

14 September 2006

Consolidated Comments on the draft UNEP reviews of Scientific Information on Cadmium and Lead (dated 18 August 2006) from U.S.A.

We appreciate the opportunity to review the UNEP draft documents on lead and cadmium. The draft documents are generally well written, contain lots of useful information, and reflect good work by the authors. However, we have many comments, as described in this paper.

The following consolidated comments are based on review by various scientists from the United States Environmental Protection Agency (U.S. EPA), U.S. Agency for Toxic Substances and Disease Registry (ATSDR), U.S. National Institute for Occupational Health and Safety (NIOSH), U.S. Department of Agriculture (USDA), and U.S. National Institute for Environmental Health Sciences (NIEHS).

Primary Contact: Chuck French, U.S. EPA
Email: French.chuck@epa.gov
Phone: 919-541-7912

A. Comments on the Extended Summary for Lead:

1. Between paragraphs 11 and 12, should add that Pb has been shown to exert a broad array of deleterious effects on multiple organ systems via widely diverse mechanisms of action.
2. para #12 - While the nervous system is a main target, it may not be appropriate to say it is the main target. It might be better to say it is the main target of concern (for a combination of various reasons, exposure levels, strength of evidence, etc) - or it would be appropriate to say it is a main target.
3. Para 13 – With regard to the statement that “Epidemiological studies show consistently that effects in children are associated with lead levels in blood (Pb-B) of about 100-150 ug/L. There are indications that lead is harmful even at blood lead concentrations considerably below 100 ug/L”

This understates the strength of the evidence that lead causes effects at levels below 100ug/L. Suggest replacing the second sentence with:

“Newly available toxicologic and epidemiologic information includes assessment of new evidence pointing towards risks of deleterious effects on certain health endpoints being induced by distinctly lower than previously demonstrated Pb-exposures indexed by blood Pb levels extending well below 10 µg/dL in children and/or adults. There may be no threshold for these effects.”

4. para 13 - both soil and dust can be impacted around lead-emitting industries. In fact, exposure to indoor dust may be a primary route of exposure to lead sourced from industrial point sources (on par with lead in soil). This is lead in dust resulting from both direct deposition,

indoors, of air lead that penetrates into the building as well as the tracking in of outdoor soil/dust indoors.

5. para #14 - Related to comment above, it would seem appropriate to say that other effects associated with Pb (in epi and/or animal studies) include effects on heme synthesis, renal function, and immune system impacts.

6. Para 16: Please see comment #21 on page 8 of this paper.

7. Para 27: Please confirm that this is an accurate, scientifically sound statement, especially the use of the term "highly". What year are these data based on? We think some revision may be needed for this paragraph to make it more factual. The paragraph is not specific enough. What concentration does "highly contaminated" refer to? What is meant by "highly contaminated" - relative to what (pristine levels?) - how about compared with aerosol measurements in the arctic taken a decade or two ago - that would be valuable info to also include in the paragraph. Lead levels may still be high compared with pristine (pre industrial levels), but they are quite lower now than levels 1-3 decades ago. Also, there should be a bit broader discussion of what trend this indicates.

8. Para 17 - Replace "particulate-bound" with "particle-bound". "Particulate" is an adjective.

9. Para 18: Please clarify the 2nd sentence, and make sure it is an accurate, balanced statement.

10. Para 26: At end of paragraph, suggest adding the following text: "then, levels decreased after about 1990 as shown in figure 2."

11. Para 28: At end of paragraph, could add some text such as the following: "However, the use of leaded petrol has decreased substantially since mid-1990s therefore anthropogenic emissions are expected be lower today than they were in mid-1990s."

12. Para 31: "In the U.S.A., emissions decreased sharply during the 1980s and early 1990s due to the phase out of lead in gasoline and reductions from industrial sources. Emissions continued to decline to a lesser extent in the mid-1990s to 2002. Overall emissions of lead decreased about 95 percent over the 21-year period 1982–2002 (U.S. EPA, 2003)."

13. In paragraph 56, 3rd sentence, please add the word "nearby" between the words "other" and "countries", and also add the following phrase: "...about 58% of deposition is due to anthropogenic sources within Germany, .."

14. Para 62: Please add a 1-2 paragraphs that summarize the available monitoring data, including levels and trends.

B. Comments on the Extended Summary for Cadmium:

1. Page 9 paragraph 40: Instead of using data from 1950 here, which does not include data from some important countries, it may be more appropriate to state the trends in consumption in the

recent past in comparison to the production such as depicted in figure 4 on pg 9. Or, change text to say “by about a factor of 2.”

2. More comments and suggested changes are shown in “track changes” in attached document

C. Comments on Lead Document:

General Comments:

1. As we mentioned in our previous comments in July 2006, we recommend inclusion of data from the U.S. CDC National Chemical Exposure Report (note: some specific text is provide in following pages) and the ATSDR Interaction Profile for Lead, Cadmium, Chromium and Arsenic in this document.

2. We are pleased that the authors have used some information from the draft EPA Lead Criteria Document (CD). However, this information must be checked again after the Criteria document is finalized, to make sure the information is correct, that the UNEP document has used the proper references/citations, etc... Moreover, it may be best to wait until both the IPCS Monograph and EPA CD document are finalized before finalizing the UNEP document, so that the IPCS Monograph and the Lead CD can be properly used as information sources for the UNEP document.

3. There are a number of typographical errors/areas where edits are needed. The whole document needs proofreading, spell check, grammar check, etc.... (for example, paragraphs 154, 155, 167, 171).

Comments on Chapter 3:

1. This document is quite weak with regard to exposure to lead paint in older homes, as well as exposure to lead paint in newer homes where lead is still used. As this document notes, a primary effect of lead is neurotoxicity in children. In the United States more children are poisoned from lead via lead paint than from any other source now that lead has been phased out from gasoline. In determining why lead is a problem in many countries, the focus should be on the contribution from local sources (such as paint, pigments used on some mini-blinds for windows, gasoline, primary lead smelters, and mining) relative to the contribution from global transport of lead. While the GC asked that the assessment focus on transport, the information of exposure from local sources would provide needed context.

2. Para #144, last sentence - We haven't seen any "metabolic" reasons that indicate greater child than adult vulnerability to effects of Pb exposure. We recommend deleting "metabolic" unless there are lead specific data on metabolism to support using this word.

3. Paragraph 146: This text understates the strength of the evidence that lead causes effects at levels below 100 ug/L. Suggest replacing the sentence:

“There are indications that lead is harmful even at blood lead concentrations considerably below 100 ug/L and there may be no threshold for these effects.”

With the following text:

“Newly available toxicologic and epidemiologic information includes assessment of new evidence pointing towards risks of deleterious effects on certain health endpoints being induced by distinctly lower than previously demonstrated Pb-exposures indexed by blood Pb levels extending well below 10 µg/dL in children and/or adults. There may be no threshold for these effects.”

Information to support this revision:

For example, in the largest available new cross-sectional study, Lanphear et al. (2000) examined the relationship between blood Pb concentrations and cognitive deficits in a nationally representative sample of 4,853 children aged 6 to 16 years children (geometric mean blood Pb of 1.9 µg/dL) who participated in NHANES III with 97.9% of the children having blood Pb concentrations <10 µg/dL. Two subtests of the WISC-R, Block Design (a measure of visual-spatial skills) and Digit Span (a measure of short-term and working memory) were given to the children. Numerous potential confounders were assessed and included in the multivariable analyses. Although no data on maternal IQ or direct observations of caretaking quality in the home were available, other variables such as the poverty index ratio and education level of the primary caregiver likely served as adequate surrogate measures of these important potential confounders. In multivariate analyses, a significant covariate-adjusted relationship was found between blood Pb level and scores on both WISC-R subtest for all children as well as among those children with blood Pb levels <10 µg/dL. Blood Pb concentration was also significantly associated with Block Design when the multivariate analysis was restricted to children with blood Pb levels <7.5 µg/dL.

Other recent studies examining the association of Pb with IQ in children with low Pb exposures have consistently observed effects at blood Pb concentrations below 10 µg/dL. Most notably, a large international pooled analysis of 1,333 children from seven different cohorts by Lanphear et al. (2005) estimated a decline of 6.2 points (95% CI: 3.8, 8.6) in full scale IQ for an increase in concurrent blood Pb levels from 1 to 10 µg/dL. A common observation among some of these studies of low level Pb exposure is the non-linear dose-response relationships between blood Pb and neurodevelopmental outcomes. Although this may seem at odds with certain fundamental toxicological concepts, it is conceivable that the initial neurodevelopmental lesions at lower Pb levels may be disrupting different biological mechanisms (e.g., early developmental processes in the central nervous system) than the more severe effects of high exposures that result in symptomatic poisoning and frank mental retardation. One ad hoc explanation may be that the predominant mechanism at very low blood Pb levels is rapidly saturated and that a

different, less-rapidly-saturated process, becomes predominant at blood Pb levels greater than 10 µg/dL.

References

1. Lanphear, B. P.; Dietrich, K.; Auinger, P.; Cox, C. (2000) Cognitive deficits associated with blood lead concentrations < 10µg/dL in U.S. children and adolescents. *Public Health Rep.* 115: 521-529.
2. Lanphear, B. P.; Hornung, R.; Khoury, J.; Yolton, K.; Baghurst, P.; Bellinger, D. C.; Canfield, R. L.; Dietrich, K. N.; Bornschein, R.; Greene, T.; Rothenberg, S. J.; Needleman, H. L.; Schnaas, L.; Wasserman, G.; Graziano, J.; Roberts, R. (2005) Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. *Environ. Health Perspect.* 113: 894-899.

4. Comment on Section 3.2:

General comment: Exposure from local sources make up a significant proportion of exposures, in most cases the overwhelming majority. This is not addressed in this section, or more importantly throughout the document. Given that the document is considering transport of lead and its contributions to a global problem, exposure from local sources should be better described and quantified. This section is too short and weak. The exposure section needs to include a more thorough description of the exposure from the sources listed, quantification of the contribution of these sources to lead exposure, and how this ranges across the globe.

5. Paragraph 159: 1st sentence – This is overly broad. In some countries this may be the case. In other countries it is not the case. In the United States, the primary exposure is lead paint.

6. Para 159: 2nd sentence – change “may also be important” to “is important”

7. Para 154 - the sentence with the 10 ug/dL is confusing and needs to be clarified (poor wording). In addition, some studies have suggested that 6-7 IQ points may be associated with exposures below 10 ug/dL (with less in the 10-20 ug/dL range) - see Canfield 2003 (Rochester Prospective Study) and the Lanphear 2005 pooled analysis.

8. Para 168 - mg/cm² is a loading measure and not a concentration measure. Please change to correct units.

9. The report is somewhat thin when it comes to dietary exposure information. There is no mention of all the work that has gone on in the U.S.A. (see suggested text in comment #13 below). The document states that dietary exposure is the major source of exposure, but then attributes reductions of population blood lead levels all to reductions in the use of leaded gasoline. While the discontinued use of tetraethyl lead has certainly resulted in blood lead reductions, so has the discontinued use of lead solder in food cans and phase out of lead in paints, etc.... In addition, referring to the diet as a major source is really a mischaracterization since in large part, particularly in considering the contribution from air, the diet is a pathway and not a source of lead like leaded gasoline, smelter emissions, paint, batteries, etc...

10. The report should also include info from the U.S. CDC National Chemical Exposure Report and the reports by Codex/CCFAC on setting MLs for lead in food based on work over the last several years. The following are several publications dealing with US dietary exposures as well as some CFSAN/FDA, CDC/NHANES and Codex/CCFAC websites.

Bolger, P.M. et al., Identification and reduction of sources of dietary lead in the United States, *Food Additives and Contaminants* 13:53-60, 1996.

Bolger, P.M., et al., Reductions in Dietary Lead Exposure in the United States, *Chemical Speciation Bioavailability* 3:31-36, 1991.

Egan, S.K., et al., US Food and Drug Administration's Total Diet Study: intake of nutritional and toxic elements, 1991-96, *Food Additives and Contaminants*, 19:103-125, 2002.

<http://www.cfsan.fda.gov/~lrd/pestadd.html>

<http://www.cfsan.fda.gov/~comm/tds-toc.html>

<http://www.cfsan.fda.gov/~comm/tds-res.html>

http://www.cdc.gov/nchs/about/major/nhanes/nhanes2003-2004/nhanes03_04.htm

<http://www.codexalimentarius.net/web/archives.jsp?lang=en>

11. Section 3.1: Some of the early statements refer to blood lead levels in terms of micrograms of lead per liter (ug/L). Then, on the second page of section 3, blood lead is referred to in terms of micrograms per deciliter (ug/dl). This difference of units is confusing. Our suggestion would be to include the units of micrograms per deciliter in brackets on the first page of section 3, and then use consistent units (e.g., ug/dl or maybe ug/L) through remainder of document. But, need to be consistent, and make sure it is clear so reader is not confused about units.

12. Para 155 - The first sentence here sounds a bit stronger than the statements from the cited study. The study reported deficits associated with mean PbB<7.5.

13. Para 164 & Table 3-1 - The following information is some dietary information being summarized for the EPA Lead Criteria Document (CD) that should be included in the UNEP Lead report in or near paragraph 164. However, please confirm it's presentation in final CD before the UNEP document is finalized (Note: the CD is on a firm schedule to be finalized on 1 October 2006):

“... recent data from the Food and Drug Administration’s Total Diet Studies show that estimates of daily Pb intake from food dropped substantially between 1982-1984 and 1994-1996 (Egan et al., 2002). For example, estimated dietary Pb intake dropped 96 percent in 2- to 5-year old children (from 30 µg/day to 1.3 µg/day) between these two study periods (Egan et al., 2002). In the 1994-1996 Total Diet Study, 74% of samples were found to be below the detection limit for Pb. Across all age groups, estimated Pb intake ranged from 0.8 to 19.6 µg/day. Infants aged 6-11 months had the lowest estimated dietary Pb intake (0.8-5.7 µg/day), and children aged 2 years had estimated dietary Pb intakes in the range of 2.4 to 10.1 µg/day. For older children and adults, dietary Pb intakes were generally in the range of

4 to 19 $\mu\text{g}/\text{day}$ (Egan et al., 2002). Similar intake levels were observed in a study of children and their mothers in Omaha, Nebraska, where the estimated rate of Pb ingestion (inclusive of dust) was 1.8 $\mu\text{g}/\text{day}$, 3.3 $\mu\text{g}/\text{day}$, 4.1 $\mu\text{g}/\text{day}$ and 7.5 $\mu\text{g}/\text{day}$, for age groups of 0 to 12 months, 13 to 24 months, 2 to 6 years, respectively (Manton et al., 2005). In one report from the NHEXAS study in Maryland, the mean intake of Pb in the diet was 7.6 $\mu\text{g}/\text{day}$ (Scanlon et al., 1999); a subsequent analysis in this study reported a daily dietary intake of 8.14 $\mu\text{g}/\text{day}$ (Ryan et al., 2001). The accompanying longitudinal study showed that Pb dietary exposures vary little over time (Scanlon et al., 1999). In the Midwest, Pb concentrations in foods consumed by children 0 to 6 years old were similar or lower than adults, but on a body weight basis Pb intake rates were 1.5 to 2.5 times higher for young children (0.26 $\mu\text{g}/\text{kg}$ body weight/day for children 0 to 7 yrs and 0.10 $\mu\text{g}/\text{kg}$ body weight for people overall) (Thomas et al., 1999). Overall, a small percentage of the population exceeded health-based intake levels set by FAO/WHO (Thomas et al., 1999). In Australia, women between 20 and 39 years of age ingest between 7.3 and 9.7 $\mu\text{g}/\text{day}$ (Gulson et al., 2001a). Infants that are breast-fed take in ~ 0.73 $\mu\text{g}/\text{day}$ compared to 1.8 $\mu\text{g}/\text{day}$ for formula-fed infants (Gulson et al., 2001a). Australian children ingest ~ 6.4 $\mu\text{g}/\text{day}$. Overall, recent studies conducted in the United States indicate that daily Pb intake from the diet ranges from about 1 to 10 $\mu\text{g}/\text{day}$. Some researchers have estimated the contribution of Pb from sources other than food in the diet. For example, Melnyk et al. (2000) estimated a daily Pb intake of 8.4 $\mu\text{g}/\text{day}$ in children based on a diet survey, but when estimated exposure due to the handling of food by children, including Pb from the floor and house dust, the daily Pb intake from ingestion was 29.2 $\mu\text{g}/\text{day}$.”

14. Para #168, 1st sentence needs a qualifier - i.e., paint dust is a primary source of lead exposure in children residing in homes with Pb paint.

15. Para 158 refers to IARC (p. 36). The document should refer to IARC classification of lead in a consistent manner – for example, the reference to IARC lead classification is slightly different on page 36 compared with page 138 (section 9.3.1).

16. Table 3-1 – the highlighted text denotes that this table is not finalized yet – the information in the Table seems somewhat “random” currently – how are the example countries chosen for inclusion?

17. Figure 3-1 shows data from Australia concerning blood lead levels and leaded petrol sales. In this graph, there are very few data points for blood lead level. It seems that there are many data that could be used to make the point of this graph, and these data from Australia seem to make it relatively weakly because of the few data points presented. Are there other data readily available to make this point better (for example, from Europe or the US)?

18. Page 35 para 151: It should be corrected to state that Pb also affects the absorption and metabolism of other metals such as Ca. Further the sentence has to be changed to reflect that Pb binds to membrane lipids and proteins rather than having affinity for cell membrane. Also it has to be noted that oxidative modifications on the cell membrane constituents (lipids and cholesterol) do occur upon Pb binding.

19. Page 35, para 155: Lanphear et al (2000) study was incorrectly characterized with reference to the IQ deficits and blood Pb concentrations and the authors should verify the original manuscript to correct it. IQ deficits are noted at blood Pb concentrations <10ug/dL (10-5 ug/dl) and possibly below 5 ug/dL. Also, several studies, including the study mentioned above, note low academic achievements to be evident at or below 5 ug/dL.

20. Page 35, para 157: The authors should verify the reference pertaining to this statement to correct their conclusions that Pb's adverse effects on blood pressure are evident at high concentration in experimental animals. The recent EPA Lead CD reported similar effects at chronic low dose exposures.

21. Para 159: Please insert the following text (which is largely from the WHO/UNECE, 2006 report) into chapter 3 between Para 159 and 160, and also in the Extended Summary between paras 15 and 16:

“On the global scale highest B-Pb levels occur in South and Central America, the Middle East, and parts of East Europe, and the former member countries of the Soviet Union. Fewtrell et al. (2004) assessed mean blood-lead concentrations in different parts of the World, based on published studies and estimated that about 25% or more of the children in these areas have B-Pb levels above 100 µg/L (as cited in WHO/UNECE, 2006).”

“Available data on the concentration of lead in air, daily intake of lead with food and Pb-B indicate a substantial decreasing trend of environmental lead exposure in many countries mainly due to the elimination of lead from gasoline, but also reducing other sources of exposure (e.g., lead in paint). For example, in the U.S. in 1970s over 80% of children had Pb-B exceeding 10 ug/dL (the blood guideline used by the U.S. Centers for Disease Control and Prevention). In a 1999–2002 survey of children in the United States, 1.6% exceeded this level (U.S. CDC,). Nonetheless, the exceedances of the guideline in the U.S. are probably mostly due to local sources (e.g., paint, contaminated soils) and not attributable to long-range transport.

In Turin, Italy, the mean B-Pb in adults dropped by 58% (from 153 to 64 µg/l) between 1985/1986 and 1993/1994 (Bono et al., 1995), and in Swedish children a dramatic decline has been observed between 1978 and 2005 (Strömberg et al., 2003; Figure 3-15). In German adults, the geometric mean lead blood levels decreased from 62 µg/l in 1985/86, to 46 µg/l in 1990/92 and to 31 µg/l in 1998 (Becker et al., 2002). For German schoolchildren (n=3,964) the geometric mean lead blood levels decreased 5 from 1979-2000 from 190 µg/l to 31 µg/l in an industrialized area and from 120 µg/l to 21 µg/l in a rural area (Wilhelm et al., 2005, 2006). Erythrocyte samples from adults indicated that there was decay in Swedes throughout the 1990's; about 4% annual decrease (Wennberg et al., 2006, and WHO/UNECE, 2006).

The decrease or removal of lead from gasoline is a main reason of the declines in blood lead levels, however, the removal of lead from soldered cans, phasing out of lead paints, and other factors also play a role. Reduced blood lead levels correlating with

reduced use of leaded gasoline have been demonstrated in a number of countries. However, the remaining local sources still contribute to a significant number of children with elevated blood levels. For example, in the United States, lead poisoning is still considered a substantial health problem, and is attributed to local sources.”

22. Page 38, para 171: Susceptibility associations would be better reflected in the following order: age, nutrition status, genetic susceptibility, tobacco smoking, alcohol consumption and health status.

23. Para 176 and Table 3-2 – More explanatory text is needed here. Please insert text explaining what Codex Alimentarius is, what the numbers represent, etc...

24. Section 3.4, page 40 – para 177 – In the last sentence, please delete “environmental chemicals” and insert the word “lead”.

25. Para 179 is confusing – there are 2 sentences in this section, each dealing with different topics/points – Please edit this section to address one primary point.

26. Page 40, para 177: The sentence has to be corrected as the word “may” undermines the deleterious effects of Pb and the cost repercussions for the society. Please delete the word “may” and insert “does”.

Chapter 5:

1. Para 247: Please add the following text to chapter 5 between 247 and 248, or other appropriate location in chapter 5:

“In the U.S.A., emissions decreased sharply during the 1980s and early 1990s due to the phase out of lead in gasoline and reductions from industrial sources. Emissions continued to decline to a lesser extent in the mid-1990s to 2002. Overall emissions of lead decreased about 95 percent over the 21-year period 1982–2002 (U.S. EPA, 2003).”

Reference: U.S. EPA [2003] National air quality and emissions trends report, and lead air quality trends data (1980 – 2001). U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards. Available at: <http://www.epa.gov/airtrends/lead2.html>.

Chapter 6:

1. Paragraph 309 – Lead carbonate (white lead) was historically widely used for wall paint in households and still is a significant source of lead exposure to the general public.

Chapter 7:

1. Please revise paragraph 342, as follows:

“342. Lead is transported by air masses on an intercontinental scale, yet due to the relatively short residence time of lead in the atmosphere (days or weeks), the airborne dispersion of this pollutant has a pronounced **local, national, or** regional character: intercontinental transport makes only minor contributions to **environmental lead levels** ~~regional pollution~~ in industrially developed regions on a long-term basis. According to the modelling results obtained with the MSCE-HM-Hem model (Figure 7-15), annual contribution of external emission sources to the total lead deposition in Europe ~~does not exceed~~ **is less than** 5 percent, and it is even lower in North America.”

2. Paragraph 344: The last sentence is subjective and policy oriented and should be removed. Further, use of word “significant” in 2nd to last sentence is not appropriate. Please revise paragraph as follows:

“344. Compared to pollutants with longer atmospheric residence time which cycle globally, like mercury and some POPs, the intercontinental transport of lead has an episodic character due to its significantly smaller residence time in the atmosphere (characteristics of the long-range transport of lead are discussed in Section 7.1.2). However, as shown above, the contribution of lead to regional pollution can be **significant higher** during short-term episodes. ~~That is why the role of intercontinental transport of lead in pollution of Europe and North America needs further investigation.~~”

3. Pg. 98. Para 379: Though the statement captures the caveats associated with utilizing air lead concentration data between measured and modeled levels, it may be appropriate to address these issues in more detail to try to get a better understanding of air concentrations across the regions, especially as these data have indirect effects in determining the potential contribution of local, national, regional and intercontinental transport of lead.

Chapter 9:

1. Page 132, Para 509. "Occupational health and safety" or under para 510. "Information and reporting requirements." The US Centers for Disease Control and Prevention conducts surveillance of blood lead levels in children, info available at: <http://www.cdc.gov/nceh/lead/> and in adults, info available at: <http://www.cdc.gov/niosh/topics/ABLES/ables.html> .

The latest Surveillance Summary report on children is:

Meyer, P., Pivetz, T., Dignam, T., Homa, D., Schoonover, J., and Brody, D. 2003.
Surveillance for Elevated Blood Lead Levels Among Children - United States, 1997--2001
MMWR (Morbidity and Mortality Weekly Report) 2003 (Vol. 52, No. SS-10)
<http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5210a1.htm> .

The latest Surveillance Summary report on adults is:

Roscoe R., Ball, W., Curran J., DeLaurier et al. 2002. Adult Blood Lead Epidemiology and Surveillance–United States, 1998-2001 MMWR (Morbidity and Mortality Weekly Report) 2002 (Vol 51 No. SS-11) <http://www.cdc.gov/mmwr/PDF/ss/ss5111.pdf> .

The latest update on adults is:

Roscoe, R. and Graydon, J. 2006. Adult Blood Lead Epidemiology and Surveillance--United States, 2003-2004. MMWR (Morbidity and Mortality Weekly Report) 2006 (Vol 55 No. 32;876-879) <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5532a2.htm>.

D. Comments on Cadmium Document:

General Comments:

1. This is a well-written comprehensive document with lots of useful information on cadmium and captures salient findings on cadmium human health effects, environmental toxicology, cadmium sources, its distribution in ambient, environmental fate and transport, etc... however we have a number of comments, as described throughout this paper.
2. This document is strongly oriented towards the European environmental scientific literature and would be strengthened by inclusion of more health oriented publications including those from non –European countries such as the USA and Japan. Some suggested reference documents are listed below. The document would be enhanced by further discussion of the exposures and health effects. In addition, the working group may also wish to consider inclusion of a short section on interactions between cadmium, lead and arsenic since these toxic elements are frequently found together in air, food and water. Exposures of biota, including humans, to cadmium do not usually occur to this element alone but more commonly in mixtures. ATSDR has developed an interaction Profile for cadmium, lead, arsenic and chromium (reference shown below) which we suggest be considered for this report.

Recommended References:

- U.S. Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Cadmium (1999), available at website: www.atsdr.cdc.gov
- U.S. ATSDR, Interaction Profile for Arsenic, cadmium, chromium and lead (May 2004), Available at website: www.atsdr.cdc.gov

Chapter 2 – Cadmium:

1. Comments on Chapter 2: Fig. 2-1 and Annex 1. If possible, we would like to include data from U.S. here, but we have not yet been able to obtain the data.

2. p-26, Section 2.3: Cadmium in aquatic environments - This section would perhaps be strengthened by a paragraph on the complexation of cadmium with chloride in seawater which has been shown to greatly influence its bioavailability and hence toxicity to marine organisms. A similar paragraph on complexation of cadmium with particulate matter in the water column might also be useful. Total cadmium concentrations in water may be a bit misleading from the toxicity perspective.

Chapters 3 and 4 cadmium:

1. Comment: Please insert the following information (from CDC National Report (U.S. CDC, 2005) and the WHO/UNECE, 2006 report) somewhere in chapter 3, such as maybe between paragraphs 146 and 147 :

“Based on a study by the U.S. Centers for Disease Control and Prevention (U.S. CDC, 2005), for years 1999-2000, based on data from a random sample of 7,970 people, the CDC found that the mean blood concentration was 0.412 micrograms cadmium per liter of blood ($\mu\text{g/L}$). For data from 1999-2002, with sample size of about 17,000 people, the 95th percentile blood level was 1.3 $\mu\text{g/L}$ (U.S. CDC, 2005). In the same study, urine levels were also analyzed, although for a smaller sample size (about 5000 people). The mean urine levels were about 0.2 $\mu\text{g/g}$ of creatinine, and the 95th percentile was about 0.92 $\mu\text{g/g}$ of creatinine. In addition, an analysis of food intake rates and food-cadmium concentrations for the U.S. population estimated a geometric mean intake of 18.9 $\mu\text{g/day}$, or 0.4 $\mu\text{g/kg/day}$ (Choudhury et al, 2001, as cited in U.S. CDC, 2005).

“The joint WHO/LRTAP Task Force on the Health Aspects of Air Pollution reported in a recent report (WHO/UNECE, 2006) that geometric mean concentrations of urinary cadmium in nonsmokers in various studies in Europe were as follows: 0.15-0.20 $\mu\text{g/g}$ creatinine in Sweden (Berglund et al., 1994; Järup et al., 1995); 0.69 $\mu\text{g/g}$ creatinine in Belgium (Roels et al., 1993), 0.5 - 0.6 $\mu\text{g/g}$ creatinine in Poland (Jakubowski, 30 1995); and 0.15 $\mu\text{g/g}$ creatinine in Germany (Becker et al., 2003).

Cadmium levels seem to increase with age. For example, according to the data obtained in the USA mean concentrations of urine cadmium in males in age categories of 12-16; 20-39; 40-59 and >60 were 0.14 ; 0.18 ; 0.28 and 0.38 $\mu\text{g/g}$ cre respectively. In females urine cadmium concentrations were higher in the respective age groups, with levels of 0.19; 0.30; 35 0.66 and 0.81 $\mu\text{g/g}$ creatinine respectively (Choudhury et al, 2001, as cited in WHO/UNECE 2006).”

3. This section of the document is very short and should be expanded to include information from other countries. The ATSDR ToxProfile on Cadmium from 1999 may be particularly useful for information on cadmium, including minimal risk levels (MRLs) and other relevant information/data. Other information can be obtained from the U.S. CDC National Exposure Report from 2005 (U.S. CDC, 2005). There is also a large amount of literature from Japan on cadmium. In any case, this section of the document should be expanded. The section could

include some discussion of possible exposures due to various activities, such as re-cycling practices. In addition, the authors should mention passive smoking as a source of exposure for the general population. Passive smoking may represent a major source of exposure for those who do not smoke and are not occupationally exposed to cadmium.

Reference: Third National Report on Human Exposure to Environmental Chemicals (2005), available at CDC website: www.cdc.gov/nceh/dls

4. Para 135, line 3: a retinal cortex organ dose (RC): should this be renal cortex dose?

5. p-35 Table 3-1, last row. United States FDA Total Diet Study reference missing in original (last column): Daily intakes of cadmium via food from Egan et.al. (2002) were 11.5-15.3 µg/kg body weight/day for 70 kg adult males and 0.14-0.2 µg/kg body weight/day for 60-kg adult females. These values are different from those in Table 3-1 in which the source of the values was not given.

6. Figure 3-1 is a bit unclear. We suggest that you try to improve this figure?

7. p 37-39 – Section 4.3.4 Aquatic Organisms

This section would be enhanced by an expanded discussion of the importance of cadmium speciation in seawater from the perspective of bioavailability and toxicity to aquatic organisms. A discussion of intracellular cadmium binding to mineral concretions and metallothionein - like proteins as mechanisms by which marine invertebrates may accumulate cadmium following exposure and not show toxicity until the binding capacity of these compartments is exceeded as a function of dose or duration of exposure would also be useful for helping to explain bioaccumulation by species consumed as food by humans. The issue of Environmental Health Perspectives cited below may also be a useful resource document for this purpose.

Reference: Environmental Health Perspectives Volume 65 (1986).
Proceedings International Conference on Metal Binding Proteins

8. Chapter 4: The information could be presented more clearly by providing some separation between topics, such as effects on animals, plants and plankton. The lack of such separation led to poor flow of information and authors could separate the pertinent information to make a clearer and more concise presentation.

9. In chapters 3 and 4 some of the statements on scientific findings presented were confusing and contradictory in some instances.

10. Please try to differentiate the potential exposures due to tobacco smoking compared to food and other sources, and how much of the exposures are due to anthropogenic sources, long-range transport, etc....

11. Para 168 - mg/cm² is a loading measure and not a concentration measure. Please fix units.

Chapter 5 cadmium:

1. p. 51 Table 5-3, subheadings Tonnes “Pb/year” should be “Cd/year”
2. p.54 para 232, lines 2-3, total releases to the land approach 2,500-15,500 tonnes per year: The numbers do not match that in Table 5-7 on p.55 which says 10,000-45,000 tonnes.

Comments on Chapter 7 cadmium:

1. Is there a more scientific way to rephrase or clarify the following paragraph?
para 326 “However, episodically the contribution of inter continental transport can be significantly higher at certain locations on these continents. Calculated model examples illustrate that daily contributions from lead transported from one continent to the other can exceed 35 percent of total deposition during these episodes.”
2. Para 303: Even though the paragraph acknowledges that the “concentrations presented are not directly comparable”, it goes on by way of a table on page 80 and in paragraph 311 on page 81 to compare the values across locations. Therefore, a caveat or footnote should be included in table to explain clearly that these values are not directly comparable because of various factors such as “different measurement periods and sampling procedures.”
3. Para 303: While the report acknowledges 2 reasons that the reader should not compare the ambient data across locations (i.e., 'different measurement periods and sampling procedures'), there are several other reasons that are just as important, including: different analysis procedures, different detection limits and process for handling data below these limits, different size fractions? (i.e., TSP, PM10, PM2.5, ultrafines), different reporting conventions (i.e., local conditions or standard temperature and pressure). None of these important potential differences in the measurements are alluded to or explained in the report. These other reasons need to be also included in this paragraph.
4. Para 319: Please add this text to chapter 7 after paragraph 319:

“Cores of ice extracted from the Greenland Summit glacier contain a well preserved record of atmospheric metal deposition dating back several hundred years. When comparing pre- and post-industrial (i.e. before and since 1800) depositional fluxes of lead the record demonstrates a 12-fold increase that peaked in the 1970s. Lead was however, used quite extensively before 1800 at which time deposition rates were already elevated. It is estimated that the peak in the 1970s represented a 200-fold increase over natural background deposition rates. Rates of lead deposition had declined by 6.5-fold by the early 1990s reflecting the introduction of unleaded gasoline (AMAP 2005).”

Reference: AMAP, (2005). AMAP Assessment 2002: Heavy Metals in the Arctic. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xvi + 265 pp. (first published as electronic document in 2004)

5. Oceanic transport of cadmium and its contribution to food from marine animals across the regions should be clearly highlighted in the document.

Chapter 9 cadmium:

1. Para 444, p.121 Has the Codex Alimentarius Commission adopted setting the Maximum Levels for cadmium in marine bivalve mollusks (excluding oysters and scallops), in cephalopods (without viscera) and in polished rice at the 29th session? If yes, enter values in Table 3-2 on page 36.

2. Information on the phase out of lead in gasoline and related efforts, in part through the Partnership for Clean Fuels and Vehicles (www.unep.org/pcfvy), that should be included in chapter 9, include the following:

- Phase out of lead in gasoline: Success. Leaded gasoline is now phased out in 49 countries of Sub-Saharan Africa. This work was done through the Partnership for Clean Fuels and Vehicles and the Clean Air Initiative for Sub-Saharan Africa. The Partnership is now moving forward with a ratcheting down of sulfur levels in fuels. Ghana has announced plans to move to 500 ppm sulfur, down from 3000 ppm.

- Air quality monitoring: EPA, with funding from USAID, has worked with Ghana and Tanzania to put in place air quality monitoring systems in Accra (completed) and Dar Es Salaam (ongoing). One of the benefits of the monitoring systems will be to measure levels of heavy metals and other pollutants which can be transported trans-Atlantically or globally.

- South Africa blood lead study: Completed. This study showed high correlation with levels of lead in gasoline, as expected, but also showed high exposures in children from leaded paint. Legislation is now being considered to ban lead in paint in South Africa. This is an issue which needs much greater attention across the continent.

Below are more Comments on the UNEP Cadmium Report, that should be considered to the extent feasible, in the report:

General Comment:

GENERAL: The UNEP Draft Document under review (Review of Scientific Information on Cadmium) does not include some important recent information on the potential impacts from Cd in soils, and thus has a number of statements about the potential impacts/uptake/exposures from Cd in agricultural pathways that may be incorrect, or inappropriate. The following comments point up inconsistencies between the draft UNEP Cadmium document and the 2001 and 2004 UN-sponsored SCOPE documents and conferences, which comprehensively examined cadmium; they will also point out a number of the important missing references, scientific deficiencies in the analysis, including failure to consider confounders, misinterpretation of studies, and the local/regional nature -- in contrast to long-range transport -- of cadmium problems that are identified, e.g., exposures stemming from previous practices in growing rice in Asia. The

comments below are provided with citations that should be considered in revisions of the document. We kindly request that the bibliographic references provided below be considered in the revision of the document.

1) Section 2.4: The document overestimates risk from Cd by failing to consider that nearly all Cd dispersal to the environment is with co-contaminating Zn. One cannot legitimately consider future risk of soil Cd without considering the Zn which may accompany Cd into the environment. Mine wastes and smelter emissions have about 200 times more Zn than Cd. Other than the Cd-batteries entering solid waste but removed before composting of the organic fraction of solid waste, the solid waste composts, biosolids and manure contain about 200-500 times more Zn than Cd. This Zn is important because Zn inhibits Cd uptake and Cd translocation from roots to shoots of plants (Chaney and Ryan, 1994). And Zn becomes phytotoxic when leaves contain about 400-500 mg Zn/kg dry weight. Because plants (except rice) accumulate Cd and Zn in proportion to the levels added to soils, leaves can reach no higher than 2-4 mg Cd/kg dry weight when Zn is causing visible symptoms of toxicity and reducing yields such that growers lose money if they don't add limestone to prevent Zn phytotoxicity (e.g., Chaney et al., 2001). Thus, the Zn that accompanies Cd in the general environment serves to limit food-chain transfer and risk of the Cd.

2) Section 3.1: The Draft Document overstates risk from dietary Cd to bone. The report notes papers from Swedish researchers who believe they have seen adverse effects of absorbed Cd on bone health (e.g., Järup and Alfvén, 2004). This conclusion is based on misuse of diagnostic criteria for urinary low molecular weight proteins as discussed below. But more important, studies in Japan with large populations with substantially higher average Cd consumption have shown that until adverse effects on kidney have occurred, there was no adverse effect on bone (Horiguchi et al., 2005). Classic "itai-itai" disease occurred where low Ca diets and high Cd exposure from rice caused kidney disease then subsequently bone disease. Evidence from the Swedish study is far weaker than the studies from Japan; it is not yet appropriate to suggest that effects of dietary Cd on bone may be of clinical significance before the well known adverse Cd effects on proximal tubular function.

3) Section 3.2: The document fails to appreciate the unique nature of rice which promoted human Cd risk from soils contaminated by mining and smelting wastes in Asia (Chaney et al., 2004; Simmons et al., 2003). Because rice is grown in flooded soils, sulfides are formed. As long as the soil is kept flooded, little uptake of Cd or Zn occurs. But growers drain the fields when flowering starts and the sulfides are rapidly oxidized (simultaneously lowering soil pH). This allows the Cd to be readily absorbed by rice roots and move directly to grain of rice, but there is no increase in grain Zn even on highly Zn contaminated soils (Simmons et al., 2003). No crop grown in aerobic soils excludes Zn from the edible plant tissue when the soil is contaminated with geogenic Cd:Zn ratio sources.

4) Section 3.1: Although human proximal tubular disease due to excessive Cd absorption has happened at many locations in Asia, this effect has not been observed in western populations. In Asia, rice soils contained no more than 5-10 mg Cd/kg dry soil which a high fraction of the over age 50 population experienced clinical tubular dysfunction. In areas in Europe and North America where humans consumed some local crops grown on soils which

contained 100 mg Cd and 10,000 mg Zn caused no adverse effects on the exposed populations (de Burbure et al, 2003; Ewers et al., 1992; Sarasua et al., 1995; Strehlow and Barltrop, 1988). These soil Cd+Zn exposure cases were studied after the case of the New Zealand oyster consumers who consumed about as much Cd as Japanese rice farmers who were harmed by dietary Cd, but the oyster consumers had no adverse effects of their dietary Cd (Sharma et al., 1983). More detailed study of the oyster consumer population showed that neither low molecular weight proteins nor kidney Cd were increased in persons who consumed large numbers of high Cd oysters (McKenzie-Parnell and Eynon, 1987); smoking was a much more important source of absorbed Cd than consumption of large numbers of oysters (Sharma et al., 1983)! Thus western populations exposed to soils with much higher total Cd contamination than caused disease in Asia had no evidence of adverse effects of Cd on kidney, very different from the rice Cd transfer cases in Asia.

5) Section 3.1: Questionable interpretation of threshold of kidney function impairment regarding effects of dietary Cd on kidney function. As noted above, a number of populations in Asia that consumed locally grown rice grown on Cd+Zn contaminated soils for many decades suffered significant proximal tubular dysfunction. Diagnosis of tubular dysfunction for exposed persons depends on the concentration of indicator low molecular weight proteins in urine which are considered to be diagnostic for Cd disease. In the last few years there have been advances in this understanding that indicate that threshold concentrations used as threshold for injury in Europe are much lower than found in Asian populations where disease is significant. Ikeda et al. (2003) reported that urinary Cd had to exceed 10 µg per g creatinine before the first true tubular dysfunction was observed. Rice-Cd consuming individuals with clinical Cd disease have urinary β_2 -microglobulin of about 100,000 µg per g creatinine (e.g., Tohyama et al., 1982); further, the diagnostic threshold for β_2 -M in urine is at least 1000 µg per g creatinine. And protein levels in urine increase with increasing age as a normal phenomenon (shown in many studies; e.g., for normal 70-79 year old US adults, the geometric mean (GSD) and 95% upper confidence limit for β_2 -M were 107.1 (3.8) and 1451 µg per L (Chaney and Ryan, 1994)). Failure to use appropriate threshold concentrations for diagnostic proteins in urine caused European researchers to claim adverse effects when the entire population studied was within the normal range. Extensive populations in Japan have been evaluated which support more realistic diagnostic thresholds (Ezaki et al., 2003; Horiguchi et al., 2004).

The document also cites a paper by Noonan et al. (2002) which reports further examination of data for two populations in Pennsylvania, USA. One group lived near a Zn smelter at Palmerton, PA, while the other was a distant control village. As shown by Sarasua et al. (1995), there was no significant difference in urinary Cd or low molecular weight proteins between the exposed (garden soils in Palmerton Borough commonly contained 100 mg Cd + 10,000 mg Zn/kg dry soil, about 200-500 times higher than background soils in this region of Pennsylvania) and control villages. So Noonan et al combined the highly Cd exposed and control populations and looked for relationships between urinary Cd and proteins. As is commonly observed, in both populations smokers had higher urine Cd than non-smokers, so the persons they considered to have excessive Cd absorption did not obtain that Cd from the highly contaminated soils where they lived, including common growing of some vegetable crops in home gardens. The thresholds for claimed adverse effects cannot be considered valid in comparison with the observations of Ikeda et al. (2003).

6) Section 3.2: The document fails to consider the special role of rice in promoting Cd absorption in humans (Reeves and Chaney, 2007-accepted manuscript). It has been shown that rice is deficient in Zn and Fe for health of subsistence rice consumers. And deficiency of Fe and Zn promote Cd absorption by animals. Recent research has indicated that Cd²⁺ is transported on the Fe²⁺ transporter of the duodenum (DMT1), so that up-regulation to obtain Fe from diets with marginal bioavailable Fe causes much higher retention of dietary Cd. In papers by Reeves and Chaney (2001; 2002; 2004), marginal supply of Fe-Zn-Ca (up-regulated transporters but did not reduce the rate of gain of growing rats) caused 10-fold higher retention of Cd. The Reeves and Chaney (2004) paper shows that the higher absorption and slower turnover of Cd in the duodenum allows net absorption to be increased. Thus, although it is correct to be concerned about bioavailable Cd in rice diets, other diets contaminated by the combined Zn+Cd source are a substantially different case. The other major grains are not so low in bioavailable Fe as rice, and they accumulate high levels of Zn under conditions that cause an increase in grain Cd (Chaney et al., 2007).

In addition, the Codex Alimentarius Commission set a new standard for maximum residue of Cd in polished rice during 2006 after a number of years of consideration of that limit. The Japanese government suggested the limit based on their extensive experience with human Cd disease from contaminated soil. The limit was set at 0.4 mg Cd per kg fresh weight of polished rice at Step 8 of the Codex Standards (Codex, 2006; http://www.codexalimentarius.net/download/report/657/al29_12e.pdf). This figure is technically well justified from the epidemiologic data in Japan (e.g., Ikeda et al., 2003; Ezaki et al., 2003; Horiguchi et al., 2004)). However, one should be concerned that limits on some other foods are unnecessarily low to protect human health from food Cd. The limit for wheat is 0.2 mg per kg fresh weight of whole grain, but rice is much more likely to cause human Cd disease than in Cd in wheat because of the other nutrients present in wheat (Fe, Zn) compared to rice (and a significant fraction of grain Cd is removed during milling, different from rice where Fe, Zn and Ca are largely removed during milling but Cd is not decreased appreciably. Clearly the UNEP document on cadmium suggests a much higher risk of cadmium to humans than was concluded by the Codex Alimentarius Commission, the UN/WHO/FAO expert function to protect food safety.

7) Section 5.2: Cd in livestock manure has not increased crop Cd. Yes, livestock manure contains Cd which is imported to the farm and will cause a slow increase in soil Cd (e.g., Nicholson et al., 2003; Keller and Schulin, 2003). But the same manure has increased Zn and phosphate which play important roles in limiting the uptake of Cd by plants. In tests of long term field plots where deposition of Cd from contaminated aerosols on the control plot was compared to addition of Cd in manure for many decades on manured plots at Rothamsted Experiment Station (Jones and Johnston, 1989). The manured plots received considerably more Cd application than the control plots. But crop uptake of Cd was greater on the control plots than on the manured plots. The combination of the usual low geogenic or lower Cd:Zn ratio in the manured soils, with the other components of manure, caused stronger binding of the Cd in soil, and lowered Cd accumulation by plants.

Cd in some rock phosphate sources is quite high (e.g., Morocco; Idaho, USA) and there is general agreement that high Cd rock sources will require decontamination before use. These ore reserves are the long term phosphate fertilizer sources on Earth, and Cd will be a consideration in manufacturing and use of these products. However, it is clear that the typical low Cd phosphates from Florida, USA, have not increased crop Cd after many decades of use as fertilizer (Mortvedt, 1984; Mortvedt, 1987; Mortvedt et al., 1981). Recent study by Huang et al. (2003; 2004) show that repeated applications of even high Cd phosphates are not additive over time in increasing Cd uptake by lettuce and other crops.

8) Section 3.2: Other foods contain Zn, phytate, fiber, and Fe which lower Cd bioavailability. As noted above, rice is deficient in Fe and Zn for subsistence rice growers which promotes Cd retention by rice consumers. In studies of other foods, humans were supplied specific Cd rich foods for long periods. In a study by Reeves et al. (2001), individuals consumed sunflower kernels or peanuts daily for one year; the amount of sunflower kernels doubled dietary Cd; *but there was no increase in blood or urinary Cd*. In a similar study by Vahter et al. (1996), non-smoking Swedish young women were omnivores who did or did not consume seafood; consuming seafood caused them to consume three-times higher amounts of Cd; but blood Cd was not increased. Subsequent analysis indicated that the shellfish supplied Zn and Fe which made the consumers have higher Fe status and absorb a lower fraction of ingested Cd. Zn in the shellfish would also be expected to inhibit Cd absorption. In other experiments, crops were grown on soils amended with biosolids and although biosolids increased Cd in Swiss chard and lettuce by 2-5 fold in strongly acidic soils, there was no increase of Cd in kidney or liver after feeding a high fraction of diet to guinea pigs and mice, respectively (Chaney et al., 1978a; 1978b). A direct test of the effect of Zn in lettuce and spinach on absorption of Cd in the crops by Japanese quail showed significant reduction in crop Cd bioavailability with increased crop Zn (McKenna et al., 1990). Thus careful tests of foods which are commonly rich in Cd compared to most foods, showed that Cd bioavailability was much lower than found for rice. Extrapolation from the rice Cd experience in Asia is scientifically inappropriate when considering the diet of western populations.

9) Section 3.2: Livestock serve to protect humans from exposure to most of the Cd that livestock ingest. In Europe and North America, most cropland is used to produce livestock feed. Feeding studies have shown that of the total Cd ingested during the lifetime of meat cattle and sheep, less than 0.1% is retained in the carcass at slaughter and most of that is in the kidney and liver which are not consistently used as human foods (e.g., Bray et al., 1985). Dairy products are not increased in Cd from feeds containing levels of Cd which would occur in forages grown on Cd+Zn enriched soils (Smith et al., 1991). Because such a high fraction of land is used for production of forages and grains for livestock feed, and so little of this crop Cd enters human diets, the logic of the document very strongly overestimates Cd transfer from fertilized or manured soils to humans.

10) Section 3.2: The case of Cd increase in kidney of older sheep in Australia is not found in other locations. It is important that readers be informed that the main reason that sheep in Australia accumulate significantly increased levels of kidney Cd by age 2 is more related to the presence of a weed in pastures than to uptake of Cd by all pasture crops. The weed, “capeweed” accumulates over 10-times more Cd than usual pasture crops of Australia (perennial ryegrass and

subterranean clover), yet only ordinary levels of Zn (McLaughlin et al., 1996). The high Cd:Zn ratio of plants consumed by the grazing sheep in Australia causes higher accumulation of Cd than found for sheep from other nations where the capeweed problem does not occur.

11) Section 3.2: Age adjustment of Joint FAO/WHO Expert Committee on Food Additives (JECFA) potentially tolerable weekly intake for Cd. Age adjustment of the PTWI number for Cd from WHO/JECFA (0.001 mg per kg BW per day) is inappropriate. Because Cd accumulates in the kidney across one's lifetime, peaking at about age 50, the development of the PTWI had to be based on a lifetime exposure model. Short exposures were considered unimportant for chronic toxicants such as Cd, and the weekly intake was introduced to help communicate that this limit is for longer periods of consideration than daily intake. The PTWI was based on models of 50 year diet intake with assumed Cd intake proportional to calorie intake across the lifetime (e.g., Friberg et al., 1985). Cd intake rate per kg BW was at least double from youths compared to adults. Thus the PTWI took into account the higher rate of food and Cd intake of infants and children vs. adults. Because infants and children ingest more food per kg body weight, they will always appear to be nearer to the PTWI. But because of the way the PTWI was developed, only adult diet comparisons should be considered valid and appropriate for Cd. Stressing that dietary Cd intake by youths is at a high fraction of the PTWI in another important overstatement of Cd risk in the UNEP Draft Document on Cadmium that needs to be corrected throughout the document.

12) Section 3.2: Workers exposed to Cd vs. dietary Cd exposure. Before adoption of air Cd limits, many workers experienced kidney disease from workplace Cd exposure. In the case of an adult worker starting at age 20, with high aerosol exposures, liver Cd accumulates rapidly and reaches levels far higher than occur in persons with slow dietary Cd exposure. This pool of liver Cd was a significant risk that even when urinalysis shows the worker should be removed from Cd exposure, as the liver Cd migrates to the kidney over time more severe kidney tubular damage will occur. This concern for exposed workers has driven some of the high interest in pre-clinical indicator criteria to protect these individuals. Although the high aerosol exposure of workers may justify use of lower diagnostic concentrations to make removal from exposure determination, there is no evidence that the rate of dietary Cd ingestion causes the remarkable accumulation of liver Cd seen in workers, and when food exposures were stopped, individuals did not experience appreciably higher tubular disease with time. The PTWI provides protection against all cases of dietary Cd source/exposure in the literature.

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Comments on Cadmium APPENDIX:

1. p. 31 Table V wrong title. Lead should be replaced by cadmium in table title and subtitle.
2. p-44 and 45. Replace lead by cadmium. Where is the link to the USA submission?

Additional References:

Reference for Egan et al. (2002): Egan SK, SS-H Tao, JAT Pennington, PM Bolger. US Food and Drug Administration's Total Diet Study: intake of nutritional and toxic elements, 1991-96. Food additives and Contaminants 19, 103-125 (2002)

Other useful references from the Surgeon General's Report The Health Consequences of Involuntary Exposure to Tobacco Smoke:

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International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Beryllium, Cadmium, Mercury, and Exposures in the Glass Manufacturing Industry. Vol. 58. Lyon (France): International Agency for Research on Cancer, 1994.

Lambers DS, Clark KE. The maternal and fetal physiologic effects of nicotine. Seminars in Perinatology 1996;20(2):115-26.

Werler MM. Teratogen update: smoking and reproductive outcomes. Teratology 1997;55(6):382-8.

Jane A. McElroy, Martin M. Shafer, Amy Trentham-Dietz, John M. Hampton, and Polly A. Newcomb Cadmium Exposure and Breast Cancer Risk J Natl Cancer Inst 2006; 98: 869-873.

More General Comments on UNEP Documents On Lead And Cadmium:

1. Since these documents are supposed to be scientific reports only, all policy related statements in the document should be deleted. The documents should contain no policy statements, no recommendations, no subjective/judgmental statements about degree of "concern", etc....
2. The scientific information presented in the form of short statements often tried to combine conclusions or inferences drawn from different studies. This led to long and winding sentences and seems to have lost focus on what they were meant to convey at several instances. The language needs to be firmed up and trimmed all through the document.

3. Color schemes used in comparative Venn diagrams lack consistency in many places and makes comparison of the data from two different time periods or regions difficult.

More Comments on Cadmium Document:

1. As stated in the document these scientific reviews serve as documents for the UN governing council to consider with regard to long-range environmental transport. The document while identifying and detailing various factors that affect these parameters has failed to adequately describe the relationships between end use pattern trends, and waste management alternatives and their bearing on the long-range transport. Lack of such discussion, if were due data gaps, has to be identified in the appropriate section (data gaps).