APPENDIX A:
Addendum to Health-based Maximum Contaminant Level Support Document for
1,2,3-Trichloropropane (DWQI, 2009)

New Jersey Drinking Water Quality Institute Health Effects Subcommittee

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Summary

The Health Effects Subcommittee has reviewed the basis for the March 2009 Health-based MCL recommendation and relevant newer information. There is no new information indicating that the 2009 cancer potency factor, 26 $(mg/kg/day)^{-1}$, should be revised. Current USEPA risk assessment guidance recommends use of age-dependent adjustment factors to the cancer potency factor, in combination with age-specific drinking water ingestion factors, to account for increased susceptibility from early life exposure to carcinogens with a mutagenic mode of action such as 1,2,3-trichloropropane. This approach was used to develop the 2015 Health-based MCL recommendation for 1,2,3-trichloropropane. **The recommended Health-based MCL is 0.0005 µg/L (0.5 ng/L)**, a 2.6-fold decrease from the Health-based MCL recommended in 2009 (0.0013 µg/L; 1.3 ng/L).

Introduction

In March 2009, the New Jersey Drinking Water Quality Institute (DWQI) Health Effects Subcommittee developed a recommended Health-based MCL of 0.0013 µg/L (1.3 ng/L) (DWQI, 2009a). The MCL recommended by the DWQI in 2009 was 0.03 µg/L (30 ng/L), based on an analytical Practical Quantitation Level (PQL) of 0.03 µg/L and the ability of treatment removal technology to achieve this level (DWQI, 2009b).

In September 2015, New Jersey Department of Environmental Protection Commissioner Bob Martin requested that the DWQI review the basis for the MCL that it had recommended in 2009. In order to determine whether the 2009 recommendation should be revised, the Health Effects Subcommittee has reviewed the basis for the 2009 Health-based MCL and relevant newer information available after March 2009. This addendum presents the results of the Health Effects Subcommittee's review.

Review of 2009 Health Effects Subcommittee assessment (DWQI, 2009a)

1,2,3-Trichloropropane is a contaminant of nematocides/fumigants applied to soil and has also been used for other industrial purposes. It is stable in the environment and has been detected in public water systems, private wells, and in ground water at contaminated sites in New Jersey and other states.

After absorption into the body, 1,2,3-trichloropropane is metabolized to reactive intermediates which are mutagenic, genotoxic, and carcinogenic. It is a potent carcinogen and caused tumors in male and female rats and mice in multiple organs in a 2-year chronic gavage study (NTP, 1993). In this study, tumors began to be detected within a year of the start of dosing, and were associated with high mortality rates of treated animals. Forestomach tumors were the most frequent tumor type in male and female mice and rats. It was concluded that the carcinogenicity of 1,2,3-trichloropropane occurs through a mutagenic mode of action.

Because the incidence of forestomach tumors was so high even at the lowest dose, a time-to-tumor model appropriate for modeling dose-response data from studies with early fatal tumor occurrence is used to develop cancer slope factors from the NTP (1993) data. Modeling of forestomach tumors in female mice gave the highest slope factor, 26 $(mg/kg/day)^{-1}$. The recommended Health-based MCL developed from this slope factor in March 2009 was 0.0013 µg/L or 1.3 ng/L (DWQI, 2009a).

Relevant information that has become available since 2009 DWQI Health-based MCL recommendation

USEPA IRIS Assessment

Cancer descriptor and cancer potency factor

The USEPA Integrated Risk Information System (IRIS) completed its assessment of 1,2,3-trichloropropane in September 2009 (USEPA, 2009). USEPA IRIS risk assessments undergo extensive public comment and peer review and are the preferred source of risk assessment information used by USEPA.

IRIS concluded that 1,2,3-trichloropropane is "likely to be carcinogenic to humans" under the USEPA Guidelines for Carcinogen Risk Assessment (USEPA, 2005a). IRIS developed an oral cancer potency factor of 30 $(mg/kg/day)^{-1}$ based on the tumor incidence in female mice in the NTP (1993) chronic study using a time-to-tumor model. The IRIS (2009) cancer assessment is consistent with the DWQI (2009) evaluation, which also was based on time-to-tumor modeling of tumor incidence in female mice in the NTP (1993) chronic study. IRIS modeling of alimentary tumors (primarily forestomach) resulted in a cancer potency factor of 26 $(mg/kg/day)^{-1}$, identical to the DWQI cancer potency factor which is based on forestomach tumors. Additional IRIS

modeling of combined incidence of tumors at all sites (alimentary system, liver, Harderian gland, and uterus) in female mice provided a slightly higher factor, 28 $(mg/kg/day)^{-1}$. IRIS rounded these two slope factors to one significant figure and recommended a cancer potency factor of 30 $(mg/kg/day)^{-1}$.

Mutagenic mode of action and age-dependent adjustment factors (ADAFs)
Comparison of studies in which exposures began during the perinatal (prenatal or early in life) period with studies in which exposure started in adulthood suggest that susceptibility to mutagenic carcinogens is higher early in life than in adulthood. Accordingly, current USEPA risk assessment guidance (USEPA, 2005b) recommends the application of age-dependent adjustment factors (ADAFs) for carcinogens with a mutagenic mode of action (MOA) when the exposure period includes early life, as is the case with chronic exposure to drinking water contaminants. The recommended ADAFs and their age groupings are 10-fold for <2 years, and 3-fold for 2 to <16 years. These 10-fold and 3-fold adjustments to the cancer potency factor are combined with age specific drinking water consumption factors when estimating cancer risks from early life (<16 years age) exposure to carcinogenic drinking water contaminants with a mutagenic MOA.

Toxicological studies of 1,2,3-trichloropropane indicate that it causes carcinogenicity through a mutagenic mode of action (DWQI, 2009a; USEPA, 2009). Therefore, USEPA IRIS (2009) recommended the application of ADAFs when assessing the cancer risk of 1,2,3-trichloropropane from exposures that include early life.

USEPA Office of Water health-based UCMR3 Reference Concentration
1,2,3-Trichloropropane is included in the USEPA Unregulated Contaminant Monitoring Rule (UCMR3) which requires nationwide monitoring of public water supplies for a list of unregulated drinking water contaminants in 2013-2015 (USEPA, 2015). The USEPA Office of Water (2015) has developed health-based Reference Concentrations for UCMR3 contaminants to provide a context for interpretation of detections of these contaminants.

The USEPA Office of Water Reference Concentrations for 1,2,3-trichloropropane are based on the USEPA cancer potency factor of 30 $(mg/kg/day)^{-1}$ with application of ADAFs (USEPA, 2005b) and age-specific drinking water ingestion factors for a 70 year assumed lifespan. The age-specific drinking water ingestion factors used to develop the UCMR3 Reference Value were provided to the Health Effects Subcommittee by the USEPA Office of Water in a spreadsheet that can be used to calculate chronic drinking water concentrations using ADAFs. The factors are shown in Table 1, and the spreadsheet is provided in Appendix A. They are expressed as daily ingestion rate in liters per kg body weight (L/kg/day) and are based on the 90th percentile estimates for community water system consumers for each age period (USEPA, 2011). The adult drinking water consumption value of 2 L/day used for previous MCLs developed by the DWQI

and USEPA is also based on the 90th percentile (USEPA, 2004). It should be noted that the time-weighted average drinking water ingestion rate over a 70 year lifetime using the factors in Table 1 is 0.035 L/kg/day, which is not a large change from the ingestion rate of 0.029 L/kg based on default adult exposure factors (2 L/day; 70 kg body weight).

The choice of the cancer risk level used as the basis for human health criteria is a policy decision, and the cancer risk levels used in drinking water risk assessment differ among states and federal programs. Therefore, USEPA Office of Water (USEPA, 2015) provides Reference Concentrations for carcinogens based on a range of cancer risk levels (10^{-4} – 10^{-6}). Health-based MCLs developed by the DWQI for carcinogens are based on a lifetime cancer risk level of 10^{-6} (one in one million), as this risk level is specified as the goal for New Jersey MCLs in the 1984 amendments to the New Jersey Safe Drinking Water Act (N.J.S.A. 58:12A-1 et seq.). The USEPA Reference Concentration at the 10^{-6} risk level used as the goal for NJ MCLs is 0.0004 µg/L (0.4 ng/L).

Table 1. ADAFs and Age-Specific Drinking Water Ingestion Factors*			
Age period	**ADAF**	**Ingestion rate (L/kg/day)**	**Fraction of Lifetime**
birth to < 1 month	10	0.235	0.001
1 to < 3 months	10	0.228	0.002
3 to < 6 months	10	0.148	0.004
6 to < 12 months	10	0.112	0.007
1 to < 2 years	10	0.056	0.014
2 to < 3 years	3	0.052	0.014
3 to < 6 years	3	0.043	0.043
6 to < 11 years	3	0.035	0.071
11 to < 16 years	3	0.026	0.071
16 to < 18 years	1	0.023	0.029
18 to <21 years	1	0.026	0.043
21 to <70 years	1	0.034	0.700

*See text above for explanation of basis and use of these factors.

Relevant information since 2009
No additional scientific studies relevant to the risk assessment of 1,2,3-trichloropropane were located in a recent PubMed search.

Two recent publications on risk assessment of 1,2,3-trichloropropane were found (Tardiff and Carson, 2010; Meek et al., 2014). Additionally, the basis for the existing Hawaii Department of Health MCL for 1,2,3-trichloropropane was reviewed in 2012 by TetraTech (2012).

<u>Tardiff and Carson (2010)</u>

Tardiff and Carson (2010) propose a drinking water concentration of 200-280 µg/L (200,000-280,000 ng/L) as protective for carcinogenic effects of 1,2,3-trichloropropane. This evaluation does not consider any scientific data that became available subsequent to the DWQI (2009a) and USEPA IRIS (2009) risk assessments, but rather is based on differing conclusions about issues that were thoroughly considered by DWQI (2009a) and USEPA IRIS (2009). The main points that are the basis for Tardiff and Carson's (2010) conclusion are briefly discussed below. Based on its review of the information presented by Tardiff and Carson (2010), the DWQI Health Effects Subcommittee has determined that the conclusions and the proposed drinking water concentration presented by Tardiff and Carson (2010) are not scientifically supportable or consistent with current risk assessment guidance (USEPA, 2005a, 2005b).

Tardiff and Carson (2010) propose that a threshold (Reference Dose) approach should be used for cancer risk assessment of 1,2,3-trichloropropane. This proposal is based on their conclusion that the dose-response curve for the mutagenicity of this chemical is non-linear (e.g. has a threshold). This approach is clearly not consistent with USEPA (2005a, 2005b) guidelines for carcinogen risk assessment. Additionally, the Health Effects Subcommittee concludes that explanations presented by Tardiff and Carson (2010) are based on other chemicals, rather than on data from studies of 1,2,3-trichloropropane itself. The recent review of 1,2,3-trichloropropane risk assessment developed for Hawaii Department of Health (TetraTech, 2012; see below) concurs with these conclusions of the Health Effects Subcommittee. TetraTech (2012) states that "there are insufficient data to support the authors' assumption that cancer incidence related to TCP would be non-linear at low doses" and that "the current data are not sufficient to support a non-linear approach for regulatory purposes." In agreement with the Health Effects Subcommittee's review, TetraTech (2012) also states that the conclusions of Tardiff and Carson (2010) about the MOA of 1,2,3-trichloropropane are speculative and are based on data from other compounds that "are not structurally or chemically related to 1,2,3-trichloropropane".

Tardiff and Carson (2010) also conclude that several of the tumor types observed in the NTP (1993) study are not relevant to humans, including forestomach tumors. As discussed above, forestomach tumors are the tumor type with the highest incidence in the NTP (1993) study, and the DWQI (2009a) and EPA IRIS (2009) slope factors are based on the incidence of these tumors. As discussed in DWQI (2009), IARC (2003) reviewed the issue of human relevance of forestomach tumors. IARC (2003) concluded that, although humans do not have a forestomach, the tissues in the upper part of the human digestive tract are comparable to the rodent forestomach. Furthermore, IARC (2003) concluded that forestomach tumors caused by

genotoxic carcinogens that also cause tumors at other sites, as is the case for 1,2,3-trichloropropane, should be considered relevant to humans. Subsequent to the DWQI (2009a) document, USEPA IRIS (2009) also considered the human relevance of forestomach tumors, including the conclusions of IARC (2003) and peer review comments that USEPA IRIS received on this issue. EPA IRIS (2009) also concluded that the forestomach tumors caused by 1,2,3-trichloropropane should be considered relevant to humans.

Finally, Tardiff and Carson (2010) state that the doses used in NTP (1993) exceeded the Maximum Tolerated Dose (MTD) based on decreased body weight and early mortality in the high dose group, and that doses exceeding the MTD should not be considered relevant for human risk assessment. However, this argument is not applicable to NTP (1993) because the decreased body weight and early mortality in the high dose group resulted from the tumors that occurred early in life, not from other types of non-cancer toxicity.

Meek et al. (2014)

Meek et al. (2014) developed a mode of action/human relevance framework for evaluating the weight of evidence for risk assessment. They used 1,2,3-trichloropropane as a case study for a chemical with strong evidence for a mutagenic MOA for carcinogenicity. It was compared to carbon tetrachloride, a carcinogen which has weak evidence for a mutagenic MOA. The study did not develop risk based values for water or other media, but rather used these chemicals to illustrate how information related to the weight of evidence for a mode of action can be evaluated.

TetraTech (2012) review of Hawaii Department of Health MCL

The basis for the existing Hawaii Department of Health MCL for 1,2,3-TCP of 0.6 μg/L was reviewed in 2012 (TetraTech, 2012). This MCL was adopted in 2005 and is based on a long term goal of 0.6 μg/L developed for Hawaii DOH by Tardiff (2001). This value was based on a cancer potency factor of 0.0588 $(mg/kg/day)^{-1}$ from the incidence of pancreatic tumors in male rats in NTP (1993) at the 10^{-6} cancer risk level (Tardiff, 2001). Adjustments for extrapolation of doses in animals to humans and ADAFs were not used in the risk assessment conducted by Tardiff (2001).

TetraTech (2012) evaluated the lifetime cancer risk level at the current Hawaii MCL, 0.6 μg/L, using a range of cancer potency factors based on data from NTP (1993). ADAFs were applied in this analysis, as consistent with current USEPA (2005b) risk assessment guidance. TetraTech (2012) did not dismiss the human relevance of forestomach tumors, but rather developed an "alternative" cancer potency factor of 5.8 $(mg/kg/day)^{-1}$ as a "compromise" approach. This factor is based on the geometric mean of the four USEPA IRIS (2009) cancer potency factors for male and female rats and mice, and included forestomach tumors. TetraTech (2012) then calculated

the lifetime cancer risk at the MCL of 0.6 µg/L based on a range of cancer potency factors that considered forestomach tumors in different ways. The cancer potency factors considered were:

- USEPA IRIS (2009) recommended cancer potency factor based on tumors at all sites, including forestomach, in female mice - 30 $(mg/kg/day)^{-1}$
- TetraTech (2012) "alternative" cancer potency factor based on geometric mean of four USEPA IRIS (2009) cancer potency factors (for male and female rats and mice, including forestomach tumors) – 5.8 $(mg/kg/day)^{-1}$
- USEPA IRIS (2009) cancer potency factor based on tumors in male and female mice with forestomach tumors excluded – 1.3 $(mg/kg/day)^{-1}$
- Earlier Tardiff (1992) cancer potency factor based on pancreatic tumors in male rats – 0.12 $(mg/kg/day)^{-1}$
- Tardiff (2001) cancer potency factor based on pancreatic tumors in male rats – 0.0588 $(mg/kg/day)^{-1}$

TetraTech (2012) reported that the range of lifetime cancer risk levels at the MCL of 0.6 µg/L based on this range of cancer potency factors, 0.0588 $(mg/kg/day)^{-1}$ to 30 $(mg/kg/day)^{-1}$, is 2.8 x 10^{-6} to 1.4 x 10^{-3}. All of these risk levels are above the 1 x 10^{-6} risk level specified as the goal for MCLs in New Jersey legislation (N.J.S.A. 58:12A-1 et seq.). Although the approach used by TetraTech to develop its "alternative" slope factor (the geometric mean of the four slope factors for each gender and species) of 5.8 $(mg/kg/day)^{-1}$ is not consistent with approach used by the DWQI, it is notable that the drinking water concentration based on the "alternative" slope factor at the 1 x10^{-6} risk level required by New Jersey legislation is quite stringent, 0.002 µg/L (2 ng/L).

<u>Health-based MCL Recommendation</u>

There is no information suggesting that the cancer potency factor, 26 $mg/kg/day^{-1}$, developed by the DWQI (2009a) should be revised. It is identical to the cancer potency factor based on alimentary tumors (forestomach and oral tumors, of which >95% were forestomach tumors) in female mice; NTP, 1993) developed by USEPA IRIS (2009). A slightly more stringent cancer potency factor, 28 $mg/kg/day^{-1}$, based on combining all tumor types in female mice was also presented by USEPA IRIS (2009). These values were rounded by USEPA IRIS to one significant figure, 30 $mg/kg/day^{-1}$, which is the cancer potency factor recommended by IRIS. The Health Effects Subcommittee concluded that the cancer potency factor recommended by USEPA IRIS (2009) is not meaningfully different from the DWQI (2009a) factor. Additionally, the DWQI has not developed slope factors based on combined tumors from different organs in its past assessments. Therefore, the 2009 DWQI cancer potency factor of 26 $mg/kg/day^{-1}$ is used to develop the recommended Health-based MCL.

As discussed above, current USEPA (2005b) risk assessment guidance indicates that ADAFs should be applied in chronic drinking water risk assessment for carcinogens with a mutagenic MOA, and USEPA IRIS (2009) recommends that ADAFs be used in the risk assessment of

1,2,3-trichloropropane. The Health Effects Subcommittee agrees with this recommendation. Therefore, the ADAFs provided by USEPA (2005b) and the age-specific drinking water ingestion factors recommended by USEPA Office of Water (Table 1) are used to develop the Health-based MCL.

As shown in Appendix A, the ADAF-Adjusted Unit Risk (risk from ingesting 1 µg/L for 70 years) is 2.0×10^{-3} (µg/L)$^{-1}$. The Age-Adjusted Unit Risk Level Concentration (drinking water concentration at the 10^{-6} risk level; i.e. Health-based MCL) is calculated as:

Risk Level ÷ ADAF-Adjusted Unit Risk = ADAF-Adjusted Unit Risk Level Concentration

or: $1 \times 10^{-6} \div 2.0 \times 10^{-3}$ (µg/L)$^{-1}$ = 0.0005 µg/L or 0.5 ng/L

Therefore, the Health-based MCL based on a cancer potency factor of 26 mg/kg/day^{-1} and a 10^{-6} (one in one million) lifetime cancer risk is **0.0005 µg/L (0.5 ng/L).**

Conclusion

The recommended Health-based MCL for 1,2,3-trichloropropane is **0.0005 µg/L (0.5 ng/L).**

Citations

DWQI (2009a). New Jersey Drinking Water Quality Institute. Maximum Contaminant Level recommendations for hazardous contaminants in drinking water. Submitted to: New Jersey Department of Environmental Protection. March 2009. Appendix A: Health Effects Subcommittee Report. Health-Based MCL Support Document: 1,2,3-Trichloropropane. p. 165-195.

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NTP (1993). National Toxicology Program. Toxicology and carcinogenesis studies of 1,2,3-trichloropropane (CAS No. 96-18-4) in F344/N rats and B6C3F1 mice (gavage studies). Public Health Service, U.S. Department of Health and Human Services; NTP TR 384.

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USEPA (2011). United States Environmental Protection Agency. Exposure Factors Handbook 2011 Edition (Final). EPA/600/R-09/052F, 2011. [http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf.]

USEPA (2015). United States Environmental Protection Agency. The Third Unregulated Contaminant Monitoring Rule (UCMR 3): Data Summary, June 2015. http://water.epa.gov/lawsregs/rulesregs/sdwa/ucmr/upload/UCMR3_Data-Summary_June-2015_508.pdf

Appendix A: Calculation of Health-based MCL for 1,2,3-Trichloropropane with Spreadsheet for ADAFs and Age-specific Drinking Water Ingestion Factors (provided by USEPA Office of Water)

$$\text{ADAF-Adjusted Unit Risk } (\mu g/L)^{-1} = \sum(\text{CSF} \times \text{ADAF} \times \text{DWI/BWR} \times \text{CW} \times \text{F})$$

CSF	Cancer Slope Factor (mg/kg/day)$^{-1}$
ADAF	The Age Dependent Adjustment Factor (ADAF) for the age group birth to two-years (ADAF=10), two years to sixteen years (ADAF=3), and sixteen to seventy years (ADAF=1)
DWI/BWR	Drinking Water Intake Body Weight Ratio (DWI/BWR) expressed as liters per kg body weight (L/kg/day) for each lifestage (90th percentile, consumers only)
CW	Unit risk concentration in drinking water of 0.001 mg/L (1 µg/L)
F	The fraction of a 70 year lifetime applicable to the age period (e.g., 2/70 for the birth to two-years, 14/70 for two years to sixteen years and 54/70 for sixteen years to seventy year periods)

Input Cancer Slope Factor (mg/kg/day)$^{-1}$ 26

Lifestage	Cancer Slope Factor (mg/kg/day)$^{-1}$	ADAF[1]	DWI/BWR (L/kg/day)[2,3]	CW (mg/L)	Fraction of Lifetime	ADAF-adjusted Unit Risk[4] (µg/L)$^{-1}$
birth to < 1 month	26	10	0.235	0.001	0.0012	7.3E-05
1 to < 3 months	26	10	0.228	0.001	0.0024	1.4E-04
3 to < 6 months	26	10	0.148	0.001	0.0036	1.4E-04
6 to < 12 months	26	10	0.112	0.001	0.0071	2.1E-04
1 to < 2 years	26	10	0.056	0.001	0.014	2.1E-04
			ADAF-adjusted unit risk for Birth to < 2 years[1]			**7.7E-04**
2 to < 3 years	26	3	0.052	0.001	0.014	5.8E-05
3 to < 6 years	26	3	0.043	0.001	0.043	1.4E-04
6 to < 11 years	26	3	0.035	0.001	0.071	2.0E-04
11 to < 16 years	26	3	0.026	0.001	0.071	1.4E-04
			ADAF-adjusted unit risk for 2 to <16 years[1]			**5.4E-04**
16 to < 18 years	26	1	0.023	0.001	0.029	1.7E-05
18 to <21 years	26	1	0.026	0.001	0.043	2.9E-05
21 to <70 years	26	1	0.034	0.001	0.700	6.2E-04
			ADAF-adjusted unit risk for 16 to 70 years[1]			**6.6E-04**

ADAF-adjusted Unit Risk for Birth to 70 years   **2.0E-03**

Calculation of ADAF-Adjusted Risk Level Concentration (ng/L)

ADAF-Adjusted Unit Risk Level Concentration = Risk Level ÷ ADAF-Adjusted Unit Risk

The lifetime ADAF-adjusted unit risk is applied to calculate the concentration in drinking water that is equivalent to specific population risk levels. The concentrations of the contaminant in drinking water associated with an increased risk of cancer (one additional case of cancer) in ten thousand (1 x 10-4), one hundred thousand (1 x 10-5), and one million (1 x 10-6) people are as follows:

Risk Level	ADAF-Adjusted Risk Level Concentration (mg/L)	ADAF-Adjusted Risk Level Concentration (µg/L)	ADAF-Adjusted Risk Level Concentration (ng/L)
1.0E-04	0.00005	0.05	51
1.0E-05	0.000005	0.005	5
1.0E-06*	**0.0000005**	**0.0005**	**0.5***

***Cancer risk level used by DWQI for recommended Health-based MCLs, as specified in the 1984 amendments to the New Jersey Safe Drinking Water Act (N.J.S.A. 58:12A-1 et seq.).

[1]The three exposure periods and their associated ADAFs [Birth to two-years (ADAF=10), two years to sixteen years (ADAF=3), and sixteen to seventy years (ADAF=1)] were established using "The Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (EPA, 2005a)" and are to be use if chemical-specific data that quantify the increased risk are lacking for mutagenic carcinogens.

[2]The estimated drinking water intake body weight ratios (L/kg/day) used for **Birth to <3 years** are the 90th percentile values of the consumers only estimates of direct and indirect water ingestion, based on 1994-1996, 1998 CSFII (community water, mL/kg-day) in Table 3-19 in the Exposure Factors Handbook 2011 Edition (Final), page 3-40. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-09/052F, 2011. [http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf.]

[3]The estimated drinking water intake body weight rations (L/kg/day) used for **3 to ≥ 21 years** are the 90th percentile values of the consumers only estimates of direct and indirect water ingestion, based on 2003-2006, (community water, mL/kg/day) in Table 3-38 in the Exposure Factors Handbook 2011 Edition (Final), page 3-59. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-09/052F, 2011. [http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf.]

[4]The ADAF-adjusted Unit Risk is defined as the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water. The risk is calculated for each of the three exposure periods with application of its ADAF and then added together to obtain the total risk for a 70 year period initiated at birth. Risks can also be calculated for any exposure duration of interest combined with the doses for the age group of interest.