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Relative source allocation of TDI to drinking water for derivation of a criterion for chloroform: A Monte-Carlo and multi-exposure assessment

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ABSTRACT

Drinking water quality standard (DWQS) criteria for chemicals for which there is a threshold for toxicity are derived by allocating a fraction of tolerable daily intake (TDI) to exposure from drinking water. We conducted physiologically based pharmacokinetic model simulations for chloroform and have proposed an equation for total oral-equivalent potential intake via three routes (oral ingestion, inhalation, and dermal exposures), the biologically effective doses of which were converted to oral-equivalent potential intakes. The probability distributions of total oral-equivalent potential intake in Japanese people were estimated by Monte Carlo simulations. Even when the chloroform concentration in drinking water equaled the current DWQS criterion, there was sufficient margin between the intake and the TDI: the probability that the intake exceeded TDI was below 0.1%. If a criterion that the 95th percentile estimate equals the TDI is regarded as both providing protection to highly exposed persons and leaving a reasonable margin of exposure relative to the TDI, then the chloroform drinking water criterion could be a concentration of 0.11 mg/L. This implies a daily intake equal to 34% of the TDI allocated to the oral intake (2 L/d) of drinking water for typical adults. For the highly exposed persons, inhalation exposure via evaporation from water contributed 53% of the total intake, whereas dermal absorption contributed only 3%.

1. Introduction

1.1. Background

Drinking water quality guideline values of threshold chemicals, which have been assumed to have safe exposure levels up to a certain threshold level, are derived by allocating a fraction of tolerable daily intake (TDI) to exposure from drinking water. This allocation is made because drinking water is not the sole source of chemical exposure, and it is essential to take into account exposure from other routes. The World Health Organization's Guidelines for Drinking-water Quality say, "Some consideration of the proportion of the ADI [acceptable daily intake] or TDI that may be attributed to different sources is therefore needed in developing guideline values" (WHO, 2011). Where sufficient information on exposure is available, the amount of intake that comes from drinking water and its relative contribution to total exposure can be estimated. However, the calculation of the allocation factor, the fraction of the TDI allocated to drinking water, is not clearly defined.

USEPA (2000) recommends the Exposure Decision Tree Approach for TDI (termed the reference dose [RfD]) allocation. The approach utilizes either the subtraction or percentage method to account for other exposures, depending on whether one or more health-based criterion is relevant for a chemical in question. The subtraction method is considered acceptable when only one criterion is relevant for a chemical, while the percentage method is recommended when multiple media criteria are under consideration. The USEPA says "The subtraction method results in a criterion allowing the maximum possible chemical concentration in water after subtracting other sources. As such, it removes any cushion between pre-criteria levels (i.e., actual "current" levels) and the RfD". In this approach, however, the drinking water intake estimate is approximately the 90th percentile value, whereas intake estimates from non-water exposures are based on arithmetic mean values. EPA says that this combination of parameter value assumptions is expected to result in a criterion that is protective of a majority of the population, but does not recommend that high-end intakes

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Abbreviations

Symbols	Definition
a_i	coefficient for the effect of cooking water on food (dimensionless)
A_D	daily oral intake (mg/day)
A_f	allocation factor (%)
A_{sk}	body surface area (cm^2)
b_k(r)	coefficient for the effect of water evaporation on the air (dimensionless, *k*=bathroom, kitchen, or residence)
b_w	body weight (kg)
b_h	body height (cm)
C_a	concentration in inhaled air (mg/L)
$\overline{C}_a(r)$	daily-average concentration in inhaled air (mg/L)
$C_{air,w,\ k}$ (r)	concentration in inhaled air in an area (*k* = bathroom, kitchen, or residence) under the influence from tap water (mg/L) ("(r)" indicates Monte-Carlo input.)
$C_{air,outdoor}$ (r)	concentration in outdoor air (mg/L)
C_{alv}	concentration in alveolar air (mg/L)
C_{art}	concentration in arterial blood (mg/L)
C_d	concentration in water for dermal adsorption (mg/L)
$\overline{C}_d(r)$	daily-average concentration in water for dermal adsorption (mg/L) ("(r)" indicates Monte-Carlo input.)
$C_{food,w,i}$	concentration in *i*th food group after cooking with tap water (mg/g)
$C_{food,0,i}$	concentration in *i*th food group after cooking with pure water (mg/g)
C_{ven}	concentration in mixed venous blood (mg/L)
C_{vf}	concentration in venous blood leaving fat (mg/L)
C_{vk}	concentration in venous blood leaving the kidneys (mg/L)
C_{vl}	concentration in venous blood leaving the liver (mg/L)
C_{vr}	concentration in venous blood leaving rapidly perfused tissues (mg/L)
C_{vs}	concentration in venous blood leaving slowly perfused tissues (mg/L)
C_{vsk}	concentration in venous blood leaving skin (mg/L)
C_w	concentration in tap water (mg/L)
D_D	dermal potential dose [mg/(kg-body d)]
D_{DO}	oral-equivalent dermal potential dose [mg/(kg-body d)]
D_I	inhalation potential dose [mg/(kg-body d)]
D_{IO}	oral-equivalent inhalation potential dose [mg/(kg-body d)]
D_O	oral potential dose [mg/(kg-body d)]
D_T	total oral-equivalent potential dose [mg/(kg-body d)]
E_D	dermal biologically effective dose [mg/(kg-organ d)]
E_I	inhalation biologically effective dose [mg/(kg-organ d)]
E_O	oral biologically effective dose [mg/(kg-organ d)]
G_v	guideline value (mg/L)
K_{mk}	Michaelis constant for enzymatic reaction for the kidneys (mg/L)
K_{ml}	Michaelis constant for enzymatic reaction for the liver (mg/L)
K_p	effective skin permeability coefficient (cm/d)
$I_{food,i,j}$ (r)	daily intake of *j*th food in *i*th food group (g/d) ("(r)" indicates Monte-Carlo input.)
I_{water}	daily drinking water consumption (L/d)
P_{ba}	blood/air partition coefficient (dimensionless)
P_{fb}	fat/blood partition coefficient (dimensionless)
P_{kb}	kidney/blood partition coefficient (dimensionless)
P_{lb}	liver/blood partition coefficient (dimensionless)
P_{rb}	rapidly perfused/blood partition coefficient (dimensionless)
P_{sb}	slowly perfused/blood partition coefficient (dimensionless)
P_{skb}	skin/blood partition coefficient (dimensionless)
P_{skw}	skin/water partition coefficient (dimensionless)
Q	breathing rate (L/d)
Q_{alv}	alveolar ventilation rate (L/d)
Q_f	blood flow rate to fat (L/d)
Q_k	blood flow rate to the kidneys (L/d)
Q_l	blood flow rate to the liver (L/d)
Q_r	blood flow rate to rapidly perfused tissues (L/d)
Q_s	blood flow rate to slowly perfused tissues (L/d)
Q_{sk}	blood flow rate to skin (L/d)
Q_t	cardiac output (L/d)
t	time (d)
$t_{bathroom}$(r)	time spent in bathroom per day (dimensionless)
$t_{kitchen}$(r)	time spent in kitchen per day (dimensionless)
$t_{residence}$(r)	time spent in residence per day (dimensionless)
$t_{outdoor}$(r)	time spent outdoors per day (dimensionless)
V_f	volume of fat (L)
V_l	volume of the liver (L)
V_k	volume of the kidneys (L)
V_{maxl}	maximum enzymatic reaction rate for the liver (mg/d)
V_{maxk}	maximum enzymatic reaction rate for the kidneys (mg/d)
V_r	volume of rapidly perfused tissues (L)
V_s	volume of slowly perfused tissues (L)
V_{sk}	volume of skin (L)
α	ratio of effective doses by single/continuous exposure (dimensionless)
α_1	ratio of oral effective doses by single/continuous exposure (dimensionless)
α_2	ratio of inhalation effective doses by single/continuous exposure (dimensionless)
α_3	ratio of dermal effective doses by single/continuous exposure (dimensionless)
$\alpha_{2/1}$	ratio of α_2 to α_1 (dimensionless)
$\alpha_{3/1}$	ratio of α_3 to α_1 (dimensionless)
β	ratio of effective/potential dose at a constant continuous administration (kg-body d/kg-organ)
β_1	ratio of oral effective/potential dose at a constant continuous administration (kg-body d/kg-organ)
β_2	ratio of inhalation effective/potential dose at a constant continuous administration (kg-body d/kg-organ)
β_3	ratio of dermal effective/potential dose at a constant continuous administration (kg-body d/kg-organ)
$\beta_{2/1}$	ratio of β_2 to β_1 (dimensionless)
$\beta_{3/1}$	ratio of β_3 to β_1 (dimensionless)
ϕ	ratio of alveolar ventilation rate to breathing rate (dimensionless)

be subtracted for every exposure source since the combination may not be representative of any actually exposed population.

For volatile compounds such as chloroform and benzene, volatilization from water, in particular when bathing, may increase exposure via inhalation, which could raise total exposure. Dermal absorption of compounds when bathing could also raise total exposure. Shehata (1985) performed a multi-route exposure assessment for benzene, toluene, and xylene. The study employs the subtraction method and suggests that 0–64% (average: 32%) of exposure can be allocated to drinking water. For trihalomethanes (THMs), exposure through inhalation while showering is estimated to be 50–200% of oral exposure via ingestion of water (Jo et al., 2005; Kim et al., 2004). The ratios of dermal exposure to oral exposure are estimated to be 30–70% for THMs (Xu et al., 2002). Ingestion of drinking water is estimated to account for 4–24% of exposure for THMs, whereas combined exposure from inhalation