



**TO:** Joint Committee on Recreational Water Facilities

**FROM:** Mr. Tom Vyles, Chairperson

**DATE:** October 7, 2022

**SUBJECT:** Proposed revision to NSF/ANSI/CAN 50 *Equipment and Chemicals for Swimming Pools, Spas, Hot Tubs and Other Recreational Water Facilities (50i190r1)*

Draft 1 of NSF/ANSI/CAN 50 issue 190 is being forwarded to the Joint Committee for balloting. Please review the changes proposed to this Standard and **submit your ballot by October 28, 2022** via the NSF Online Workspace (<http://standards.nsf.org>).

Please review all ballot materials. When adding comments, please include the section number applicable your comment and add all comments under one comment number whenever possible. If additional space is needed, you may upload a word or .PDF version of your comments online via the browser function.

**Purpose**

This ballot will make revisions to the method of treatment chemical evaluation, switching from the current TOE method to a TTC approach.

**Background**

An issue paper submitted in 2019 recommended the Joint Committee reevaluate the 10 ppb threshold for evaluation of treatment chemicals. A motion to send the issue paper to the RWF Task Group on Pool Chemical Evaluation. That group met multiple times to review and discuss the topic, eventually deciding to adopt a TTC evaluation approach, with similar language being drafted for NSF Drinking Water standards.

If you have any questions about the technical content of the ballot, you may contact me in care of:

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[Note – the recommended changes to the standard which include the current text of the relevant section(s) indicate deletions by use of ~~strikeout~~ and additions by **grey highlighting**. Rationale Statements are in *italics* and only used to add clarity; these statements will NOT be in the finished publication.]

## NSF/ANSI/CAN Standard

# Equipment and Chemicals for Swimming Pools, Spas, Hot Tubs, and other Recreational Water Facilities

Evaluation criteria for materials, components, products, equipment, and systems for use at recreational water facilities

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## 27 Treatment chemicals used in recreational water and facilities

### 27.1 Scope

#### 27.1.1 Products included in scope

Treatment chemicals requiring a health effects evaluation includes those directly added to the waters of pools and spas. These treatment chemicals shall not impart undesirable levels of either chemical constituents or contaminants to the water.

Swimming pool treatment chemical constituents evaluated under this Standard shall include:

- the swimming pool treatment chemical constituents;
- the product-specific contaminants identified in the formulation review or by testing; and
- other constituents as identified in the formulation review or by testing.

Excluded from the scope of this evaluation procedure are contaminants produced as by-products through reaction of the treatment chemical with a constituent of the treated water. Also excluded from the scope of this evaluation procedure are the potential effects of the accumulation of pool treatment chemicals in the pool water based on multiple dosages over time. The rationale for these exclusions is based on the variability of pool-specific parameters that may influence such determinations which include, but are not limited to, water chemistry, variability in recirculation, different filtration rates/types, water replacement rates, and splash-out rates.

#### 27.1.2 Products excluded from scope

Excluded from health effects evaluations are any chemicals not added directly to the water that only have incidental contact.

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NOTE — The excluded treatment chemicals are not diluted in the recreational water, thus a health effects assessment must consider user exposure to the concentrated chemical under different circumstances. This exposure is best evaluated using a different hazard assessment than the framework outlined in Annex N-12.

## **27.2 Definitions**

**27.2.1 benchmark dose:** The lower 95% confidence limit on the dose that would be expected to produce a specified response in X% of a test population. This dose may be expressed as BMDx (adapted from Barnes et al., 1995). For the purposes of this Standard, the benchmark dose shall be calculated at the 10% response level.

**27.2.2 continuous data:** A measurement of effect that is expressed on a continuous scale, e.g., body weight or serum enzyme levels (US EPA 1995).

**27.2.3 critical effect:** The first adverse effect, or its known precursor, that occurs as the dose rate increases (US EPA, 2011a).

**27.2.4 genetic toxicity:** Direct interaction with DNA that has the potential to cause heritable changes to the cell.

### **27.2.5 health hazards (types of) (US EPA, 1999 and 2011a)**

**27.2.5.1 acute toxicity:** Effects that occur immediately or develop rapidly after a single administration of a substance. Acute toxicity may also be referred to as immediate toxicity.

**27.2.5.2 allergic reaction:** Adverse reaction to a chemical resulting from previous sensitization to that chemical or to a structurally similar one.

**27.2.5.3 chronic effect:** An effect that occurs as a result of repeated or long-term (chronic) exposures.

**27.2.5.4 chronic exposure:** Multiple exposures occurring over an extended period of time or a significant fraction of an animal's or individual's lifetime.

**27.2.5.5 chronic toxicity:** The capability of a substance to cause adverse human health effects as a result of chronic exposure.

**27.2.5.6 irreversible toxicity:** Toxic effects to a tissue that cannot be repaired.

**27.2.5.7 local toxicity:** Effects that occur at the site of first contact between the biological system and the toxicant.

**27.2.5.8 reversible toxicity:** Toxic effects that can be repaired, usually by a specific issue's ability to regenerate or mend itself after chemical exposure.

**27.2.5.9 systemic toxicity:** Effects that are elicited after absorption and distribution of a toxicant from its entry point to its target tissue.

**27.2.6 lowest observed adverse effect level (LOAEL):** The lowest exposure concentration at which statistically or biologically significant increases in frequency or severity of effects are observed between the exposed population and its appropriate control group (US EPA, 2011a).

**27.2.7 margin of exposure (MoE):** The LED10 or other point of departure divided by the environmental dose of interest (US EPA, 2011a).

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**27.2.8 model:** A mathematical function with parameters that can be adjusted so the function closely describes a set of empirical data. A mechanistic model usually reflects observed or hypothesized biological or physical mechanisms and has model parameters with real world interpretation. In contrast, statistical or empirical models selected for particular numerical properties are fitted to data; model parameters may or may not have real world interpretation. When data quality is otherwise equivalent, extrapolation from mechanistic models (e.g., biologically based dose often carries higher confidence than extrapolation using empirical models (e.g., logistic model) US EPA, 2011a).

**27.2.9 no observed adverse effect level (NOAEL):** The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects (US EPA, 2011a).

**27.2.10 nonregulated substance:** A substance for which a statutory concentration limit does not exist.

**27.2.11 peer review:** A documented critical review of a scientific or technical work product conducted by qualified individuals or organizations that are independent of those who performed the work, but who are collectively equivalent or superior in technical expertise to those who performed the work. It includes an in-depth assessment of the assumptions, calculations, extrapolations, alternate interpretations, methodology, acceptance criteria, and conclusions pertaining to the work product and the documentation that supports the conclusions reached in the report. Peer review is intended to ensure that the work product is technically adequate, competently performed, properly documented, and that it satisfies established requirements (US EPA, 1998a).

**27.2.12 point of departure:** A data point or an estimated point that can be considered to be in the range of observation. The standard point of departure is the LED10, which is the lower 95% confidence limit on a dose associated with 10% extra risk (adapted from Barnes et al., 1995).

**27.2.13 quantal data:** A dichotomous measure of effect; each animal is scored “normal” or “affected,” and the measure of effect is the proportion of scored animals that are affected (US EPA, 1995).

**27.2.14 quantitative risk assessment:** An estimation of the risk associated with exposure to a substance using a methodology that employs evaluation of dose response relationships.

**27.2.15 range of extrapolation:** Doses that are outside the range of empirical observation in animal studies, human studies, or both (adapted from Barnes et al., 1995).

**27.2.16 range of observation:** Doses that are within the range of empirical observation in animal studies, human studies, or both (adapted from Barnes et al., 1995).

**27.2.17 reference dose (RfD):** An estimated (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA’s non-cancer health assessments, [Durations include acute, short-term, subchronic, and chronic and are defined individually in this glossary (US EPA, 2011a)].

**27.2.18 regulated substance:** A substance for which a quantitative human health risk assessment has been performed and utilized in promulgation of a statutory concentration limit for drinking water.

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**27.2.19 short-term exposure level (STEL):** A maximum concentration of a contaminant that is permitted for an acute exposure.

**27.2.20 total allowable concentration (TAC):** The maximum concentration of a non-regulated contaminant allowed in a public drinking water supply.

**27.2.21 toxicodynamics:** Variations in the inherent sensitivity of a species or individual to chemical-induced toxicity, resulting from differences in host factors that influence the toxic response of a target organ to a specified dose (TERA, 1996).

**27.2.22 toxicokinetics:** Variations in absorption, distribution, metabolism, and excretion of a compound that account for differences in the amount of parent compound or active metabolite(s) available to a target organ (TERA, 1996).

**27.2.23 weight of evidence:** The extent to which the available biomedical data support the hypothesis that a substance causes cancer or other toxic effects in humans (adapted from US EPA, 2011a).

### **27.3 Formulation submission**

The manufacturer shall submit, at a minimum, the following information for each swimming pool treatment chemical:

- a proposed maximum dose rate for the product;
- complete formulation information, which includes the following:
  - the composition of the formulation (in percent or parts by weight for each chemical in the formulation);
  - the reaction mixture used to manufacture the chemical, if applicable;
  - Chemical Abstracts Registry Number (CASRN), chemical name and supplier for each chemical present in the formulation; and
  - a list of known suspected impurities within the treatment chemical formulation and the maximum percent or parts by weight of each impurity.
- a description or classification of the process in which the treatment chemical is manufactured, handled and packaged.

#### **27.3.1 Formulation review**

The formulation information provided by the manufacturer shall be reviewed and this review shall determine the formulation-dependent chemical constituents required to be evaluated in accordance with Sections 27.5 and 27.7. For those swimming pool treatment chemicals that have regulatory approval for use in pools by the US EPA under the Federal Insecticide, Fungicide, Rodenticide Act (FIFRA), such regulatory approval may be used to exempt the swimming pool treatment chemical constituents from evaluation against the requirements of Sections 27.5 and 27.7; however, contaminant testing and evaluation shall still be required as set forth under Section 27.4.

#### **27.3.2 Determination of swimming pool water concentrations**

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Utilizing the formulation information and maximum dose rate provided, the maximum residual concentration of each chemical constituent in the product may be calculated as follows:

$$\frac{\text{mg constituent}}{\text{mg product}} \times \frac{\text{mg product}}{\text{L pool water}} = \frac{\text{mg constituent}}{\text{L pool water}}$$
$$[\% \text{ formulation}] \quad \left[ \begin{array}{c} \text{maximum} \\ \text{dose rate} \end{array} \right] \quad \left[ \begin{array}{c} \text{maximum pool} \\ \text{water concentration} \end{array} \right]$$

NOTE — Unit conversions may be required in order to convert the provided maximum dose rate into mg product/L pool water value.

The maximum pool water concentration of each chemical constituent in the product must be calculated and then initially compared to the criteria in Sections 27.5 and 27.7.

## 27.4 Contaminant testing

Swimming pool treatment chemicals shall be tested according to the test methodologies in NSF/ANSI/CAN 60 Annex N-1 and analyzed for contaminants per the requirements of NSF/ANSI/CAN 60, Sections 3, 4, 5, 6, and 7 regarding minimum test batteries and formulation dependent analytes. Any identified contaminants shall not exceed criteria in Sections 27.5 and 27.7.

### 27.4.1 Determination of swimming pool water contaminant concentrations

Utilizing the maximum dose rate, the concentration of each chemical contaminant in the product may be calculated as follows:

$$\frac{\text{mg product}}{\text{L pool water}} \times \frac{\text{L laboratory volume}}{\text{mg laboratory dose}} \times \mu\text{g/L contaminant} = \frac{\mu\text{g contaminant}}{\text{L pool water}}$$
$$\left[ \begin{array}{c} \text{maximum} \\ \text{dose rate} \end{array} \right] \quad \left[ \begin{array}{c} \text{laboratory} \\ \text{test conditions} \end{array} \right] \quad \left[ \begin{array}{c} \text{laboratory} \\ \text{contaminant} \\ \text{result} \end{array} \right] \quad \left[ \begin{array}{c} \text{pool water} \\ \text{concentration} \end{array} \right]$$

NOTE — Unit conversions may be required in order to convert the provided maximum dose rate into mg product/L pool water value.

The maximum pool water concentration of each chemical contaminant in the product must be calculated and then initially compared to the criteria in Sections 27.5 and 27.7.

## 27.5 Toxicology review and evaluation procedures for swimming pool treatment chemicals

### 27.5.1 General requirements

This section defines the toxicological review and evaluation procedures for the evaluation of the health effects of swimming pool treatment chemicals. It is intended to establish the human health risk, if any, of chemicals imparted to recreational water under the anticipated use conditions of the product. The toxicology review procedure may be utilized to evaluate the chemicals and contaminants contained in the finished product.

The following general procedure may be used to evaluate swimming pool treatment chemicals under this Standard.

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a) Based on the formulation information, the concentration of each swimming pool treatment chemical (and/or contaminants, if applicable) in the swimming pool water at the maximum recommended dose rate shall be determined. As an initial toxicity screening evaluation, any chemical constituent (or contaminant) in the product formulation that has a concentration in the swimming pool water less than or equal to the criteria listing in Section 27.5 at the maximum recommended dose does not require further toxicology evaluation. All chemical constituents (or contaminants) that exceed the criteria identified in this Section at or below the maximum recommended dose require toxicology evaluation as described hereafter.

b) For chemical constituents (or contaminants) with concentrations in the swimming pool water that exceed the criteria identified in this Section at or below the maximum recommended dose require, an exposure assessment shall be performed utilizing equations and assumptions described in Sections 27.6 and 27.7.

c) Following the determination of exposure levels (in mg/kg-d) for chemical constituents (or contaminants) with concentrations in the swimming pool water that exceed established criteria in Section 27.5 at or below the maximum recommended dose, the following approaches may be utilized to determine the acceptability of the calculated exposure:

—a determination shall be made as to whether a published (publicly available in printed or electronic format) and peer-reviewed quantitative risk assessment for the chronic exposure to the substance is available. When a quantitative risk assessment is available, the assessment and its corresponding reference dose shall be reviewed for their appropriateness in evaluating the human health risk of the swimming pool treatment chemical constituent (or contaminant).

—as an alternative approach, the total allowable concentration (TAC) values as reported in NSF/ANSI/CAN 600 may be utilized if available for the specific chemical constituent (or contaminant) by converting the TAC value into a mg/kg-d rate by utilizing default body weight and drinking water consumption assumptions (70 kg and 2 L), respectively. The resulting mg/kg-d rate may be compared with the estimated exposure at the maximum recommended dose to determine acceptability.

—if a TAC value or other published risk assessment value is unavailable, a risk assessment for the specific chemical constituent (or contaminant) may be conducted in accordance with the procedures outlined in Section 27.7; however, in lieu of determining a TAC value, the identified point of departure may be utilized to conduct a Margin of Exposure (MoE) analysis.

—if a TAC value or other published risk assessment value is unavailable and there are insufficient toxicity data from which to perform a risk assessment in accordance with Section 27.7, the chemical exposure cannot be assessed and presence of the chemical in the formulation is precluded at a concentration greater than 10 µg/L.

#### **27.5.2 Approved standard evaluation levels (STELs)**

The contents of Table 27.1 lists chemicals used in the treatment of recreational water. The standardized evaluation level has been previously approved under Section 27 for use in recreational water and listed chemicals may be used at the stated dose, or less, without further toxicological evaluation. However, this does not exempt the recreational water treatment products from contaminant testing or the evaluation of any measured contaminants to the requirements of Section 27.

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**Table 27.1**  
**Approved standardized evaluation levels**

Chemical	Synonyms	Strength	CAS #	Standardized evaluation level (mg/L)	Standardized evaluation level (lb/10,000 gal)
<b>Dechlorinator chemicals<sup>1</sup></b>					
calcium thiosulfate		100%	10124-41-1	90	7.5 lb
hydrogen peroxide		35%	772-84-1	60	1.5 gal of 35%
sodium thiosulfate		100%	7772-98-7	100	8.3 lb
sodium sulfite		100%	7757-83-7	70	5.8 lb
sodium bisulfite		100%	7631-90-5	60	5 lb
sodium metabisulfite		100%	7681-57-4	60	5 lb
<b>Alkalinity and pH adjustment chemicals</b>					
calcium carbonate		100%	471-34-1	400	33.4 lb
calcium hydroxide	slaked lime	100%	1305-62-0	650	54 lb
calcium oxide		100%	1305-78-8	500	42 lb
carbon dioxide		100%	124-38-9	600	50 lb
hydrochloric acid	muriatic acid	32%	7647-01-0	500	13.5 gal of 32%
magnesium hydroxide		100%	1309-42-8	150	12.5 lb
magnesium oxide		100%	1309-48-4	100	8.3 lb
potassium carbonate		100%	584-08-7	280	23.4 lb
potassium hydroxide	caustic soda	50%	1310-58-3	100	1.3 gal of 50%
sodium carbonate	soda ash	100%	497-19-8	212	17.7 lb
sodium bicarbonate	baking soda	100%	144-55-8	165	13.8 lb
sodium bisulfate		100%	7681-38-1	500	42 lb
sodium hydroxide		50%	1310-73-2	100	1.3 gal of 50%
sodium percarbonate		100%	15630-89-4	315	26 lb
sodium sesquicarbonate		100%	533-96-0	190	15.9 lb
sulfuric acid		38%	7664-93-9	550	7.9 gal of 38%
<b>Calcium hardness</b>					
calcium chloride		100%	10043-52-4	400	33 lb
<b>Stabilizer</b>					
cyanuric acid		100%	108-80-5	50	4.2 lb
sodium tetraborate pentahydrate		69%	12179-04-3	330	27.5 lb



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Other					
ascorbic acid		100%	50-81-7	12	1 lb
sodium ascorbate		100%	134-03-2	12	1 lb
citric acid		100%	77-92-9	20	1.7 lb
sodium citrate		100%	68-04-2	20	1.7 lb
<sup>1</sup> Standardized evaluation levels for dechlorinating compounds at minimum can neutralize 40 ppm of free available chlorine.					

### 27.5.3 Maximum pool water concentrations for metals

The following metal contaminants will be limited to the TAC criteria as set forth under NSF/ANSI/CAN 600. Any metals listed here will be evaluated per the procedures outline in the remainder of this section.

**Table 27.2**  
**Limitations on metal contaminants**

Metal	Criteria (mg/L)
antimony	0.006
arsenic	0.01
barium	2
beryllium	0.004
cadmium	0.005
chromium	0.1
lead	0.005
mercury	0.002
selenium	0.05
thallium	0.002

### 27.5.4 Threshold of Toxicology Concern

As an initial toxicity screen to determine the need for further toxicological assessment, chemical constituents (or contaminants) in the product formulation may be evaluated using the Threshold of Toxicology Concern (TTC) approach as described herein. The TTC approach has been developed to screen and prioritize the risk assessment of substances when the chemical structure of the substance is known and where human oral exposure can be estimated to be relatively low (Munro et al., 1996, 2008; Kroes et al., 2004, 2007; Boobis et al., 2017).

#### 27.5.4.1 Determination of TTC Screening Criteria

The original TTC approach utilized the classification method from Cramer et al. (1978) to examine the distribution of NOAEL for each of the three Cramer structural classes using a database of 613 chemicals with 2,941 NOAEL values (Munro et al., 1996). The 613 chemicals consisted of a broad range of chemicals (industrial, food, environmental, agricultural, pharmaceuticals and consumer product chemicals) and resulted in 137, 28 and 448 chemicals in Cramer Classes I, II and III, respectively. From the available toxicity data for each of the 613 chemicals, the most conservative NOAEL was selected, based on the most sensitive species, sex and endpoint. If a subchronic NOAEL was identified, it was divided by a factor of

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three to extrapolate to a chronic NOAEL. From the identified NOAEL values, the 5th percentile NOAEL (in mg/kg-day) was calculated for each structural class and an uncertainty factor of 100x was applied resulting in TTC values of 1.5, 9 and 30 µg/kg-day for Cramer I, II and III, respectively. For potentially genotoxic substances (DNA-reactive mutagens), Kroes et al. (2004) derived a TTC value of 0.00025 µg/kg-day based on a 10<sup>-6</sup> cancer risk level. To extrapolate the TTC values for use in swimming pool applications, the highest swimmer intake rate (children ages 6-11) of 0.0024 L/kg-day obtained from U.S. EPA Exposure Factor Handbook (U.S. EPA, 2019) may be utilized resulting in screening criteria provided in Table 27.3 below:

**Table 27.3**  
**Threshold of Toxicology Concern Screening Criteria**

<b>Classification</b>	<b>TTC value (µg/kg-day)</b>	<b>Screening Criteria (µg/L)<sup>1</sup></b>
Genotoxicity Structural Alert (highest concern)	0.0025 <sup>2</sup>	6 <sup>3</sup>
Cramer Class III (high concern)	1.5	200
Cramer Class II (intermediate concern)	9	1000
Cramer Class I (low concern)	30	4000

<sup>1</sup> Calculated using intake rate for children 6-11 of 0.0024 L/kg-day based on 0.077 L/day with body weight of 32 kg (U.S. EPA, 2019) where Threshold Limit = TTC value / intake rate / 3x adjustment factor (rounded to 1 sig. figure)  
<sup>2</sup> Based on 10<sup>-6</sup> cancer risk level  
<sup>3</sup> Threshold limit is based on 10<sup>-5</sup> risk level (equivalent to NSF 600 TAC approach for linear carcinogens) using a default age-dependent adjustment factor of 1.7 (from U.S. EPA, 2005a)

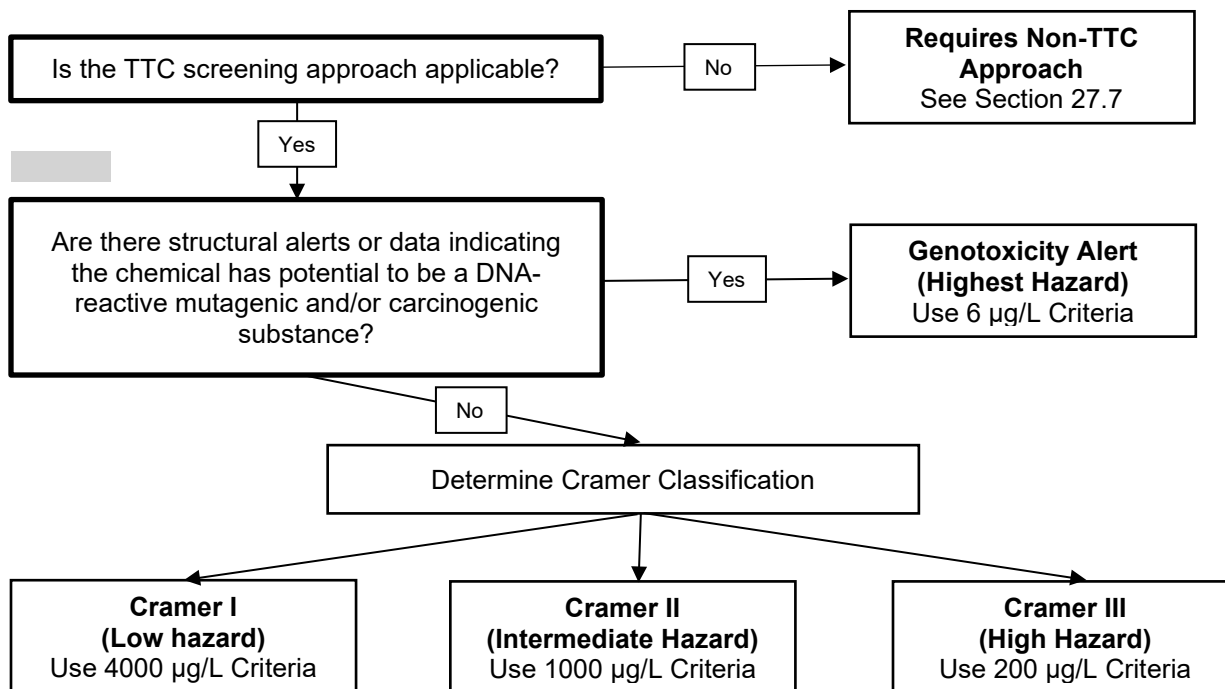
From Table 27.3, the calculation of the TTC Screening Criteria for swimming pool chemicals includes an additional adjustment factor of 3x. This adjustment factor is to account for possible inhalation or dermal exposures to the constituent (or contaminant) as the TTC values are based on oral exposure.

#### 27.5.4.2 Application of TTC Screening Criteria

To apply the TTC Screening Criteria from Table 27.3, the applicable TTC Screening Criteria must be compared to the maximum concentration of the constituent (or contaminant) in the swimming pool water. If the maximum concentration is less than the applicable Screening Criteria, no further toxicology evaluation is required. However, there are several categories of chemicals that are excluded from using the TTC screening approach and must be evaluated per Section 27.7 if present: inorganic substances, proteins, steroids, nanomaterials, radioactive substances, organosilicon substances, metals, high-potency carcinogens (e.g. aflatoxin-like, azoxy- or N-nitroso substances and benzidines) and bioaccumulative compounds (e.g. polyhalogenated-dibenzodioxins, -dibenzofurans and -biphenyls). Additionally, the TTC screening process shall not apply to any substance for which available toxicity data and sound scientific judgment indicate that the potential for any adverse health effects is significant at a swimming pool water concentration below the applicable TTC Screening Criteria.

The applicable TTC Threshold Limit is determined by the following steps:

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For any chemical constituent (or contaminant) in a product formulation where use of the TTC screening approach is appropriate and the maximum concentration in the swimming pool water is below the applicable TTC Screening Criteria, no additional toxicology evaluation is required.

#### 27.5.4 Threshold of evaluation

~~As an initial toxicity screen to determine the need for further toxicological assessment, any chemical constituent (or contaminant) in the product formulation that has a maximum concentration in the swimming pool water of  $\leq 10$  µg/L at the maximum recommended dose does not require further toxicology evaluation. However, this threshold of evaluation concentration of 10 µg/L shall not apply to any substance for which available toxicity data and sound scientific judgment indicate that the potential for any adverse health effect is significant at a swimming pool water concentration of  $\leq 10$  µg/L.~~

~~NOTE — When assessing whether the threshold of evaluation concentration of 10 µg/L may be utilized, emphasis should be placed on whether the chemical is a strong sensitizing agent, a genotoxic agent or, a potential human carcinogen. Structure activity relationships may also be considered.~~

~~Therefore, for any chemical constituent (and/or contaminant) in a product formulation where use of the threshold of evaluation limit is appropriate and the maximum concentration in the swimming pool water is below 10 µg/L, no additional toxicology evaluation is required.~~

##### 27.5.4.1 Determination of the threshold of evaluation

~~Under Section 3.6.1 of NSF/ANSI/CAN 600, a threshold of evaluation for chronic exposure to a chemical in drinking water was determined to be 3 µg/L (static conditions). The use of the threshold of evaluation criteria under NSF/ANSI/CAN 600 is based on an assumed drinking water intake of 2 L/d (US EPA, 2012). For pool water, a study by Dufour et al. (2006), an oral exposure to pool water of 0.05 L/h or swimming event was estimated for children of ages 6 to 11 yr. Based on this intake, a threshold of evaluation for chemicals found in pool water may be determined as follows:~~

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FDA threshold of regulation — 0.5 µg/kg food (from 21 CFR 170.39)

Average food intake in children (6 to 11 yr) — 1.118 kg/d (from EFH, US EPA, 1997)

Pool water ingested per swimming event — 0.05 L (from Dufuor et al., 2006)

$$\text{threshold of evaluation} = \frac{(0.5 \mu\text{g/kg food}) \times (1.118 \text{ kg food/d})}{(0.05 \text{ L pool water ingested})} = 11.18 \mu\text{g/L} \approx 10 \mu\text{g/L}$$

**NOTE** — While derived from an oral route of exposure only, the resulting 10 µg/L threshold of evaluation level for pool chemicals is only approximately three-fold higher than the drinking water threshold of evaluation of 3 µg/L from NSF/ANSI/CAN 600 despite the estimated oral intake of pool water being twenty-fold less. While exposure to pool treatment chemicals by skin contact and inhalation is potentially greater than from ingestion, the 10 µg/L threshold of evaluation level for pool chemicals allows for a margin that may account for this.

## 27.6 Swimming pool exposure assessment methodology

### 27.6.1 General requirements

For chemical concentrations in the pool water at the maximum recommended dose that are above applicable TTC screening criteria (or where TTC criteria cannot be applied) ~~exceed 10 µg/L at or below the maximum recommended dose~~, an exposure assessment shall be performed as detailed in Section 27.6. For chemicals present in swimming pools, there is the potential for post-application dermal, oral, and inhalation exposures. To address potential systemic effects associated with dermal, inhalation, and incidental oral exposures, exposures are estimated using equations from US EPA SWIMMODEL software (2003a). US EPA SWIMMODEL software was developed as a screening tool to conduct exposure assessments of pesticides found in swimming pools and spas. It utilizes screening exposure assessment equations to calculate the high-end exposure for swimmers expressed as a mass-based intake value (mg/event).

**NOTE** — Depending on the properties of the specific chemical being assessed, available toxicity data and sound scientific judgment, determination of the contribution of inhalation or dermal exposures to the total exposure dose may not be required:

— **inhalation:** Chemical properties to consider when assessing the contribution of inhalation exposure include, but are not limited to, volatility, water solubility, and/or direct reactivity with tissues; and

— **dermal:** Chemical properties to consider when assessing the contribution of dermal exposure include, but are not limited to, molecular weight and/or  $K_{ow}$ .

Using US EPA SWIMMODEL (2003a) equations and the assumptions provided in the, exposure estimates may be calculated for adults (men and women), children (ages 11 to < 16 yr) and children (ages 6 to < 11 yr). Additionally, the available assumptions allow for exposure estimates for each age group based on whether the individual is a competitive or non-competitive swimmer. For noncompetitive swimmers, the equations and assumptions provided in this herein allow for differing exposure concentrations depending on acute or chronic endpoints.

Limitations and caveats in the equations from US EPA SWIMMODEL (2003a) include the following:

—the model focuses on potential chemical intakes only and does not take into account metabolism or excretion of the chemical being assessed;

—the model uses the following absorption facts for each route of exposure:

—**ingestion:** 100% absorption of ingested chemicals is assumed;

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- dermal**: Chemical-specific decimal Kp is used; and
- inhalation**: 100% absorption of inhaled chemical is assumed;
- the model does not account for the effect of ambient temperature on intake; and
- the exposure estimates are derived based on use of the chemical in swimming pools only.

When estimating swimming exposure, the US EPA Office of Pesticides uses a procedure (US EPA, 2015) in which some of the inputs and parameters utilized by US EPA SWIMODEL (2003a) have been modified. Among the updates were modifications of the exposure times which allow for assessment of short-term and long-term exposure. When deriving exposure estimates, the short-term exposure concentrations shall first be determined by the calculation of the potential daily dose (PDD) and then assessed according to the toxicology evaluation process described in Section 27.7. If the short-term exposure concentration (the calculated PDD) exceeds the acceptance criteria based on lifetime exposure effects identified by the toxicology review requirements described herein, then the average daily dose (ADD) may then be calculated and compared against the lifetime exposure acceptance criteria; however, the short-term exposure concentration shall be addressed by comparing against a short-term acceptance criteria identified according to the toxicology evaluation process described in Section 27.7.

## 27.6.2 Swimming pool dermal exposures (systemic)

Dermal exposure estimates are predicated on a single compartment model of the skin with the rate-limiting step being the penetration of the stratum corneum. The model utilizes Fick's Law of Diffusion to calculate a general exposure value without regard for differences in the skin permeability of specific body parts. As the permeability constant provides estimates of an internal dose following dermal exposure, the oral toxicity acceptance criteria identified under Section 27.7 rather than dermal specific acceptance criteria may be used to assess the risks of adverse systemic effects from the dermal exposure route.

### 27.6.2.1 Short-term swimming pool dermal exposures

The following equation is taken from US EPA SWIMODEL (2003a) and shall be used to estimate short-term dermal doses when the critical adverse effect for the chemical being assessed is a systemic effect.

$$PDD = \frac{C_w \times K_p \times SA \times ET \times CF}{BW}$$

where:

*PDD* = potential daily dose (mg/kg-d)  
*C<sub>w</sub>* = chemical concentration in pool water (mg/L)  
*K<sub>p</sub>* = permeability constant (see equation below)  
*SA* = surface area (cm<sup>2</sup>)  
*ET* = exposure time (h/d)  
*CF* = conversion factor (0.001 L/cm<sup>3</sup>)  
*BW* = body weight (kg)

$$K_p = 10^{[-2.72 + (0.71 \times \log K_{OW}) - (0.0061 \times MW)]}$$

where:

*K<sub>p</sub>* = permeability constant (cm/h)  
*K<sub>OW</sub>* = octanol water coefficient

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*MW* = molecular weight

*C<sub>w</sub>*: Chemical concentration in pool water (mg/L) is chemical specific and based on label rates.

*K<sub>p</sub>*: Permeability constant (cm/h) is chemical specific and can be estimated based on a above equation for organic chemicals provided by US EPA's *Dermal Exposure Assessment: Principles and Applications* (US EPA, 1992). The default *K<sub>p</sub>* value for inorganic chemicals is 1E-3 cm/h (US EPA, 1992).

**Table 27.34**  
**Assumptions for short-term swimming pool dermal exposure and dose estimate**

Age	Adult		11 to < 16 years		6 to < 11 years	
Type of swimmer	Comp	Non-comp	Comp	Non-comp	Comp	Non-comp
ET (h/d)	3 <sup>1</sup>	1 <sup>2</sup>	2 <sup>1</sup>	1 <sup>2</sup>	1 <sup>1</sup>	1 <sup>2</sup>
SA (cm <sup>2</sup> )	19,500 <sup>3</sup>		15,900 <sup>4</sup>		10,800 <sup>4</sup>	
BW (kg)	80 <sup>5</sup>		57 <sup>6</sup>		32 <sup>6</sup>	

<sup>1</sup> ET (competitive swimmers): The exposure times for competitive swimmers are based on the ACC's swimmer survey (ACC, 2002).

<sup>2</sup> ET (noncompetitive swimmers): The exposure times for non-competitive and/or recreational swimmers are based on NHAPs 90<sup>th</sup> percentile exposure durations (US EPA, 1996a).

<sup>3</sup> SA (adult): The body surface area exposed to pool water is 19,500 cm<sup>2</sup> which represents the entire body including the head. This value is the recommended average provided by the EPA Exposure Factors Handbook (US EPA, 2011d).

<sup>4</sup> SA (child): The body surface areas exposed to pool water are 10,800 cm<sup>2</sup> for children age 6 to < 11 yr and 15,900 cm<sup>2</sup> for children age 11 to < 16 yr, based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

<sup>5</sup> BW (adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights (US EPA, 2011d).

<sup>6</sup> BW (child): The body weight is 57 kg for children age 11 to < 16 yr, and 32 kg for children age 6 to < 11 yr based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

### 27.6.2.2 Long-term swimming pool dermal exposure

The following equation is taken from US EPA SWIMODEL (2003a) and shall be used to estimate long-term dermal doses when the critical effect endpoint for the chemical being assessed is based on systemic effects:

$$ADD = \frac{C_w \times K_p \times SA \times ET \times EF \times CF}{BW \times 365 \frac{\text{day}}{\text{year}}}$$

where:

*ADD* = average daily dose (mg/kg-d)  
*C<sub>w</sub>* = chemical concentration in pool water (mg/L)  
*K<sub>p</sub>* = permeability constant (see equation below)  
*SA* = surface area (cm<sup>2</sup>)  
*ET* = exposure time (hours/day)  
*EF* = exposure frequency (events/year)

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$CF$  = conversion factor (0.001 L/cm<sup>3</sup>)  
 $BW$  = body weight (kg)

$$Kp = 10^{[-2.72 + (0.71 \times \log K_{OW}) - (0.0061 \times MW)]}$$

where:

$Kp$  = permeability constant (cm/h)  
 $K_{OW}$  = octanol water coefficient  
 $MW$  = molecular weight

**Table 27.45**  
**Assumptions for long-term swimming pool dermal exposure and dose estimate**

Age	Adult		11 to <16 years		6 to <11 years	
Type of swimmer	Comp	Non-comp	Comp	Non-comp	Comp	Non-comp
ET (h/d)	3 <sup>1</sup>	0.3 <sup>2</sup>	2 <sup>1</sup>	0.5 <sup>2</sup>	1 <sup>1</sup>	0.5 <sup>2</sup>
EF (events/year)	238 <sup>3</sup>	88 <sup>4</sup>	189 <sup>5</sup>	72 <sup>4</sup>	65 <sup>6</sup>	102 <sup>4</sup>
SA (cm <sup>2</sup> )	19,500 <sup>7</sup>		15,900 <sup>8</sup>		10,800 <sup>8</sup>	
BW (kg)	80 <sup>9</sup>		57 <sup>10</sup>		32 <sup>10</sup>	

<sup>1</sup> ET (competitive swimmers): The exposure times for competitive swimmers are based on the ACC's swimmer survey (ACC, 2002).

<sup>2</sup> ET (noncompetitive swimmers): The exposure times for non-competitive and/or recreational swimmers are based on NHAPs mean values (US EPA, 1996a).

<sup>3</sup> EF (adult competitive): Mean values for master's and collegiate swimmers ranged from 187 to 238 d/yr. For collegiate swimmer, ACC (2002) assumed (5 events/wk) × (52 wk/yr) × (11 mo/yr) / (12 mo/yr).

<sup>4</sup> EF (noncompetitive): Mean yearly frequency values obtained from NHAPS (US EPA, 1996a).

<sup>5</sup> EF (11 to < 16 yr competitive): Mean value from ACC (2002) which assumed (4 events/wk) × (52 wk/yr) × (11 mo/yr) / (12 mo/yr).

<sup>6</sup> EF (6 to < 11 yr competitive): Mean value from ACC (2002) assumed (2.5 events/wk) × (52 wk/yr) × (6 mo/yr) / (12 mo/yr).

<sup>7</sup> SA (adult): The body surface area exposed to pool water is 19,500 cm<sup>2</sup> which represents the entire body including the head. This value is the recommended average provided by the EPA Exposure Factors Handbook (US EPA, 2011d).

<sup>8</sup> SA (child): The body surface areas exposed to pool water are 10,800 cm<sup>2</sup> for children age 6 to < 11 yr and 15,900 cm<sup>2</sup> for children age 11 to < 16 yr, based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

<sup>9</sup> BW (adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights (US EPA, 2011d).

<sup>10</sup> BW (child): The body weight is 57 kg for children age 11 to < 16 yr and 32 kg for children age 6 to < 11 yr based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

### 27.6.3 Swimming pool dermal exposures (localized)

For certain chemicals, the observed treatment-related adverse effect is the result of local skin irritation or sensitization rather than a systemic effect that occurs after the chemical is absorbed through the skin. As

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US EPA SWIMODEL (2003a) is based on the assumption that dermal absorption has taken place, it is not appropriate to use the model to estimate dermal exposure for skin irritants or sensitizing agents. In this case it is recommended that the concentration of the chemical used in the dermal toxicity study be compared directly with the concentration of the chemical in the pool water. Based on the available dermal toxicity studies, a weight of evidence approach should be used to identify an appropriate NOAEL (for irritation effects) or a NESIL (No Expected Sensitization Induction Level) that may then be compared to the concentration of the chemical in the pool water using a Margin of Exposure assessment. The acceptability of the calculated Margin of Exposure shall be determined by the uncertainty assigned to the identified NOAEL or NESIL using current methodology described by WHO (2008) or other authoritative body. If this is not possible because the applied dose was reported in terms of mass per unit area (i.e.,  $\mu\text{g}/\text{cm}^2$ ), a film thickness approach shall be used to calculate the exposure in terms of  $\mu\text{g}/\text{cm}^2$  as shown in the following equation:

$$\text{Exposure} = C_w \times FT$$

where:

*Exposure* = chemical concentration on skin exposed to treated pool water ( $\mu\text{g}/\text{cm}^2$ )  
*C<sub>w</sub>* = chemical concentration in pool water ( $\text{mg}/\text{L} = \mu\text{g}/\text{cm}^3$ )  
*FT* = film thickness of water on the skin (cm)

assumptions:

*C<sub>w</sub>*: Chemical concentration in pool water ( $\text{mg}/\text{L} = \mu\text{g}/\text{cm}^3$ ) is chemical specific and based on label rates

*FT*: The film thickness of water on the skin of 0.0049 cm is based on the value EFAST users' manual (US EPA, 2007)

NOTE — Identical exposures for adults and children and competitive and noncompetitive swimmers are assumed because the exposure duration is not a factor considered when using the film thickness approach.

#### 27.6.4 Swimming pool oral exposures

##### 27.6.4.1 Short-term swimming pool oral exposures

The following equation is taken from US EPA SWIMODEL software (2003a) and shall be used to calculate post-application short-term oral exposures:

$$PDD = \frac{C_w \times IgR \times ET}{BW}$$

where:

*PDD* = potential daily dose ( $\text{mg}/\text{kg}\cdot\text{d}$ )  
*C<sub>w</sub>* = chemical concentration in pool water ( $\text{mg}/\text{L}$ )  
*IgR* = ingestion rate of pool water ( $\text{L}/\text{h}$ )  
*ET* = exposure time ( $\text{h}/\text{d}$ )  
*BW* = body weight (kg)

*C<sub>w</sub>*: Chemical concentration in pool water ( $\text{mg}/\text{L}$ ) is chemical specific and based on label rates



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**Table 27.56**  
**Assumptions for short-term swimming pool oral exposure and dose estimate**

Age	Adult		11 to <16 years		6 to <11 years	
Type of swimmer	Comp	Non-comp	Comp	Non-comp	Comp	Non-comp
IgR (L/h)	0.025 <sup>1</sup>	0.05 <sup>1</sup>	0.025 <sup>1</sup>	0.05 <sup>1</sup>	0.05 <sup>1</sup>	0.05 <sup>1</sup>
ET (h/d)	3 <sup>2</sup>	1 <sup>3</sup>	2 <sup>2</sup>	1 <sup>3</sup>	1 <sup>2</sup>	1 <sup>3</sup>
BW (kg)	80 <sup>4</sup>		57 <sup>5</sup>		32 <sup>5</sup>	

<sup>1</sup> IgR: The ingestion rate for noncompetitive swimmer is 0.05 L/h (US EPA, 2015). The ingestion rate for competitive swimmers age 11 or above is assumed to be 0.025 L/h based on based on the opinion of swim coaches interviewed during the ACC swimmer survey that competitive swimmers ingest less water than noncompetitive swimmers because they have learned how to control their breathing (ACC, 2002).

<sup>2</sup> ET (competitive swimmers): The exposure times for competitive swimmers are based on the ACC’s swimmer survey (ACC, 2002).

<sup>3</sup> ET (noncompetitive swimmers): The exposure times for non-competitive and/or recreational swimmers are based on NHAPs 90<sup>th</sup> percentile exposure durations (US EPA, 1996a).

<sup>4</sup> BW (adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights (US EPA, 2011d).

<sup>5</sup> BW (child): The body weight is 57 kg for children age 11 to < 16 yr and 32 kg for children age 6 to < 11 yr based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

#### 27.6.4.2 Long-term swimming pool oral exposures

The following equation is taken from US EPA SWIMODEL software (2003a) and shall be used to calculate post-application long-term oral exposures:

$$ADD = \frac{C_w \times IgR \times ET \times EF}{BW \times 365 \frac{\text{day}}{\text{year}}}$$

where:

**ADD** = average daily dose (mg/kg-d)  
**C<sub>w</sub>** = chemical concentration in pool water (mg/L)  
**IgR** = ingestion rate of pool water (L/h)  
**ET** = exposure time (h/d)  
**EF** = exposure frequency (events/yr)  
**BW** = body weight (kg)

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**Table 27.67**  
**Assumptions for long-term swimming pool oral exposure and dose estimate**

Age	Adult		11 to <16 years		6 to <11 years	
Type of Swimmer	Comp	Non-Comp	Comp	Non-Comp	Comp	Non-Comp
IgR (L/h)	0.025 <sup>1</sup>	0.05 <sup>1</sup>	0.025 <sup>1</sup>	0.05 <sup>1</sup>	0.05 <sup>1</sup>	0.05 <sup>1</sup>
ET (h/d)	3 <sup>2</sup>	0.3 <sup>3</sup>	2 <sup>2</sup>	0.5 <sup>3</sup>	1 <sup>2</sup>	0.5 <sup>3</sup>
EF (events/yr)	238 <sup>4</sup>	88 <sup>5</sup>	189 <sup>6</sup>	72 <sup>5</sup>	65 <sup>7</sup>	102 <sup>5</sup>
BW (kg)	80 <sup>8</sup>		57 <sup>9</sup>		32 <sup>9</sup>	

<sup>1</sup> IgR: The ingestion rate for noncompetitive swimmer is 0.05 L/h (US EPA, 2015). The ingestion rate for competitive swimmers age 11 or above is assumed to be 0.025 L/h based on based on the opinion of swim coaches interviewed during the ACC swimmer survey that competitive swimmers ingest less water than noncompetitive swimmers because they have learned how to control their breathing (ACC, 2002).

<sup>2</sup> ET (competitive swimmers): The exposure times for competitive swimmers are based on the ACC's swimmer survey (ACC, 2002).

<sup>3</sup> ET (noncompetitive swimmers): The exposure times for non-competitive and/or recreational swimmers are based on NHAPs mean values (US EPA, 1996a).

<sup>4</sup> EF (adult competitive): Mean values for master's and collegiate swimmers ranged from 187 to 238 d/yr. For collegiate swimmer, ACC (2002) assumed (5 events/wk) × (52 wk/yr) × (11 mo/yr) / (12 mo/yr).

<sup>5</sup> EF (noncompetitive): Mean yearly frequency values obtained from NHAPS (US EPA, 1996a).

<sup>6</sup> EF (11 to < 16 yr competitive): Mean value from ACC (2002) which assumed (4 events/wk) × (52 wk/yr) × (11 mo/yr) / (12 mo/yr).

<sup>7</sup> EF (6 to <11 yr competitive): Mean value from ACC (2002) assumed (2.5 events/wk) × (52 wk/yr) × (6 mo/yr) / (12 mo/yr).

<sup>8</sup> BW (adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights (US EPA, 2011d).

<sup>9</sup> BW (child): The body weight is 57 kg for children age 11 to < 16 yr and 32 kg for children age 6 to < 11 yr based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

## 27.6.5 Swimming pool inhalation exposures

### 27.6.5.1 Short-term swimming pool inhalation exposures

The following equation is taken from US EPA SWIMODEL (2003a) and shall be used to calculate post-application short-term inhalation exposures:

$$PDD = \frac{V_p \times IR \times ET}{BW}$$

where:

**PDD** = potential daily dose (mg/kg-d)  
**V<sub>p</sub>** = chemical vapor concentration (see equation below)  
**IR** = inhalation rate (m<sup>3</sup>/h)  
**ET** = exposure time (h/d)  
**BW** = body weight (kg)

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$$Vp = Cw \times H' \times 1,000 \text{ L/m}^3$$

where:

$Vp$  = Chemical vapor concentration (mg/m<sup>3</sup>)  
 $Cw$  = Chemical concentration in pool water (mg/L)  
 $H'$  = Henry's Law constant (unitless)

$Cw$ : Chemical concentration in pool water (mg/L) is chemical specific and based on label rates  
 $H'$ : The unitless Henry's Law constant is chemical specific and calculated using

$$H' = \frac{HLC}{(R \times T)}$$

where:

$HLC$  = Henry's law constant  
 $R$  (gas constant) =  $8.19 \times 10^{-5} \text{ atm} \cdot \text{m}^3/\text{mole} \cdot \text{K}$   
 $T$  (ambient temperature in terms of Kelvin units) =  $25^\circ \text{C} + 273^\circ \text{K}$

NOTE — The exposures estimated using this equation are considered by the US EPA to be conservative because the effects of dilution by outdoor air at outdoor pools or mechanical ventilation at indoor pools are not included in the equation used to calculate the air concentration for the chemical being assessed.

**Table 27.78**  
**Assumptions for short-term swimming pool inhalation exposure and dose estimate**

Age	Adult		11 to < 16 years		6 to < 11 years	
Type of swimmer	Comp	Non-comp	Comp	Non-comp	Comp	Non-comp
IR (m³/h)	3.2 <sup>1</sup>	1.0 <sup>1</sup>	2.9 <sup>2</sup>	1.5 <sup>2</sup>	2.5 <sup>2</sup>	1.3 <sup>2</sup>
ET (h/d)	3 <sup>3</sup>	1 <sup>4</sup>	2 <sup>3</sup>	1 <sup>4</sup>	1 <sup>3</sup>	1 <sup>4</sup>
BW (kg)	80 <sup>5</sup>		57 <sup>6</sup>		32 <sup>6</sup>	

<sup>1</sup> IR (adult): The inhalation rates for adults are based on the values presented in EPA's Exposure Factors Handbook (US EPA, 2011d).

<sup>2</sup> IR (child): The inhalation rates for adults are based on the values presented in EPA's Exposure Factors Handbook (US EPA, 2011d).

<sup>3</sup> ET (competitive swimmers): The exposure times for competitive swimmers are based on the ACC's swimmer survey (ACC, 2002).

<sup>4</sup> ET (noncompetitive swimmers): The exposure times for non-competitive and/or recreational swimmers are based on NHAPs 90<sup>th</sup> percentile exposure durations (US EPA, 1996a).

<sup>5</sup> BW (adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights (US EPA, 2011d).

<sup>6</sup> BW (child): The body weight is 57 kg for children age 11 to < 16 yr and 32 kg for children age 6 to < 11 yr based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

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### 27.6.5.2 Long-term swimming pool inhalation exposures

The following equation is taken from US EPA SWIMODEL (2003a) and shall be used to calculate post-application short-term inhalation exposures:

$$ADD = \frac{V_p \times IR \times ET \times EF}{BW \times 365 \frac{\text{day}}{\text{year}}}$$

where:

ADD = average daily dose (mg/kg-d)  
 $V_p$  = chemical vapor concentration (see equation below)  
 $IR$  = inhalation rate (m<sup>3</sup>/h)  
 $ET$  = exposure time (h/d)  
 $EF$  = exposure frequency (events/yr)  
 $BW$  = body weight (kg)

$$V_p = C_w \times H' \times 1,000 \text{ L/m}^3$$

where:

$V_p$  = chemical vapor concentration (mg/m<sup>3</sup>)  
 $C_w$  = chemical concentration in pool water (mg/L)  
 $H'$  = Henry's Law constant (unitless)

$C_w$ : Chemical concentration in pool water (mg/L) is chemical specific and based on label rates  
 $H'$ : The unitless Henry's Law constant is chemical specific and calculated using:

$$H' = \frac{HLC}{(R \times T)}$$

where:

$HLC$  = Henry's law constant  
 $R$  (gas constant) = 8.19E-5 atm-m<sup>3</sup>/mole-K  
 $T$  (ambient temperature in terms of Kelvin units) = 25 °C + 273 °K

**Table 27.89**  
**Assumptions for long-term swimming pool inhalation exposure and dose estimate**

Age	Adult		11 to < 16 years		6 to < 11 years	
Type of swimmer	Comp	Non-comp	Comp	Non-comp	Comp	Non-comp
IR (m³/h)	3.2 <sup>1</sup>	1.0 <sup>1</sup>	2.9 <sup>2</sup>	1.5 <sup>2</sup>	2.5 <sup>2</sup>	1.3 <sup>2</sup>
ET (h/d)	3 <sup>3</sup>	0.3 <sup>4</sup>	2 <sup>3</sup>	0.5 <sup>4</sup>	1 <sup>3</sup>	0.5 <sup>4</sup>
EF (events/yr)	238 <sup>5</sup>	88 <sup>6</sup>	189 <sup>7</sup>	72 <sup>6</sup>	65 <sup>8</sup>	102 <sup>6</sup>
BW (kg)	80 <sup>9</sup>		57 <sup>10</sup>		32 <sup>10</sup>	
<sup>1</sup> IR (adult): The inhalation rates for adults are based on the values presented in EPA's Exposure Factors Handbook (US EPA, 2011d).						

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<sup>2</sup> IR (child): The inhalation rates for adults are based on the values presented in EPA's Exposure Factors Handbook (US EPA, 2011d).

<sup>3</sup> ET (competitive swimmers): The exposure times for competitive swimmers are based on the ACC's swimmer survey (ACC, 2002).

<sup>4</sup> ET (noncompetitive swimmers): The exposure times for non-competitive and/or recreational swimmers are based on NHAPs mean values (US EPA, 1996a).

<sup>5</sup> EF (adult competitive): Mean values for master's and collegiate swimmers ranged from 187 to 238 d/yr. For collegiate swimmer, ACC (2002) assumed  $(5 \text{ events/wk}) \times (52 \text{ wk/yr}) \times (11 \text{ mo/yr}) / (12 \text{ mo/yr})$ .

<sup>6</sup> EF (noncompetitive): Mean yearly frequency values obtained from NHAPS (US EPA, 1996a).

<sup>7</sup> EF (11 to < 16 yr competitive): Mean value from ACC (2002) which assumed  $(4 \text{ events/wk}) \times (52 \text{ wk/yr}) \times (11 \text{ mo/yr}) / (12 \text{ mo/yr})$ .

<sup>8</sup> EF (6 to < 11 yr competitive): Mean value from ACC (2002) assumed  $(2.5 \text{ events/wk}) \times (52 \text{ wk/yr}) \times (6 \text{ mo/yr}) / (12 \text{ mo/yr})$ .

<sup>9</sup> BW (adult): The average body weight of adult males and females is 80 kg which is the average of the median male and female body weights (US EPA, 2011d).

<sup>10</sup> BW (child): The body weight is 57 kg for children age 11 to < 16 yr and 32 kg for children age 6 to < 11 yr based on the recommended values from the EPA Exposure Factors Handbook (US EPA, 2011d).

## 27.7 Swimming pool chemical toxicology evaluation procedure

### 27.7.1 General requirements

Following the determination of exposure levels (in mg/kg-d) for chemical constituents (or contaminants) with concentrations in the swimming pool water that exceed 10 µg/L at or below the maximum recommended dose, the following approaches may be utilized to determine the acceptability of the calculated exposure levels.

—a determination shall be made as to whether a published (publicly available in printed or electronic format) and peer-reviewed quantitative risk assessment for the chronic exposure to the substance is available to be utilized in assessing the acceptability of the estimated swimming pool chemical exposure.

—if a published and peer-reviewed risk assessment is not currently available for the chemical being assessed, the Total Allowable Concentration (TAC) values as contained in NSF/ANSI/CAN 600 may be utilized (if available) by converting the TAC value into a mg/kg-d rate by incorporating default body weight and drinking water consumption assumptions (70 kg and 2 L), respectively (US EPA, 2012). The resulting mg/kg-d rate may be compared with the estimated total systemic exposure (all exposure routes) to determine acceptance (unless the endpoint of concern identified is a local effect).

—if an NSF/ANSI/CAN 600 TAC value or other published risk assessment value is unavailable, a risk assessment for the specific chemical constituent (or contaminant) may be conducted in accordance with the procedures outlined in Section 27.7.4.

—if an NSF/ANSI/CAN 600 TAC value or other published risk assessment value is unavailable and there is insufficient toxicity data from which a risk assessment may be performed in accordance with Section 27.7.4, the chemical exposure cannot be assessed and presence of the chemical in the formulation is precluded at a concentration greater than 10 µg/L at or below the maximum recommended dose.

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### **27.7.2 Utilization of published risk assessment**

Evaluation of all published risk assessments shall include review of the written risk assessment document and a determination of whether additional toxicity data exists that was not considered in the assessment. If additional toxicity data are identified that were not considered in the risk assessment, the risk assessment shall be updated in accordance with Section 27.7.4.

The following shall be documented when utilizing an existing risk assessment:

- the source of the risk assessment;
- identification and discussion of any data not addressed by the assessment; and
- comparison and contrast of the existing risk assessment to the requirements of Section 27.7.4, with respect to selection of uncertainty factors or other assumptions.

#### **27.7.2.1 Evaluation of multiple published risk assessments**

When multiple published assessments are available for a chemical being assessed, the available assessments shall be reviewed, and a rationale shall be provided for the selection of the assessment considered to be the most appropriate for the evaluation of human exposure to recreational water treatment chemicals. Factors used to determine the appropriate assessment shall include, but not be limited to, the following:

- completeness and currency of the data review of each assessment;
- technical competence of the organization(s) that sponsored the assessment; and
- species and route(s) of exposure for which the assessment was performed.

When multiple published risk assessments are reviewed and are determined to be of equivalent quality, the following hierarchy shall be used to select the appropriate assessment, based on sponsoring organization:

1. US EPA;
2. Health Canada;
3. International bodies such as the World Health Organization (WHO) or the International Programme on Chemical Safety (IPCS);
4. European bodies such as the Drinking Water Inspectorate (DWI) and KIWA; or
5. Entities such as other federal or state regulatory agencies, private corporations, industry associations, or individuals.

#### **27.7.2.2 Risk assessment for published assessments – Noncarcinogenic endpoints**

As described in Section 27.6, the equations utilized to estimate exposures attributable to dermal, oral and inhalation routes (excluding local effects) facilitate the determination of a total systemic exposure in mg/kg-d. If route-specific sensitization and irritation effects are not anticipated based on the available data, an oral reference dose (RfD) obtained from a published peer-reviewed risk assessment may be used to evaluate the estimated systemic exposure to the chemical being assessed.

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The RfD is an estimate of a daily exposure to the human population that is likely to be without an appreciable risk of deleterious effects during a lifetime. Before comparing the RfD with the estimated systemic exposure for the chemical being assessed, a Relative Source Contribution (RSC) must be applied to account for exposure to the chemical from other sources outside of swimming pool water. Default RSCs are used in the absence of quantitative data to determine the swimming pool water contribution of a substance. Thus, a default RSC of 80% shall be applied to the RfD if no other uses for the chemical outside of pool water uses can be identified. If other uses can be identified, a default RSC of 20% shall be used.

Therefore, the acceptability of exposure may be determined based on the following:

- If  $RfD \text{ (mg/kg-d)} \times RSC \geq PDD \text{ (mg/kg-d, systemic, all routes)}$  then acceptable; or
- If  $RfD \text{ (mg/kg-d)} \times RSC < PDD \text{ (mg/kg-d, systemic, all routes)}$  then unacceptable.

If the PDD exceeds the  $RfD \times RSC$  value, the ADD may be used in place of the PDD for evaluation purposes with the additional requirements that the PDD value must then be evaluated against a short-term effect level criteria. The short-term effect level (STEL) criteria may be calculated under Section 27.7.4.5 or may be obtained from published risk assessments.

As an alternate approach, if the published peer-reviewed risk assessment has derived a drinking water criteria (mg/L) for the chemical being assessed, the drinking water criteria may be converted into a mg/kg-d dose which shall then be compared to the PDD (systemic, all routes) calculated utilizing the equations in Section 27.6 (again assuming that local adverse effects are not anticipated).

$$\text{Drinking water criteria } \left( \frac{\text{mg}}{\text{L}} \right) \times \frac{DWI \left( \frac{\text{L}}{\text{d}} \right)}{BW \text{ (kg)}} = \text{comparison criteria } \left( \frac{\text{mg}}{\text{kg-d}} \right)$$

where:

$DWI$  = drinking water intake (verify assumptions used in deriving the drinking water criteria)  
 $BW$  = body weight (verify assumptions utilized in deriving the drinking water criteria)

After obtaining the comparison criteria value, it shall be compared with the PDD (systemic, all routes) calculated under Section 27.6 to determine acceptability. If the PDD exceeds the comparison criteria value, the ADD may be used in place of the PDD for evaluation purposes; however, the PDD must also then be evaluated against a short-term effect level criteria (as established under Section 27.7.4.5).

### 27.7.2.3 Risk estimation for published assessments – Carcinogenic endpoints

If a carcinogenic endpoint has been identified as the critical effect in the available published peer-reviewed risk assessment, the point of departure from the risk assessment shall be utilized to perform a margin of exposure (MoE) analysis with the ADD calculated in Section 27.6. The MoE shall be calculated as follows:

$$\text{MoE} = \text{point of departure (mg/kg-d)} / \text{ADD (mg/kg-d, systemic, all routes)}$$

If the calculated MoE is greater than or equal to 10,000, the exposure to the chemical of concern shall be acceptable.

NOTE — The use of an acceptance MoE of 10,000 for carcinogenic compounds is based on the opinion EFSA Scientific Committee (2005).

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### 27.7.3 Utilization of total allowable concentration (TAC)

If a published peer-reviewed risk assessment is unavailable for the chemical of concern, a total allowable concentration (TAC) as determined by Section 3 under NSF/ANSI/CAN 600 may be utilized if available and sensitization or adverse local effects are not anticipated. The TAC value may be converted into a mg/kg-d dose which may then be compared to the PDD (systemic, all routes) calculated utilizing the equations in Section 27.6.

$$\text{drinking water criteria } \left( \frac{\text{mg}}{\text{L}} \right) \times \frac{DWI \left( \frac{\text{L}}{\text{day}} \right)}{BW \text{ (kg)}} = \text{comparison criteria } \left( \frac{\text{mg}}{\text{kg-d}} \right)$$

where:

$DWI$  = drinking water intake (2 L for an adult)  
 $BW$  = body weight (70 kg for an adult)

After obtaining the comparison criterion value, it shall be compared with the PDD (systemic, all routes) calculated under Section 27.6 to determine acceptability. If the PDD exceeds the comparison criteria value, the ADD may be used in place of the PDD for evaluation purposes; however, the PDD must also then be evaluated against a short-term effect level criteria (as established under Section 27.7.4.5).

### 27.7.4 Risk estimation using new or updated risk assessments

#### 27.7.4.1 Data requirements for new or updated risk assessments

For each substance requiring a new or updated risk assessment, toxicity data to be considered shall include, but not be limited to assays of genetic toxicity, acute toxicity (1- to 14-d exposure), short-term toxicity (14- to 28-d exposure), subchronic toxicity (90-d exposure), reproductive toxicity, developmental toxicity, immunotoxicity, neurotoxicity, chronic toxicity (including carcinogenicity), and human data (clinical, epidemiological, or occupational) when available. For a fuller understanding of the toxic potential of the substance, supplemental studies shall be reviewed, including, but not limited to, mode or mechanism of action, pharmacokinetics, pharmacodynamics, sensitization, endocrine disruption, and other endpoints. Structure activity relationships, physical and chemical properties, and any other chemical specific information relevant to the risk assessment shall also be reviewed.

Toxicity testing shall be performed in accordance with the most recently adopted toxicity testing protocols such as those described by the Organization for Economic Cooperation and Development (OECD), US Environmental Protection Agency (US EPA), and US Food and Drug Administration (US FDA). All studies shall be reviewed for compliance with Good Laboratory Practice (21 § CFR, Part 58; 40 CFR, Part 792).

NOTE — Review of the study according to the approach suggested in Klimisch et al, 1997 may also be used to determine the quality of reported data.

A weight-of-evidence approach shall be employed in evaluating the results of the available toxicity data. This approach shall include considering the likelihood of hazard to human health and the conditions under which such a hazard may be expressed. A characterization of the expression of such effects shall also be included, as well as the consideration of the substance's apparent mode of action.



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#### **27.7.4.2 Data requirements for quantitative risk assessment**

Toxicity testing requirements for the quantitative risk assessment procedure are defined in Table 27.910. A minimum data set consisting of a gene mutation assay, a chromosomal aberration assay, and a subchronic toxicity study shall be required for the performance of a quantitative risk assessment. The required studies and preferred criteria are defined in Table 27.910. Modifications to the minimum data set shall be permitted when well supported by peer-reviewed scientific judgment and rationale.

NOTE — Modifications may include, but are not limited to, acceptance of studies using alternate routes of exposure, alternate assays of genetic toxicity, and supplemental studies other than those specified.

Required studies, additional studies, and available supplemental studies shall be reviewed in order to perform a quantitative risk estimation in accordance with Section 27.7.4.3.

Additional studies for the evaluation of reproductive and developmental toxicity (as specified in Table 27.910) shall be required to be reviewed when:

- results of the required minimum data set studies and any supplemental studies indicate toxicity to the reproductive or endocrine tissues of one or both sexes of experimental animals; or
- the compound under evaluation is closely related to a known reproductive or developmental toxicant.

#### **27.7.4.3 Risk estimation for new or updated risk assessments**

The method of risk estimation used for new and updated risk assessments shall be determined by the quantity and quality of toxicity data identified for the contaminant of concern (see Section 27.7.4). When available toxicity data are sufficient to identify an appropriate Point of Departure for a chemical with a non-carcinogenic endpoint, the Point of Departure shall be determined by the toxicologic endpoint identified as the critical effect utilizing either the NOAEL/LOAEL or BMDL approach.

Selected NOAEL/LOAEL/BDL values from animal studies shall be converted to human equivalent doses (HEDs) using a cross-species weight scaling approach, as outlined in US EPA's guidance document (2011c). This method to convert data between animal and human species for both cancer and noncancer endpoints should be used when physiologically-based toxicokinetics (PBPK) modeling is not feasible and no chemical-specific data on interspecies weight conversion are available.

##### **27.7.4.3.1 NOAEL or LOAEL approach**

The substance data set shall be reviewed in its entirety, and the highest NOAEL for the most appropriate test species, relevant route of exposure, study duration, mechanism, tissue response, and toxicological endpoint shall be identified. If a NOAEL cannot be clearly defined from the data, the lowest LOAEL for the most appropriate test species, relevant route of exposure, and toxicological endpoint shall be utilized. The general procedure for calculating the TAC using this approach is as follows.

Determine the critical study and effect from which the NOAEL or LOAEL will be identified according to the following hierarchy (US EPA, 1993 and Dourson et al., 1994):

1. Adequate studies in humans;
2. Adequate studies in animal models most biologically relevant to humans (e.g., primates), or that demonstrate similar pharmacokinetics to humans;

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3. Adequate studies in the most sensitive animal species (the species showing an adverse effect at the lowest administered dose using an appropriate vehicle, an adequate study duration, and a relevant route of exposure); and

4. Effects that are biologically relevant to humans.

#### **27.7.4.3.2 Benchmark dose approach**

The benchmark dose level (BMDL) for the substance shall be calculated by modeling the substance's dose response curve for the critical effect in the region of observed responses. The benchmark response (BMR) concentration shall be determined by whether the critical response is a continuous endpoint measurement or a quantal endpoint measurement. The BMR shall be calculated at the 10% response level. The BMDL is the lower confidence limit on the dose that produces a specified magnitude of change (10%) in a specified adverse response (BMD<sub>10</sub>).

Curve-fitting models shall be selected based on the characteristics of the response data in the observed range. The model shall be selected, to the extent possible, based on the biological mode of action of the substance taken together in a weight-of-evidence evaluation of the available toxicological and biological data. The selected model shall be used to determine the BMDL.

#### **27.7.4.3.3 Margin of exposure evaluation**

Following determination of the point of departure (either by the NOAEL/LOAEL approach or the BMDL approach), the point of departure shall be utilized to perform a margin of exposure (MoE) analysis with the PDD calculated in Section 27.6. The PDD shall be divided by the RSC to account for exposure to the chemical from other sources outside of swimming pool water. Default RSC values are used in the absence of quantitative data to determine the swimming pool water contribution of a substance. Thus, a default RSC of 80% shall be used if no other applications for the chemical outside of pool water uses can be identified. If other uses can be identified, a default RSC of 20% shall be used. The MoE shall be calculated as follows:

$$\text{MOE} = \frac{\frac{\text{point of departure } \frac{\text{mg}}{\text{kg-d}}}{\text{PDD } (\frac{\text{mg}}{\text{kg-d}} \text{ systemic, all routes)}}}{\text{RSC}}$$

An acceptable MoE shall be determined based on the uncertainty factors as set forth in Table 27.4011. A default value of 10 shall be used for individual areas of uncertainty when adequate data are not available to support a data-derived uncertainty factor. Selection of the values of each uncertainty factor shall consider the criteria (adapted from Dourson et al., 1996) as set forth in Sections 27.7.4.3.3.1 through 27.7.4.3.3.5.

Following determination of the acceptable MoE based on the selected uncertainty factors, the calculated MoE based on the above equation may be compared to the acceptable MoE to determine the acceptability of the exposure to the chemical of concern.

If the calculated MoE using the PDD exceeds the acceptable MoE, the ADD may be used in place of the PDD for evaluation purposes, however, the PDD must also then be evaluated against a short-term effect level criterion (as established under Section 27.7.4.5).

If a point of departure cannot be determined for a chemical of concern due to lack of toxicity data and the chemical concentration in the pool water exceeds the threshold value of 10 µg/L at or below the minimum recommended dose, the product cannot meet the requirements of this Standard.

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#### **27.7.4.3.3.1 Human variability**

Selection of the human variability factor shall be based on the availability of data that identify sensitive subpopulations of humans. If sufficient data are available to quantitate the toxicokinetic and toxicodynamic variability of humans (see Sections 27.2.19 and 27.2.20), factor values of 3, 1, or a value determined from the data shall be considered. In the absence of these data, the default value of 10 shall be used (Dourson et al., 1996).

#### **27.7.4.3.3.2 Interspecies variability**

Selection of the interspecies variability factor shall be based on the availability of data that allow for a quantitative extrapolation of animal dose to the equivalent human dose for effects of similar magnitude or for a NOAEL. This includes scientifically documented differences or similarities in physiology, metabolism and toxic response(s) between experimental animals and humans. If sufficient data are available to quantitate the toxicokinetic and toxicodynamic variabilities between experimental animals and humans (see Sections 27.2.19 and 27.2.20), factor values of 3, 1, or a value determined from the data shall be considered. When HED conversion is conducted by use of body weight (BW)<sup>3/4</sup> scaling, the interspecies uncertainty factor default value may be reduced from 10 to 3. In the absence of these data, the default value of 10 shall be used (Dourson et al., 1996).

#### **27.7.4.3.3.3 Subchronic to chronic extrapolation**

Selection of the factor for subchronic extrapolation shall be based on the availability of data that allow for quantitative extrapolation of the critical effect after subchronic exposure to that after chronic exposure. Selection shall also consider whether NOAELs differ quantitatively when different critical effects are observed after subchronic and chronic exposure to the compound. When the critical effect is identified from a study of chronic exposure, the factor value shall be 1. When sufficient data are available to quantitate the difference in the critical effect after subchronic and chronic exposure, or when the principal studies do not suggest that duration of exposure is a determinant of the critical effects, a factor value of 3 or a value determined from the data shall be considered. In the absence of these data, the default value of 10 shall be used (Dourson et al., 1996).

#### **27.7.4.3.3.4 Database sufficiency**

Selection of the factor for database sufficiency shall be based on the ability of the existing data to support a scientific judgment of the likely critical effect of exposure to the compound. When data exist from a minimum of five core studies (two chronic bioassays in different species, on two-generation reproductive study, and two development toxicity studies in different species), a factor value of 1 shall be considered. When several, but not all, of the core studies are available, a factor value of 3 shall be considered. When several of the core studies are unavailable, the default value of 10 shall be used (Dourson et al., 1996).

#### **27.7.4.3.3.5 LOAEL to NOAEL Extrapolation**

Selection of the factor for LOAEL to NOAEL extrapolation shall be based on the ability of the existing data to allow the use of a LOAEL rather than a NOAEL for non-cancer risk estimation. If a well-defined NOAEL is identified, the factor value shall be 1. When the identified LOAEL is for a reversible or minimally adverse toxic effect, a factor value of 3 shall be considered. When the identified LOAEL is for a severe or irreversible toxic effect, a factor value of 10 shall be used (Dourson et al., 1996).

#### **27.7.4.4 Procedure for identifying a class-based point of departure**

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If insufficient toxicology data exists for the chemical of concern to identify a point of departure, a point of departure may be identified based on a chemical class-based approach.

#### **27.7.4.4.1 Establishment of the chemical class**

The chemical class for which the class-based evaluation criteria are to be established shall consist of clearly defined and closely related group of substances, and shall be defined according to chemical structure (e.g., aliphatic or aromatic), primary chemical functional group(s) (e.g., alcohol, aldehyde, or ketone), and molecular weight or weight range.

#### **27.7.4.4.2 Review of chemical class toxicity information**

Once the chemical class has been defined according to Section 27.7.4.4.1, information on chemicals of known toxicity that are included in the defined chemical class shall be reviewed. An appropriate number of chemicals of known toxicity shall be reviewed to confirm the class-based evaluation approach. Sources of data for chemicals of known toxicity shall include, but not be limited to, the following:

- US EPA risk assessments, including Maximum Contaminant Levels (MCL), Health Advisories, and Integrated Risk Information System (IRIS) entries;
- Health Canada or other regulatory entity risk assessments;
- state or provincial drinking water standards and guidelines; and
- World Health Organization (WHO) or other international drinking water standards and guidelines.

A point of departure shall be identified for each chemical of known toxicity that is being used to determine the class-based point of departure. Carcinogenic potential shall be evaluated using a quantitative structure-activity relationship program to verify that the carcinogenic potential of the chemical of unknown toxicity is no greater than that of the chemicals being used to determine the class-based point of departure.

#### **27.7.4.4.3 Determination of the class-based evaluation criteria**

After review of the available toxicity information specified in Section 27.7.4.4.2, the class-based point of departure shall not exceed the lowest point identified for the chemicals of known toxicity in the defined chemical class. The point of departure identified for the chemical class may then be utilized in performing the margin of exposure analysis as described in Section 27.7.4.3.3, until such time as sufficient toxicity data are available to determine a chemical-specific point of departure.

The class-based point of departure shall not be applied to any substance for which available data and sound scientific judgment, such as structure-activity relationship considerations, indicate that adverse health effects may result. If, after a chemical class is defined and its point of departure established, a substance of greater toxicological significance is identified within the class, the class-based evaluation criteria shall be re-evaluated and revised to the acceptable concentrations of the new substance.

#### **27.7.4.5 Procedure for identifying a short-term effect level**

##### **27.7.4.5.1 Data requirements for evaluating short-term exposures**

Short-term exposure paradigms, appropriate for potentially high initial substance concentrations, shall be used to evaluate potential acute risk to human health of short-term exposures. Sound scientific judgment shall be used to determine whether calculation of a short-term exposure level (STEL) is appropriate for a

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given contaminant. The NOAEL or LOAEL for the critical short-term hazard of the substance shall be identified. The following types of studies shall be considered for identification of short-term hazard:

- short-term (less than 90-d duration) toxicity study in rodents or other appropriate species with a minimum of 14-d post-treatment observation period, clinical observations, hematology and clinical chemistry, and gross pathology (preferably an oral study in rodents);
- reproduction or developmental assay (for substances that have these endpoints as the critical effects); or
- subchronic 90-d study in rodents or other species (preferably an oral study in rats).

The critical study shall be used to calculate a Short-Term Exposure Level (STEL) in accordance with Section 27.7.4.5.2.

Selection of uncertainty factors for calculation of a STEL shall consider the quality and completeness of the database for assessing potential short-term effects. Selection of uncertainty factors shall also consider data that quantify interspecies and intraspecies variations. Other parameters that shall be considered in the determination of a STEL include identification of any sensitive subpopulations, the potential for adverse taste and odor, and solubility limitations at the calculated STEL.

#### **27.7.4.5.2 Risk estimation for short-term exposure**

The STEL shall be calculated using the following equation:

$$\text{STEL} \left( \frac{\text{mg}}{\text{kg-d}} \right) = \frac{\text{NOAEL or LOAEL} \frac{\text{mg}}{\text{kg-d}}}{\text{UF}}$$

NOTE — When other than daily dosing was used in the critical study, the STEL calculation shall be adjusted to reflect the dosing schedule.

The calculated STEL shall be rounded to one significant figure.

where:

*NOAEL* = Highest NOAEL for the critical effect in a study of less than or equal to 90-d duration (see Section 27.6); if an NOAEL is not defined, the LOAEL shall be used with a corresponding adjustment to the uncertainty factor (see Table 27.4011).

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**Table 27.910**  
**Quantitative risk assessment data requirements**

Study type	Preferred criteria
<b>Required studies</b>	
gene mutation assay <sup>1</sup>	bacterial reverse mutation assay performed with and without exogenous metabolic activation using <i>Salmonella typhimurium</i> (preferred strains are TA97, TA98, TA100, TA102, TA1535, and TA1537) or <i>Escherichia coli</i> (preferred strains are WP2 <i>uvrA</i> or WP2 <i>uvrA</i> (pKM101))
chromosomal aberration assay <sup>1</sup> ( <i>in vitro</i> preferred)	metaphase analysis in mammalian cells and without exogenous metabolic activation
( <i>in vivo</i> )	metaphase analysis or micronucleus assay in mammalian species
subchronic toxicity <sup>1</sup>	90-d assay in rodent species by oral route of exposure
<b>Additional studies (required as indicated)</b>	
reproduction assay <sup>2</sup>	two generation reproductive assay in a rodent species
developmental assay <sup>2</sup>	teratology study (two species, one rodent and one non-rodent, are preferred)
chronic study <sup>3</sup>	2-yr bioassay in rodent species by oral route of exposure
<b>Supplemental studies</b>	
supplemental genotoxicity studies	mouse lymphoma, SCE, <sup>4</sup> UDS, <sup>5</sup> HGPRT, <sup>6</sup> DNA binding (post labeling assay)
bioaccumulation potential	octanol / water partition coefficient
pharmacokinetics	absorption, distribution, metabolism, and excretion data in humans, other mammalian species, or both
structural/functional assessment	structure / activity relationship analysis
acute or short-term toxicity <sup>7</sup>	1- to 14-d or 14- to 28-d study using oral exposure
cell proliferation / cell cycle assays	proliferating cell nuclear antigen (PCNA)
sensitization	guinea pig intradermal injection
<i>in vivo</i> gene mutation assay	transgenic gene mutation assays
endocrine disruption assays	receptor binding / transcriptional activation assays, frog metamorphosis assay, steroidogenesis assay
human data	epidemiological, occupational, or clinical studies
<sup>1</sup> The gene mutation assay, the chromosomal aberration assay ( <i>in vitro</i> or <i>in vivo</i> ), and the subchronic toxicity study shall constitute the minimum data set required to perform a quantitative risk assessment. When one or both <i>in vitro</i> genotoxicity studies are positive, the <i>in vivo</i> assay shall be required to be reviewed.	

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**Table 27.910**  
**Quantitative risk assessment data requirements**

Study type	Preferred criteria
<sup>2</sup> It is recommended that results of a screening assay, such as OECD No. 422, <i>Combined repeated dose toxicity study with reproduction/developmental toxicity screening test</i> , or data from other repeated dose assays that include histopathological examination of the reproductive tissues of each sex be reviewed prior to a determination that these assays are required for evaluation.	
<sup>3</sup> A chronic study with evaluation of carcinogenic endpoints is required when review of the minimum data set concludes that the substance is likely to be a human health hazard at exposures of 10 µg/L or less.	
<sup>4</sup> Sister chromatid exchange assay; SCEs are not considered to be mutagenic effects because the exchange is assumed to be reciprocal with no gain, loss, or change of genetic material. However, they do indicate that the test material has interacted with the DNA in a way that may lead to chromosome damage. In <i>in vitro</i> studies, SCEs do not provide adequate evidence of mutagenicity, but do identify the need for definitive chromosomal aberration studies. When evidence of <i>in vitro</i> clastogenicity exists, the induction of SCEs is often used as evidence of likely <i>in vivo</i> clastogenic activity because the <i>in vitro</i> aberration data demonstrate the clastogenic activity of the compound and the <i>in vivo</i> SCE data demonstrate that the compound interacted with the DNA in the target tissue.	
<sup>5</sup> Unscheduled DNA synthesis assay.	
<sup>6</sup> Hypoxanthine guanine phosphoribosyl transferase assay.	
<sup>7</sup> Minimum reported parameters include clinical observations, hematology and clinical chemistry, and gross pathology.	

**Table 27.4011**  
**Uncertainty factors**

Areas of uncertainty	Factor
<b>Intraspecies extrapolation (species variation):</b> This factor accounts for variations in chemical sensitivity among individuals in a species including toxicokinetic and toxicodynamic parameters.	1, 3, or 10
<b>Interspecies extrapolation (animal to human):</b> This factor accounts for variations in chemical sensitivity between experimental animals and humans, including toxicokinetic and toxicodynamic parameters.	1, 3, or 10
<b>Less than lifetime duration of exposure:</b> This factor is intended to extrapolate experimental results from subchronic to chronic exposure.	1, 3, or 10
<b>Use of LOAEL rather than NOAEL<sup>1</sup>:</b> This factor addresses the uncertainty in developing a reference dose from a LOAEL rather than a NOAEL.	1, 3, or 10
<b>Lack of database completeness:</b> This factor accounts for the absence of data for specific toxic endpoints.	1, 3, or 10
<sup>1</sup> This adjustment is not required for BMD calculations.  NOTE — When uncertainties exist in four areas, a 3,000-fold composite uncertainty factor is appropriate. When uncertainties exist in five areas, a 10,000-fold composite uncertainty factor is appropriate. This consolidation of individual factors recognizes that each individual factor is conservative, and multiplication of four or five uncertainty factors is likely to result in an overly conservative RfD. Datasets that would result in a composite uncertainty factor of greater than 10,000-fold are considered too weak for quantitative risk assessment (Dourson, 1994).	