Department of Defense Comments on the Draft Final IRIS Toxicological Assessment for Inorganic Arsenic Toxicological Assessment, Revised 09 April 2009					
Comments submitted by: Office of the Secretary of Defense Chemical and Material Risk Management Directorate			Organization: Department of Defense	Date Submitted: 15 May 2009	
*Comment categories: Science or methods (S); Editorial, grammar/spelling, clarifications needed (E); or Other (O). Also please indicate if Major i.e. affects the outcome, conclusions or implementation of the assessment.					
Comment No.	**Section**	**Page & Paragraph (enter "Global" if report section-wide)**	**Comment**	**Suggested Action, Revision and References (if necessary)**	**Category***
1.	Global	Global	We are satisfied with the U.S. EPA's response to comments from DOD on the previous (2008) version of this arsenic toxicological assessment. We also wish to acknowledge the improvements that the U.S. EPA authors have made in updating significant portions 2008 draft in response to the U.S. EPA Science Advisory Board (SAB) (Appendix A) and other peer reviewer's comments and recommendations.	No suggested action required.	O
2.	Section 5.3.1, "Background: History of Cancer Risk Assessments for Arsenic."	Page 98	New text on page 98 states that "*The Office of Pesticide Programs (OPP) also recently applied cancer slope factors based on the U.S. EPA (2001) assessment in their Reregistration Eligibility Decision (RED) Documents for organic arsenic pesticides (U.S. EPA, 2006c) and for Inorganic Arsenicals and/or Chromium Based Wood Preservatives (U.S. EPA, 2008).*" It would be useful to compare the key assumptions and conclusions from the U.S. EPA OPP's toxicological assessment related to inorganic arsenic's carcinogenicity to this assessment in support of U.S. EPA's IRIS program.	Consideration should be given to providing additional information for comparison purposes between the two inorganic arsenic carcinogenicity assessments, if feasible and time permits.	S
3.	Section 5.3.1. "Background:	Pages 103, 104	New analysis was included in the assessment using a modified version of the "BEIR IV" relative risk	Consider, discussing how factors, such as potential genetic differences, lifestyle (for	S

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	History of Cancer Risk Assessments for Arsenic."		model, and is described in Appendix E. A key assumption underlying this model is that "…*the risk of arsenic-related cancer mortality or incidence for the U.S. population is a constant multiplicative function of the current background age profile of cancer risks in the same U.S. population*." The text does not discuss how factors, such as potential genetic differences, lifestyle (for example, smoking history), and cumulative exposures to other potentially carcinogenic materials may impact the validity of this key assumption.	example, smoking), and cumulative exposures to other potentially carcinogenic materials may impact the validity of this key assumption and how these variations could impact the quantitative risk assessment.	
4.	Section 5.3.4. "Selection of Cancer Endpoints and Estimation of Risks for U.S. Populations."	Page 107, 108	New text included in this section states, "*The ED_{01} and LED_{01} values are estimated using a variation on the "BEIR IV" model derived for use in estimating population cancer risks for radionuclide exposures (NRC, 2001). This method, which is described further in Section 5.3.7.3 and Appendix E.2, includes the application of relative cancer risk estimate derived from the Taiwanese dose-response assessment multiplicatively to age-specific cancer risks for the U.S. In this model, the background hazard consists of age-specific cancer incidence*	Again, we recommend that the text should discuss the potential impact of differences in lifestyles between the U.S. and Taiwanese populations (for example, smoking history; access to better medical treatment, etc. having an impact on cancer survival rates.	S

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			data for bladder and lung cancer from the United States for the years 2000-2003 (NCI, 2006). The ratios of cancer mortality to incidence for arsenic-related cancers are assumed to be the same in the U.S. and Taiwanese populations." The text does not discuss the impact of differences in lifestyles (for example, smoking history; access to better medical treatment, etc.) having an impact on cancer survival rates.		
5	Section 5.3.5. "Non-Water Arsenic Intake and Drinking Water."	Page 108.	The U.S. EPA assessment used 10 µg/day non-water dietary intake in the baseline analysis for both the exposed and reference populations in southwest Taiwan. Page 108, which states that "*It does not include the arsenic intake value from water used for cooking rice or produce, which was addressed separately via sensitivity analysis modeling with higher water intake values*…" This new information helps clarify what constituted "non-water arsenic," which had been an area of concern related to water used for cooking potentially contributing to a higher inorganic arsenic intake than 10 ug/l.	No suggested action required.	S

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6.	Section 5.3.7. "Risk Assessment Methodology. "" Section 5.3.7.3. "Estimation of LED_{01} Values Using Relative Risk Models." Section 5.3.8.2. "Comparison to Previous Cancer Risk Estimates." U.S. EPA "Response to OMB Comment TR 5.3.7.2," Page 16, dated March 2009.	Pages 111, 114, 117-119.	Page 111 states that "*U.S. bladder and lung cancer incidence data for the years 2000-2003 (NCI [National Cancer Institute] (2006) were used as the reference values for calculating U.S. lifetime cancer risks. Thus, the LED_{01} values are expressed in terms of lifetime cancer incidence for the U.S. population (see Section 5.3.7.3).*" Page 118 text states that, "*In the analyses that follow, some of the risk comparisons are based on mortality estimates that have been converted to incidence using recent U.S. incidence-mortality ratios. This conversion introduces additional uncertainty into the comparisons; different results would have been obtained had the incidence been modeled directly rather than estimated after the fact*." The "Response to Comment" states that "*Adoption of more recent background U.S. mortality and cancer incidence data may have resulted in the current risk estimates being about 50% increased compared to what the would have been if older data had been used*." This more quantitative comparison would be useful to include in Section 5.3.8.2.	We recommend including this more quantitative comparison in Section 5.3.8.2.	S