

## 8. REGULATIONS AND ADVISORIES

The international and national regulations and guidelines pertaining to arsenic and its metabolites in air, water, and other media are summarized in Table 8-1.

ATSDR has not derived inhalation MRLs or an intermediate-duration oral MRL for inorganic arsenic, or any MRLs for organic arsenic, due to lack of suitable data.

ATSDR has derived an acute-duration oral MRL for inorganic arsenic of 0.005 mg As/kg/day based on a LOAEL of 0.05 mg As/kg/day for gastrointestinal effects and facial edema in Japanese people who ingested arsenic-contaminated soy sauce for 2–3 weeks (Mizuta et al. 1956). An uncertainty factor of 10 (10 for use of a LOAEL and 1 for human variability) was applied.

ATSDR has derived a chronic-duration oral MRL of 0.0003 mg/kg/day for inorganic arsenic based on a NOAEL of 0.0008 mg As/kg/day for dermal effects in a Taiwanese farming population exposed to arsenic in well water (Tseng 1977; Tseng et al. 1968). An uncertainty factor of 3 (for human variability) was applied.

EPA (IRIS 2007) has derived a chronic oral reference dose (RfD) of 0.0003 mg As/kg/day for inorganic arsenic, based on a NOAEL of 0.0008 mg As/kg/day for dermal effects and possible vascular complications in a Taiwanese farming population exposed to arsenic in well water (Tseng 1977; Tseng et al. 1968). An uncertainty factor of 3 (to account for the lack of reproductive data and uncertainty in whether the NOAEL accounts for all sensitive individuals) was applied. No reference concentration (RfC) for chronic inhalation exposures to arsenic was reported. EPA is currently revising the assessment for inorganic arsenic.

The Department of Health and Human Services (DHHS) has determined that inorganic arsenic is known to be a human carcinogen (NTP 2005). The EPA has determined that inorganic arsenic is a human carcinogen and has assigned it the cancer classification, Group A (IRIS 2007). EPA's quantitative estimates of carcinogenic risk from oral exposures include a cancer slope factor of 1.5 mg/kg/day and a drinking water unit risk of  $5 \times 10^{-5}$  µg/L. The inhalation unit risk for cancer is 0.0043 µg/m<sup>3</sup> (IRIS 2007).

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**Table 8-1. Regulations and Guidelines Applicable to Arsenic and Arsenic Compounds**

| Agency   | Description   | Information                                 | Reference                      |
|--|---|---|--------------------------------|
| <b>INTERNATIONAL</b>   |   |   |                                |
| Guidelines:  |   |   |                                |
| IARC   | Carcinogenicity classification for arsenic and arsenic compounds  | Group 1 <sup>a</sup>                        | IARC 2004                      |
| WHO  | Air quality guidelines  | $1.5 \times 10^{-3}$ unit risk <sup>b</sup> | WHO 2000                       |
|  | Drinking water quality guidelines for arsenic   | 0.01 mg/L <sup>c</sup>                      | WHO 2004                       |
| <b>NATIONAL</b>  |   |   |                                |
| Regulations and Guidelines:  |   |   |                                |
| a. Air   |   |   |                                |
| ACGIH  | TLV (TWA) for arsenic and inorganic compounds   | 0.01 mg/m <sup>3</sup>                      | ACGIH 2004                     |
| EPA  | Hazardous air pollutant (arsenic and inorganic compounds, including arsine)                             | Yes   | EPA 2004b<br>42 USC 7412       |
| NIOSH  | REL (15-minute ceiling limit) for arsenic and inorganic compounds <sup>d</sup>                          | 0.002 mg/m <sup>3</sup>                     | NIOSH 2005a                    |
| OSHA   | IDLH for arsenic and inorganic compounds <sup>d</sup>   | 5 mg/m <sup>3</sup>                         |                                |
|  | PEL (8-hour TWA) for general industry for arsenic organic compounds                                     | 0.5 mg/m <sup>3</sup>                       | OSHA 2005d<br>29 CFR 1910.1000 |
|  | PEL (8-hour TWA) for general industry for arsenic inorganic compounds                                   | 10 µg/m <sup>3</sup>                        | OSHA 2005c<br>29 CFR 1910.1018 |
|  | PEL (8-hour TWA) for construction industry for arsenic organic compounds                                | 0.5 mg/m <sup>3</sup>                       | OSHA 2005b<br>29 CFR 1926.55   |
|  | PEL (8-hour TWA) for shipyard industry for arsenic organic compounds                                    | 0.5 mg/m <sup>3</sup>                       | OSHA 2005a<br>29 CFR 1915.1000 |
| b. Water   |   |   |                                |
| EPA  | Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act       | Yes   | EPA 2005d<br>40 CFR 116.4      |
|  | Arsenic pentoxide, arsenic trioxide, calcium arsenate, and sodium arsenite                              |   |                                |
|  | Drinking water standards and health advisories for arsenic  |   | EPA 2004a                      |
|  | DWEL  | 0.01 mg/L                                   |                                |
|  | National primary drinking water standards for arsenic   |   | EPA 2002a                      |
|  | MCLG  | Zero  |                                |
|  | MCL   | 0.01 mg/L <sup>e</sup>                      |                                |
|  | Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act |   | EPA 2005e<br>40 CFR 117.3      |
| Arsenic pentoxide, arsenic trioxide, calcium arsenate, sodium arsenite | 1 pound   |   |                                |

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| Agency                  | Description   | Information                                | Reference                  |
|-------------------------|---|--|----------------------------|
| <b>NATIONAL (cont.)</b> |   |  |                            |
| EPA                     | Water quality criteria for human health consumption of arsenic:   |  | EPA 2002b                  |
|                         | Water + Organism  | 0.018 µg/L <sup>f</sup>                    |                            |
|                         | Organism only   | 0.14 µg/L <sup>f</sup>                     |                            |
| <b>c. Food</b>          |   |  |                            |
| EPA                     | Tolerances for residues   |  |                            |
|                         | Dimethylarsinic acid  |  | EPA 2005i                  |
|                         | Cotton (undelinted seed)  | 2.8 ppm                                    | 40 CFR 180.311             |
|                         | Methanearsonic acid   |  | EPA 2005j                  |
|                         | Cotton (undelinted seed)  | 0.7 ppm                                    | 40 CFR 180.289             |
|                         | Cotton, hulls   | 0.9 ppm                                    |                            |
|                         | Fruit, citrus   | 0.35 ppm                                   |                            |
| FDA                     | Bottled drinking water  | 0.01 mg/L                                  | FDA 2005<br>21 CFR 165.110 |
| USDA                    | Nonsynthetic substances prohibited for use in organic crop production   | Arsenic                                    | USDA 2004<br>7 CFR 205.602 |
| <b>d. Other</b>         |   |  |                            |
| ACGIH                   | Carcinogenicity classification for arsenic and arsenic compounds  | A1 <sup>g</sup>                            | ACGIH 2004                 |
|                         | Biological exposure indices for inorganic arsenic plus methylated metabolites in urine at the end of the workweek | 35 µg As/L                                 |                            |
| EPA                     | Carcinogenicity classification  | Group A <sup>i</sup>                       | IRIS 2007                  |
|                         | Oral slope factor   | 1.5 per mg/kg/day                          |                            |
|                         | Inhalation unit risk  | 4.3x10 <sup>-3</sup> per µg/m <sup>3</sup> |                            |
|                         | RfC   | No data                                    |                            |
|                         | RfD   | 3x10 <sup>-4</sup> mg/kg/day               |                            |
|                         | Superfund, emergency planning, and community right-to-know  |  |                            |
|                         | Designated CERCLA hazardous substance   |  | EPA 2005f                  |
|                         | Reportable quantity   |  | 40 CFR 302.4               |
|                         | Arsenic   | Not applicable <sup>j</sup>                |                            |
|                         | Arsenic acid, arsenic pentoxide, arsenic trioxide, calcium arsenate, dimethylarsinic acid, and sodium arsenite    | 1 pound                                    |                            |
|                         | Effective date of toxic chemical release reporting for arsenic  | 01/01/87                                   | EPA 2005h<br>40 CFR 372.65 |

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| Agency                           | Description  | Information            | Reference              |
|----------------------------------|--|------------------------|------------------------|
| <b>NATIONAL</b> ( <i>cont.</i> ) |  |                        |                        |
| EPA                              | Superfund, emergency planning, and community right-to-know |                        |                        |
|                                  | Extremely hazardous substances                             |                        | EPA 2005g              |
|                                  | Reportable quantity  |                        | 40 CFR 355, Appendix A |
|                                  | Arsenic pentoxide, calcium arsenate, and sodium arsenite   | 1 pound                |                        |
|                                  | Threshold planning quantities                              |                        |                        |
|                                  | Arsenic pentoxide  | 100/10,000 pounds      |                        |
|                                  | Calcium arsenate and sodium arsenite                       | 500/10,000 pounds      |                        |
| NTP                              | Carcinogenicity classification                             | Known human carcinogen | NTP 2005               |

<sup>a</sup>Group 1: carcinogenic to humans

<sup>b</sup>Cancer risk estimates for lifetime exposure to a concentration of 1 µg/m<sup>3</sup>.

<sup>c</sup>Provisional guideline value: as there is evidence of a hazard, but the available information on health effects is limited.

<sup>d</sup>NIOSH potential occupational carcinogen

<sup>e</sup>MCL will become effective on 01/23/06.

<sup>f</sup>This criterion is based on carcinogenicity of 10<sup>-6</sup> risk.

<sup>g</sup>A1: confirmed human carcinogen

<sup>h</sup>A3: confirmed animal carcinogen with unknown relevance to humans

<sup>i</sup>Group A: known human carcinogen

<sup>j</sup>Indicates that no reportable quantity is being assigned to the generic or broad class.

ACGIH = American Conference of Governmental Industrial Hygienists; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NAS/NRC = National Academy of Sciences/National Research Council; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TLV = threshold limit values; TWA = time-weighted average; USC = United States Code; USDA = United States Department of Agriculture; WHO = World Health Organization

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EPA is currently revising the assessment for inorganic arsenic. The International Agency for Research on Cancer (IARC) cites sufficient evidence of a relationship between exposure to arsenic and human cancer. IARC classification of arsenic is Group 1 (IARC 2004). The American Conference of Governmental Industrial Hygienists (ACGIH) classifies arsenic (elemental and inorganic compound) as a confirmed human carcinogen, cancer category A1 (ACGIH 2004).

ATSDR has derived an intermediate-duration oral MRL of 0.1 mg MMA/kg/day for MMA based on a BMDL<sub>10</sub> of 12.38 mg MMA/kg/day for diarrhea observed in rats exposed to MMA in the diet for 13 weeks (Arnold et al. 2003) and an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

ATSDR has derived a chronic-duration oral MRL of 0.01 mg MMA/kg/day for MMA based on a BMDL<sub>10</sub> of 1.09 mg MMA/kg/day for increased incidence of progressive nephropathy in male mice exposed to MMA in the diet for 2 years (Arnold et al. 2003) and an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

ATSDR has derived a chronic-duration oral MRL of 0.02 mg DMA/kg/day for DMA based on a BMDL<sub>10</sub> of 1.80 mg DMA/kg/day for increased vacuolization of the urothelium in the urinary bladder of female mice exposed to DMA in the diet for 2 years (Arnold et al. 2006) and an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

EPA has not derived RfD values for organic arsenicals (IRIS 2007).