

Comments on Cumulative Assessment of MMA, DMA and Inorganic Arsenic

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Introduction

- EPA suggests “cumulative exposure” assessment for DMA^V, MMA^V, and InAs using levels of DMA^{III} produced in humans (p. 187, Appendix E)
 - ◆ Based on “...DMA^{III} may be form of arsenic associated with greatest relative effect...”

Introduction

- Inappropriate to combine risk assessments for InAs and ingested MMA/DMA, based on
 - ◆ Analysis of relationship of DMA and disease in epidemiology studies of InAs exposure
 - ◆ Limited metabolism of ingested MMA/DMA

Epidemiology Studies

- Several studies demonstrate high proportion of metabolically-formed DMA^V (from inorganic arsenic metabolism) in urine not associated with adverse health effects
 - ◆ Bladder cancer
 - ◆ Skin cancer/skin lesions
 - ◆ Peripheral vascular disease

Case control study (Chen *et al.*, 2003)

- Role of cumulative arsenic exposure and of methylation in 49 Taiwanese bladder cancer cases
- Higher DMA/ MMA ratio in controls (11.5) than in bladder cancer patients (8.24)
- Increased metabolism of MMA to DMA associated with lower risk of bladder cancer at high cumulative arsenic exposure

Other Epidemiology Studies

- Skin cancer/skin lesions
 - ◆ Hsueh *et al.*, 1997 - cohort study
 - ◆ Yu *et al.*, 2000 - case control study
 - ◆ Chen *et al.*, 2003 – case control study
 - ◆ Valenzuela *et al.*, 2005 – cohort study
- Peripheral vascular disease
 - ◆ Tseng *et al.*, 2005 – cohort study

Conclusions

- High levels of metabolically-formed DMA from InAs exposure not associated with bladder cancer or other adverse health effects
- Ingested MMA and DMA undergo much less metabolism to reactive intermediates than does InAs
- Inappropriate to combine risk assessments for InAs and MMA/DMA