Evaluation of Swimming Pool Treatment Chemicals Health Effects under NSF/ANSI Standard 50

Presentation Outline

- About NSF International
- NSF/ANSI 50 Overview
- Development Process of Annex R
- Annex R Requirements
- Application of Annex R - Examples
- Question and Answers

NSF International: An Introduction

Our Values

NSF's Mission and History

Today

NSF Around the World

Capabilities

Services from NSF International

Our Mission

NSF International is dedicated to being the leading global provider of public health and safety-based risk management solutions while serving the interests of all stakeholders, namely the public, the business community and government agencies.

NSF International is a global, independent, public health and safety organization.

Our mission and focus has always been protecting and improving human health.

NSF helps people live safer.

We carry out this human health and safety mission by:

STANDARDS

Writing standards to promote food, drinking water, indoor air, dietary supplements, consumer products and environmental safety

TESTING

Testing products to these and other standards

CERTIFICATION

Certifying products to these standards

AUDITING

Conducting safety audits for the food, water and consumer goods industries

CONSULTING

Providing strategic and technical consulting for the dietary supplement, pharmaceutical, medical device, food and beverage industries

TRAINING

Developing training and education programs

A Historical Perspective

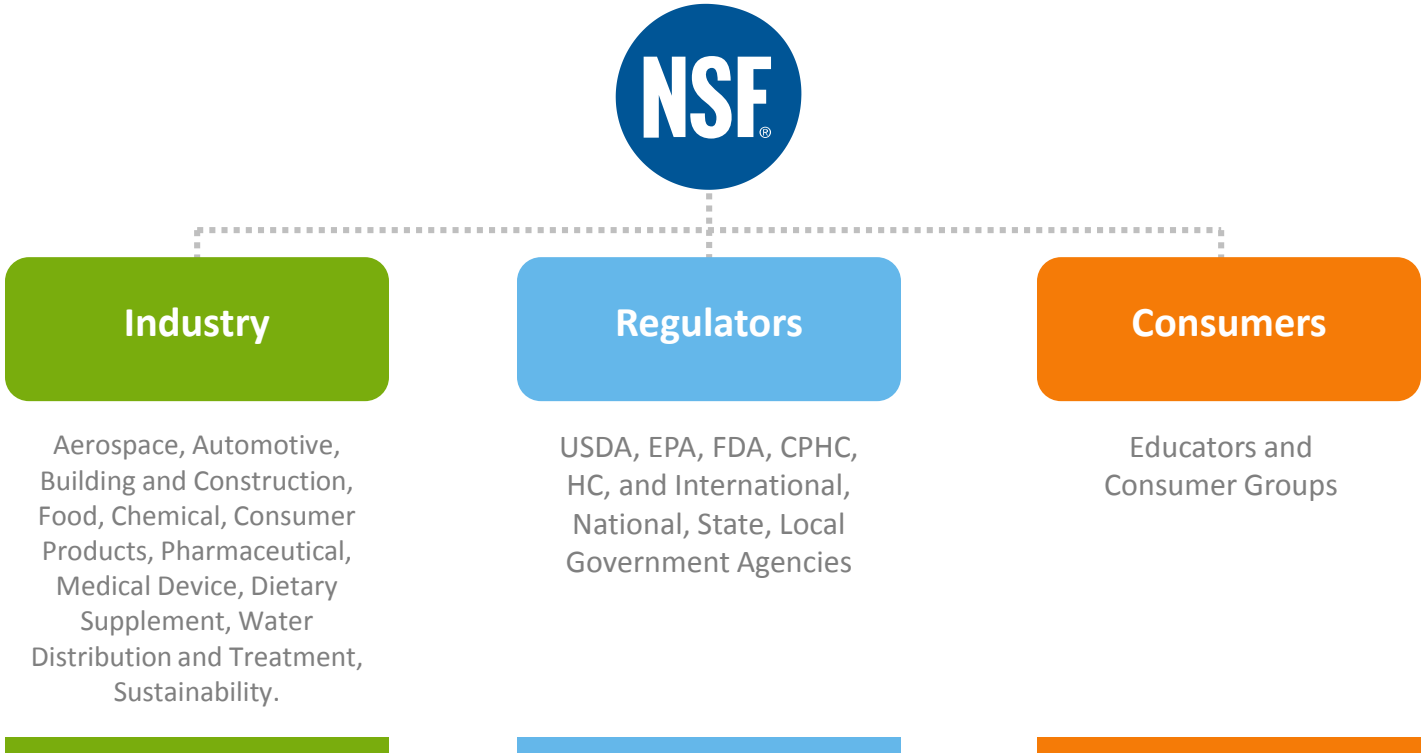
Americans began dining out in the late 1930's

Inconsistent rules and regulations arose, varying from town to town, state to state. Hence…

State health officials monitored food service establishments for sanitation using a variety of criteria.

A need for uniform national standards; NSF brings regulators, industry, consumers and public health officials together.

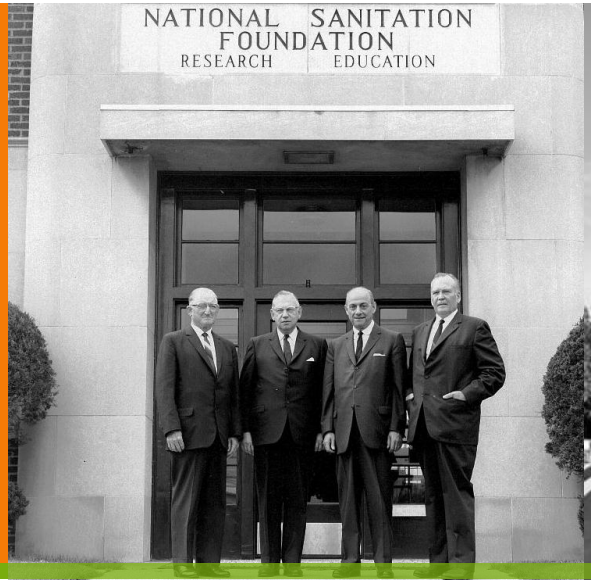
Bringing Industry, Regulatory and Consumers Together



Our Founding

In 1944,

NSF was founded as the National Sanitation Foundation in the University of Michigan's School of Public Health.



Today,

we are now *NSF International*, with corporate headquarters in Ann Arbor, MI, USA, and 51 office and lab locations worldwide.

Today, NSF is a Global Leader in Public Health and Safety

Developer of over **90** national consensus standards

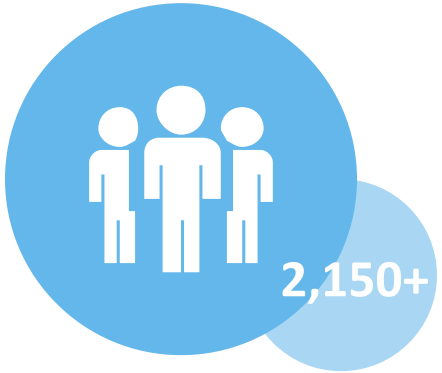
Steadfast ties with key associations and government agencies.

NSF works closely with international, federal, state and local regulators : FDA, USDA, EPA , U.S. Government & Legislature

Pan American Health Organization/World Health Organization Collaborating Center on Food Safety, Water Quality and Indoor Environment

Service provider to thousands of organizations in **168 countries**

An Unmatched Professional Staff and Facility



Experienced Professionals

microbiologists, toxicologists, chemists, engineers and public health experts

293,000 ft² of state-of-the-art laboratories
in North America, Europe, Latin America and Asia, plus partner labs around the world

NSF laboratories are ISO/IEC 17025 accredited
(testing and calibration)

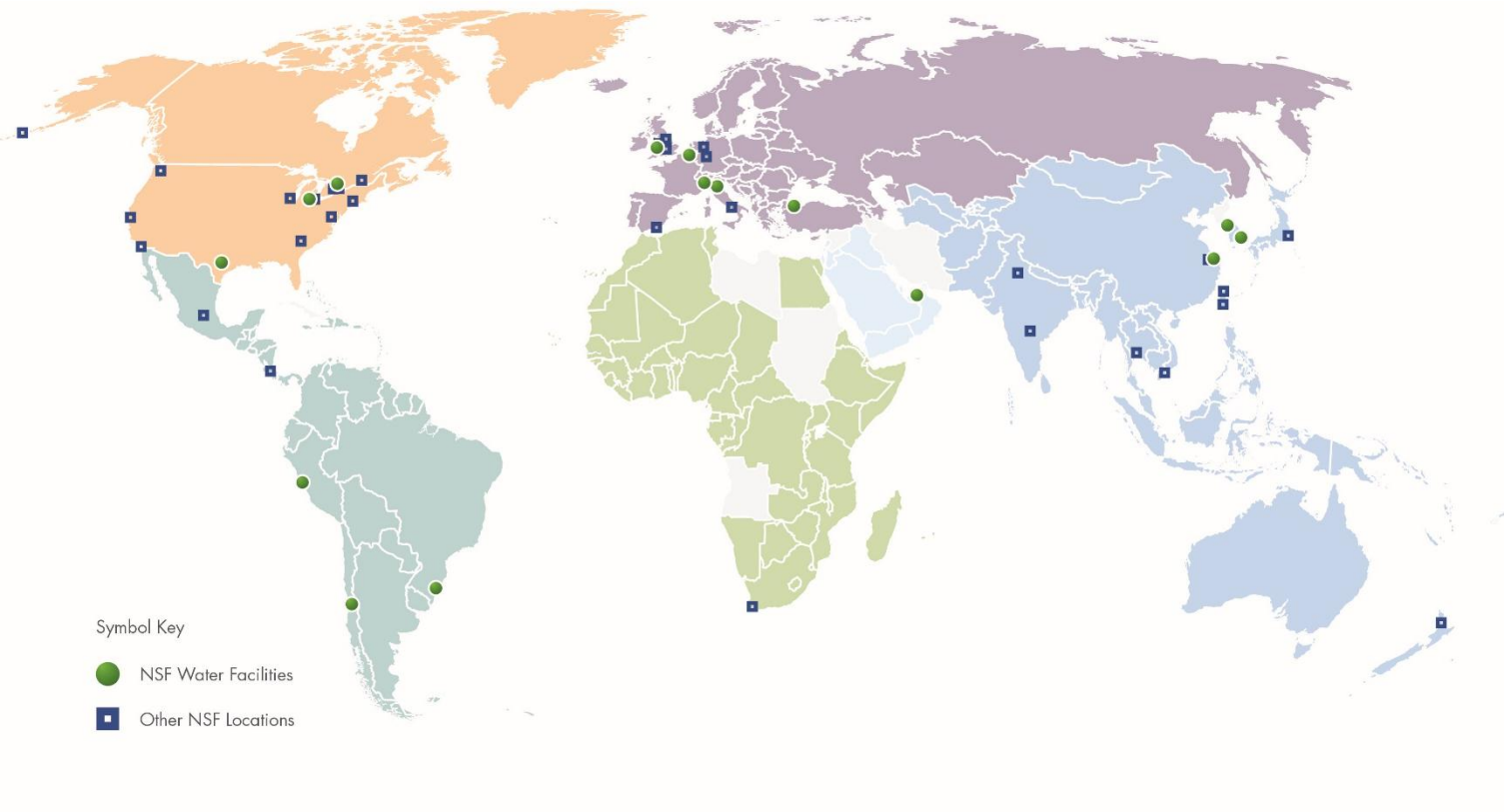
provide testing, certification and technical services for a wide range of industries

NSF's Applied Research Center
provides custom R&D services

contract method development, testing and consulting services in chemistry, microbiology, genomics and toxicology, product claim verification, lab quality/management, methods training and human health risk assessment

NSF Around the Globe

NSF provides services in 168 countries with 51 office and laboratory locations.



NSF/ANSI Standard 50

Recreational Water Products

NSF/ANSI 50

- History: Around since the early 60s
- NSF/ANSI 50 plus ASTM, ASME, UL, NSPI standards
- Filters, pumps, drains, feeders, skimmers, valves, chlorinators, generators, water test kits, pool covers, etc.
- More than 150 clients
- Standard has expanded to incorporate treatment chemicals – New Annex R (2015)
- Heavily referenced in U.S. codes

Purpose and Scope of NSF/ANSI 50

Purpose

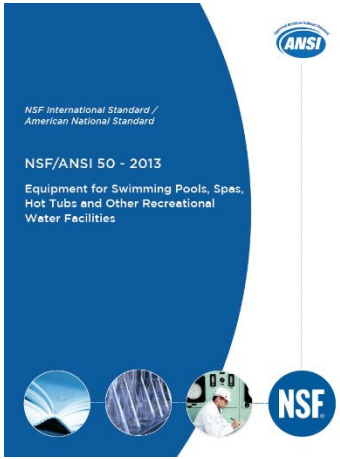
- Establishes minimum criteria for:
  - Chemical and Material health effects
  - Design and Construction
  - Performance and Durability

Scope

Materials, components, products, equipment and systems related to public and residential recreational water facility operation

NSF/ANSI 50 Joint Committee

- **Developed Standard in 1977**
- **Meets regularly to revise standard**
- **Functions via equal 3-part voting**



Manufacturers
Producers
Trade Associations

Public Health
EPA
CDC
Health Canada
Academia
State
Local

Users
Consumers
Government
Specifiers
Certifiers
Testing Labs
Retailers
NGOs

NSF/ANSI Standard 50

Sections 1-4
Scope and References, Definitions, Chemical and Material Requirements, Design and Construction

Section 5
Filters

Section 6
Centrifugal Pumps

Section 7
Non-Integral Strainers

Section 8
Valves

Section 9
Skimmers

Section 10
Mechanical Feeders

Section 11
Flow-Through Feeders

Section 12
Filtration Media

Section 13
Ozone Generators

Section 14
UV Systems

Section 15
In-line electrolytic chlorinators

Section 16
Brine/Batch type electrolytic chlorine or bromine generators

Section 17
Copper/Silver Ion Generators

Section 18
Automated Controllers

Section 19
Water Quality Test Devices (WQTD)

Section 20
Spas and Hot Tubs

Section 21
Fittings for Water Park, Spray Pad, Pool, or Spay

Section 22
Heat Exchangers, Heaters, Coolers, and solar water heating systems

Development of Annex R

Development of Annex R

- 2011 – Public Health officials presented concerns regarding treatment chemicals to NSF/ANSI Standard 50 Recreational Water Facility Joint Committee (RWFJC)

- RWFJC established a task group to develop methodology for evaluating the toxicity, contents, performance and claim verification of recreational water treatment chemicals
  - Task Group Chair – Suzie Campbell, Oklahoma City-County Health Department
  - Bob Vincent, Florida Department of Health

Development of Annex R

- Task Group originally considered whether NSF/ANSI Standard 60 could be utilized
  - Florida code requires Standard 60 Certification
- RWFJC task group contacted the U.S. EPA Office of Pesticides
  - Received information on swimmer exposure assumptions (SWIMODEL)
- Also contacted and received input from various state health departments
  - New York, California

Health Effects Assessments

NSF/ANSI Standard 60

Lifetime Exposure
2 L per Day for 70 years

Oral

12-50mL per day
1-5 days a week

Inhalation

½ -3 hours per day
1-5 days a week

Dermal

½ -3 hours per day
1-5 days a week

NSF/ANSI Standard 50

Challenges in assessing Health Effects

- Assessing accumulation of chemicals in the pool water based on multiple dosages overtime
- Handling contaminants produced by the reaction of the treatment chemical with constituents of the treated water
- Variability of pool-specific parameters including:
  - Water chemistry, recirculation, filtration rates/types, water replacement rates, splash out rates, etc.

Development of Annex R

- RWJFC Task Group decided on a simplified approach that may be used to assess treatment chemicals dosed at a maximum dose rate

- Method is based predominantly on two sources:
  - Annex A of NSF/ANSI Standards 60 and 61
  - Swimming pool exposure methodologies from U.S. EPA Office of Pesticide Programs

- Annex R was approved by the RWJFC and NSF CPHC and published in NSF/ANSI Standard 50 on October 9, 2015

Annex R Requirements

NSF/ANSI Standard 50 – Annex R

- What chemicals are subject to review under Annex R requirements?
  - Chemical constituents of the product
  - Contaminants detected in the product

- Section 3.2.2 sets forth one exception to the Annex R review requirements:
  - If chemical is registered under FIFRA it is exempt from Annex R review but is still subject to contaminant testing

Annex R Requirements – General Overview

- Initial requirement is to obtain product formulation information
  - Must include identification of all unique chemical constituents
  - Product use instructions must be provided that designate a maximum recommended dose rate

- Based on the formulation information and maximum recommended dose rate, the concentration of each chemical constituent in the swimming pool water is determined

Annex R Requirements – General Overview

- As an initial toxicity screen, any chemical constituent that has a concentration in the swimming pool water of ≤10 µg/L does not require further toxicological evaluation
  - This threshold value does not apply to any substance for which there is a concern for adverse health effects at concentrations ≤10 µg/L based on available toxicity data and scientific judgment
  - Threshold of 10 µg/L based on FDA Threshold of Regulation value from 21 CFR 170.39

Determination of Threshold Value

Threshold of 10 µg/L based on U.S. FDA Threshold of Regulation value from 21 CFR 170.39

FDA Threshold of Regulation = 0.5 µg/kg food (from 21 CFR 170.39)

Average food intake in children (6-11 years) = 1.118 kg/day (from EFH, U.S. EPA, 1997)

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

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

Annex R Requirements – General Overview

- For chemical constituents or contaminants that exceed 10 µg/L in the swimming pool water, three additional steps are utilized:
  - Exposure assessment using exposure assumptions and equations obtained from the U.S. EPA Office of Pesticide Programs
    - Accounts for oral, dermal and inhalation routes of exposure
  - Determination of acceptable exposure levels for each chemical constituent
    - Based on published peer-reviewed assessments or determined utilizing an approach similar to Annex A in Standards 60/61
  - Comparison of estimated exposures with the acceptable exposure levels to determine product acceptance.

Exposure Assessment

Exposure Assessment

- Exposure equations derived from U.S. EPA SWIMODEL software (2003a)
  - Exception of localized dermal exposure equation under R.5.3
- Exposure assumptions obtained from U.S. EPA Office of Pesticide Programs
- If localized effects (irritation or sensitization) are not significant, exposure equations allow for an estimate of total systemic exposure from oral, dermal and inhalation routes
- Equations allow for estimation of Potential Daily Dose (PDD) and Average Daily Dose (ADD)

Exposure Assessment

- Using U.S. EPA SWIMMODEL (2003a) equations and the assumptions provided in this Annex R, exposure estimates may be calculated for adults (men and women), children (ages 11 to <16) and children (ages 6 to <11).

- The available assumptions allow for exposure estimates for each age group based on whether the individual is a competitive or non-competitive swimmer.

Exposure Assessment

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 include, but are not limited to, volatility, water solubility, and/or direct reactivity with tissues.

- Dermal: Chemical properties to consider include, but are not limited to, molecular weight and/or Kow.

Exposure Assessment

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

- The model focuses does not take into account metabolism or excretion

- The model uses the following absorption facts for each route of exposure:
  - Ingestion: 100% absorption of ingested chemicals is assumed;
  - Dermal: Chemical-specific decimal Kp is used;
  - Inhalation: 100% absorption of inhaled chemical is assumed;

- The model does not account for the effect of ambient temperature on intake;

- The exposure estimates are derived based on use of the chemical in swimming pools only.

Oral Exposure Equations

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

Where:
PDD = Potential daily dose (mg/kg-day)
Cw = Chemical concentration (mg/L)
IR = Ingestion rate of pool water (L/hr)
ET = Exposure time (hrs/day)
BW = Body weight (kg)

$$ADD = \frac{Cw \times IR \times ET \times EF}{BW \times 365\ day/yr}$$

Where:
ADD = Average daily dose (mg/kg-day)
Cw = Chemical concentration (mg/L)
IgR = Ingestion rate of pool water (L/hr)
ET = Exposure time (hrs/day)
EF = Exposure frequency (events/year)
BW = Body weight (kg)

Oral Exposure Assumptions

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/hr)	0.0125	0.025	0.025	0.05	0.05	0.05
ET (hr/day)	3	1	2	1	1	1
BW (kg)	70		54		29	

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/hr)	0.0125	0.025	0.025	0.05	0.05	0.05
ET (hr/day)	3	0.3	2	0.5	1	0.5
EF (events/year)	238	88	189	72	65	102
BW (kg)	70		54		29	

Dermal Exposure

$$PDD = \frac{CW \times Kp \times SA \times ET \times CF}{BW}$$

Where:
PDD = Potential Daily Dose (mg/kg-day)
CW = Chemical Concentration in Water (mg/liter)
Kp = Permeability Constant (cm/hr)
SA = Surface Area (cm2)
ET = Exposure Time (hours/day)
CF = Conversion Factor (0.001 Liter/cm3)
BW = Body Weight (Kg)

$$ADD = \frac{CW \times Kp \times SA \times ET \times EF \times CF}{BW \times 365\ day/year}$$

Where:
ADD = Average Daily Dose (mg/kg-day)
CW = Chemical Concentration in Water (mg/liter)
Kp = Permeability Constant (cm/hr)
SA = Surface Area (cm2)
ET = Exposure Time (hours/day)
EF = Exposure frequency (events/year)
CF = Conversion Factor (0.001 Liter/cm3)
BW = Body Weight (Kg)

Dermal Exposure Assumptions

Assumptions for Short-Term Swimming 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 (hr/day)	3	1	2	1	1	1
SA (cm^2)	18,200		15,700		10,500	
BW (kg)	70		54		29	

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 (hr/day)	3	0.3	2	0.5	1	0.5
EF (events/year)	238	88	189	72	65	102
SA (cm^2)	18,200		15,700		10,500	
BW (kg)	70		54		29	

Inhalation Exposure

$$\textbf{PDD} = \frac{\textbf{Vp x IR x ET}}{\textbf{BW}}$$

Where:
Vp = Chemical vapor concentration
IR = Inhalation rate (m^3/hr)
ET = Exposure time (hrs/day)
BW = Body weight (kg)

Vp = Cw x H' x 1,000 L/m^3
Where:
Vp = Chemical vapor concentration (mg/m^3)
Cw = Chemical concentration in pool water (mg/L)
H' = Henry's Law constant (unitless)

$$\textbf{ADD} = \frac{\textbf{Vp x IR x ET x EF}}{\textbf{BW x 365 day/yr}}$$

Where:
ADD = Average daily dose (mg/kg-day)
Vp = Chemical vapor concentration
IR = Inhalation rate (m^3/hr)
ET = Exposure time (hrs/day)
EF = Exposure frequency (events/year)
BW = Body weight (kg)

Inhalation Exposure Assumptions

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 (m^3/hr)	3.2	1.0	2.9	1.5	2.5	1.3
ET (hr/day)	3	1	2	1	1	1
BW (kg)	70		54		29	

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 (m^3/hr)	3.2	1.0	2.9	1.5	2.5	1.3
ET (hr/day)	3	0.3	2	0.5	1	0.5
EF (events/year)	238	88	189	72	65	102
BW (kg)	70		54		29	

Exposure Assessment – KEY POINTS

- Oral, Dermal and Inhalation exposures are combined to calculate a **systemic dose**
- Localized (irritation and sensitization) effects must be address separately
- Physical/Chemical properties of target chemical may indicate if evaluation of dermal and/or inhalation exposure are required

Annex R - Toxicology Evaluation Procedures

Toxicology Evaluation Procedure

- Procedure adapted predominantly from Annex A of NSF/ANSI Standards 60 and 61
- Goal is to identify an **oral** reference dose (RfD) to compare with estimated **systemic** exposure
- An RfD is an estimate of a daily exposure to the human population that is likely to be without an appreciable risk during a lifetime

Toxicology Evaluation Procedure – Generally

- Applies only to chemicals that exceed a concentration of 10 µg/L (in the pool water) at the maximum dose rate
- **Does not apply to chemicals regulated under FIFRA**
- Risk assessment values are obtained from the following:
  - Publically available peer-reviewed risk assessments
  - Drinking water criteria (ex. NSF 60/61)
  - Prepare risk assessment in accordance with Annex R
- If there is insufficient toxicity data, chemicals can not be cleared passed the 10 µg/L threshold

Published Risk Assessments

- Published Assessment can be from variety of sources
  - **Examples: U.S. EPA, Health Canada, U.S. FDA, World Health Organization, published peer-reviewed literature**
- Prior to using the assessment, an updated review of the available toxicology literature on the chemical in question is reviewed
- If multiple assessment are located for the same chemical, the strengths and weakness of each assessment are evaluated
  - U.S. EPA assessments are typically given deference over other agencies

Published Risk Assessment – Non-carcinogenic endpoints

- Oral RfD value obtained from assessment is compared with Potential Daily Dose (PDD)
- Oral RfD is adjusted by a Relative Source Contribution (RSC) of either 0.8 or 0.2 depending on identified uses of the chemical
- If RfD x RSC ≥ PDD then the exposure is acceptable

Published Risk Assessment – Carcinogenic endpoints

- For risk assessments for carcinogens, the published risk assessment identifies a Point of Departure (PoD)
- A Margin of Exposure of 10000 utilized to determine acceptance between Average Daily Dose (ADD) and identified PoD
- If calculated MoE ≥ 10000, acceptable

Adapting Drinking Water Criteria

- Drinking water criteria (mg/L) may be used to calculate a comparison criteria (mg/kg-day)
  - WHO values, TAC values from NSF Standards 60/61
- Convert to mg/kg-day using intake (L/day) and body weight (kg) from source of drinking water criteria
- Compare with PDD to determine acceptance (or ADD if needed)

New or Updated Risk Assessments

- If a new or updated risk assessment is needed, requirements are set forth in Section R.6.4
- Toxicity data considered includes the following when available:
  - Genetic toxicity, acute toxicity, short-term (14- to 28-day exposure), sub-chronic (90-day), reproductive toxicity, developmental toxicity, immunotoxicity, neurotoxicity, chronic toxicity
- Human data is also considered:
  - Clinical, epidemiological or occupational studies
- Minimum data required for quantitative assessment consists of gene mutation assay, chromosomal aberration assay and a subchronic toxicity study

New or Updated Risk Assessments

- Determine a Point of Departure using either NOAEL/LOAEL or BMDL
- Generally, the NOAEL/LOAEL approach identifies the highest NOAEL below the lowest LOAEL
- Benchmark dose (BMD) is a statistical approach to model the dose response curve to obtain a Bench Mark Response (typically a 10% response rate)

New or Updated Risk Assessments

- Following determination of Point of Departure (PoD), a Margin of Exposure is calculated with the PDD
- The RSC is applied to account for exposure to the chemical outside of pool water (either 0.2 or 0.8)

MOE = PoD / (PDD/RSC)

New or Updated Risk Assessments

- What is an acceptable Margin of Exposure?
- Determined by uncertainty related to the derived Point of Departure (PoD)
  - Human Variability (1x, 3x or 10x)
  - Interspecies Variability (1x, 3x or 10x)
  - Subchronic to Chronic Extrapolation (1x, 3x or 10x)
  - Database Sufficiency (1x, 3x or 10x)
  - LOAEL to NOAEL Extrapolation (1x, 3x or 10x)
- If Total Uncertainty **is less than** your calculated MOE, result is acceptable

New or Updated Risk Assessments

- What if the calculation using the PDD results in unacceptable exposures?
  - Use the ADD instead; use of the PDD is a conservative first pass as it is comparing a short-term exposure against a long-term criteria
  - If the ADD is used, you still must address the PDD exposure by determining a Short-term Effect Level (STEL)
- Procedure for determining a STEL is set forth under Annex R Section 6.4.4
  - Allows for use of studies less than 90 days in duration

Class-Based Chemicals

- If there is in insufficient toxicity data for a specific chemical, a point of departure may be identified based on chemical class-based approach
- Chemical Class must be clearly defined:
  - Chemical structure
  - Primary chemical functional groups
  - Molecular weight range

Annex R
Hypothetical Examples

Example 1: Sodium Tetraborate Pentahydrate

- Product consists of 2% sodium tetraborate pentahydrate
- Maximum dose level of 75 mg product/L
- Results in 1.5 mg/L in the pool water as sodium tetraborate penahydrate
- The resulting exposure as boron is 0.22 mg/L

Example 1: Sodium Tetraborate Pentahydrate

- Based on physical/chemical properties of sodium tetraborate pentahydrate, oral route is the only route of concern
  - Non-volatile
  - Inorganic compound exhibits very low dermal penetration

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
Oral Exposure (mg/kg-day)	1.2E-04	3.9E-05	2.0E-04	2.0E-04	**3.8E-04**	**3.8E-04**

Example 1: Sodium Tetraborate Pentahydrate

- Worst case PDD is 0.38 µg/kg-day for children ages 6 to <11
- U.S. EPA chronic oral reference dose of 0.2 mg/kg-day (IRIS Database)
- An RSC of 0.2 applied due to exposure to boron from foods and in drinking water
- Acceptable exposure is 40 µg/kg-day > PDD; therefore ACCEPTABLE

Example 2: Tetra Sodium EDTA (CAS#64-02-8)

- Product consists of 1% sodium tetra sodium EDTA (87% strength)
- Maximum dose level of 75 mg product/L
- Results in 0.66 mg/L in the pool water as tetrasodium
- The resulting exposure as EDTA (CAS# 60-00-4) is 0.51 mg/L

Example 2: Tetra Sodium EDTA (CAS#64-02-8)

- Based on physical/chemical properties of EDTA, oral route and dermal routes are the only route of concerns
  - Henry law = 1.17×10^{-23}
  - Log P = -3.80, Molecular weight 292.24

Short-Term Swimming Pool Oral and 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**
Oral Exposure (mg/kg-day)	2.7E-04	9.1E-05	4.7E-04	4.7E-04	**8.8E-04**	**8.8E-04**
Dermal Exposure (mg/kg-day)	2.5E-08	8.4E-09	1.9E-08	9.3E-09	1.2E-08	1.2E-08

Example 2: Tetra Sodium EDTA (CAS#64-02-8)

- Worst case PDD is 0.88 µg/kg-day for children ages 6 to <11
- JECFA Acceptable Daily Intake of 1.9 mg/kg-day as EDTA (World Health Organization)
- An RSC of 0.2 applied due to exposure to EDTA from other sources outside of pool use
- Acceptable exposure is 380 µg/kg-day > PDD; therefore ACCEPTABLE

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