

**Comments on DECOS draft document on Cadmium and Selected Compounds**  
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SECTION & PARAGRAPH	COMMENT
<b>General Comments</b>	The Committee's recommendations are appropriate.
<b>Specific Comments</b>	
<b>Page 14, lines 5-13</b>	This document could be improved by a brief description of types of exposure routes as the majority of data presented in the document concerns oral exposure. It could also be noted that Cadmium can be considered an environmental exposure.
<b>Page. 15, line 8-9</b>	Would omit or expand the sentence "Several factors can influence inhalation and oral absorption efficiency."
<b>Page. 15, line 26</b>	Define the rate that cadmium can cross the placenta.
<b>Page 15, line 32</b>	When discussing the mean urinary cadmium concentrations in non-exposed workers, it would be beneficial to include any data on exposed workers, if available. If not available, please note.
<b>Table 5.1 Adverse effects on sexual function and fertility</b>	This table would benefit greatly from being organized into sections pertaining to males, females, and mixed studies. This format would present the data more effectively. It was confusing to follow the merit of the studies pertaining to male or female mouse studies.
<b>Section 5.1.1</b>	I would again suggest that the sections be separated into male, female, and mixed gender studies for better presentation of the data. Also, please denote what the form of cadmium was in each study, if available. Toxicology of a substance can be altered by the type of substance (i.e., Cadmium versus Cadmium Chloride as shown in the previous table).
<b>Page 29, line 22</b>	Re-word "drinking water study."
<b>Page 30, lines 29-32</b>	Was the phase of mouse oestrous noted in this study when speaking of the results? If so, this is important data to include because lengthening or arrest of particular phases of the oestrous cycle can have implications on the outcome of the study.
<b>Page 43, lines 29-35</b>	I would suggest omitting this study from the document. It does not strengthen the document, or the points made for effects of cadmium exposure on male reproductive markers in seminal fluid in

	humans due to lack of consideration of confounders in the statistical model.
<b>General Statement</b>	It would be useful in the beginning of the document to note occupational exposure limits of OSHA, NIOSH, European Union, others. Also, it would be beneficial to know the permissible amount of cadmium in drinking water.
<b>Page 54</b>	I agree with the conclusions of the committee that cadmium should be classified, at this time, as a Group 1B. There are not sufficient data in humans that consistently correlate with reproductive toxicity in humans. Also, many studies did not observe hormonal measurements in males or females in both humans and mice that denote specific mechanisms and ramifications in reproductive health. However, consistent effects were seen pertaining to male spermatogenesis and female cycle changes. Further, many of these studies involve environmental exposure and not occupational exposure in humans.
<b>Section 5.4.1, begins on page 76</b>	Denote the types of cadmium in the studies, particularly the animal studies as this can directly affect the toxicity seen within the results of each study.
<b>Page 76, line 21</b>	Consider changing the beginning to “Some females were sacrificed...”
<b>Page 102</b>	I agree with the finding of the committee that cadmium should be classified as a Group 1B. The studies have insufficient human data and a severe lack of adjustment for co-exposures as well as adjustment for other factors involved in decreased fertility among human women such as disease, decreased availability of oocytes, endometriosis, etc. However, the rodent studies show a correlation between lowered successful births, live pups, and neural tube defects as well as other birth defects apparent at birth and within two months post-partum.
<b>Page 104, line 29</b>	This conclusion is not, to date, supported by research in humans.
<b>Page 104, Lines 19-25</b>	The single study presented for human research suggests that cadmium may be present at calculated toxic levels in environmentally exposed lactating women. However, it does not address occupational exposures and could meet the criteria for the first point (a). Based upon the three animal studies that showed excretion in the breast milk to the pups and lambs but did not examine the toxicological effects on the offspring, the second (b) criteria is not, in my opinion, met. CLP criteria

	<p>(c), is not met by the studies presented. No absorption, metabolism, or excretion studies are presented in sufficient quantities that would provide more data to be able to strongly recommend that there is evidence of harm to breastfed children. It is my opinion that there are insufficient data to classify cadmium as H362 to date.</p>
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