NSF International Standard /
American National Standard

NSF/ANSI 60 - 2009

Drinking Water Treatment Chemicals - Health Effects



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Chair, Joint Committee on Drinking Water Treatment Chemicals
c/o NSF International
789 North Dixboro Road, P.O. Box 130140
Ann Arbor, Michigan 48113-0140 USA
Phone: (734) 769-8010 Telex: 753215 NSF INTL
FAX: (734) 769-0109
E-mail: info@nsf.org
Web: http://www.nsf.org

NSF International Standard/
American National Standard
for Drinking Water Additives —

Drinking water treatment chemicals — Health effects

Standard Developer
NSF International

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Foreword[2]

In response to a competitive request for proposals from the U.S. Environmental Protection Agency (USEPA), a Consortium led by NSF International (NSF) agreed to develop voluntary third-party consensus standards and a certification program for all direct and indirect drinking water additives. Other members of the Consortium include the Water Research Foundation (formerly the American Water Works Association Research Foundation), the Association of State Drinking Water Administrators, the Conference of State Health and Environmental Managers, and the American Water Works Association. (COSHEM has since become inactive as an organization.) Each organization was represented on a steering committee with oversight responsibility for the administration of the cooperative agreement. The Steering Committee provided guidance on overall administration and management, and the member organizations will remain active after the expiration of the cooperative agreement.

The standards were developed using a voluntary consensus process. All parties at interest were represented, including regulatory agencies, industry, and water suppliers; consultants; and other users of products covered by the standards.

Two standards for additives products have been adopted. NSF/ANSI 61: *Drinking water system components - Health effects* currently covers indirect additives. NSF/ANSI 60, and subsequent product certification against it, will replace the USEPA Additives Advisory Program for drinking water treatment chemicals. For more information with regard to USEPA's actions, refer to the July 7, 1988 *Federal Register* (53FR25586).

NSF/ANSI 60 has been developed to establish minimum requirements for the control of potential adverse human health effects from products added to water for its treatment. It does not attempt to include product performance requirements, which are currently addressed in standards established by such organizations as the American Water Works Association, the American Society for Testing and Materials, and the American National Standards Institute. Because this Standard complements the standards of these organizations, it is recommended that products also meet the appropriate requirements specified in the standards of such organizations.

The Standard and the accompanying text are intended for voluntary use by certifying organizations, utilities, regulatory agencies, and/or manufacturers as a basis of providing assurances that adequate health protection exists for covered products.

This version of NSF/ANSI 60 – 2009 includes the following revisions:

- Issue 42 Prep K weights which modifed the minimum recorded weight in the method for Preparation K (B.3.12) to provide practical limitations for weights recorded during the estimation of chemical tested on a dry weight basis

Please note that the footnote in Table D1 that states that the Single Product Acceptable Concentration (SPAC) for bromate will be lowered to 0.003 mg/L is still under evaluation by the NSF Joint Committee on Drinking Water Treatment Chemicals. At this time, it has not been demonstrated that the drinking water industry demand for hypochlorite chemicals cannot be adequately met at the lower SPAC. The next revision of this standard will be made up to date with the decision of the Joint Committee.

This Standard was developed by the NSF Joint Committee on Drinking Treatment Chemicals using the consensus process described by the American National Standards Institute.

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Suggestions for improvement of this Standard are welcome. Comments should be sent to Chair, Drinking Water Additives, c/o NSF International, Standards Department, PO Box 130140, Ann Arbor, Michigan 48113-0140, USA.

Consortium Organizations

NSF International

Popularly referred to as NSF, NSF International is a non-commercial agency. It is incorporated under the laws of Michigan as a not-for-profit organization devoted to research, education, and service. It seeks to solve problems involving man and his environment. It wishes to promote health and enrich the quality of life through conserving and improving that environment. Its fundamental principle of operation is to serve as a neutral medium in which business and industry, official regulatory agencies, and the public come together to deal with problems involving products, equipment, procedures, and services related to health and the environment. It is conceived and administered as a public service organization.

NSF is perhaps best known for its role in developing Standards and Criteria for equipment, products, and services that bear upon health. NSF was the lead organization in the Consortium responsible for developing this Standard. NSF conducts research; tests and evaluates equipment, products, and services for compliance with standards and criteria; and grants and controls the use of NSF registered Marks.

NSF offers product certification (Listing Services) for all products covered by its Standards. Each program has established policies governing the associated product evaluation, Listing Services, follow-up and enforcement activities. The NSF Listing Mark is widely recognized as a sign that the product or service to which it relates complies with the applicable NSF Standard(s).

Water Research Foundation

The mission of the Water Research Foundation (WRF) is to sponsor practical, applied research in behalf of the drinking water industry of North America. The scope of the research program embraces all aspects of water supply operation, from development and maintenance of water resources to treatment technologies and water quality issues, from storage and distribution system operations to health effects studies and utility planning and management activities. WRF serves as the centralized industry institution for planning, managing, and funding cooperative research and development in drinking water, including the subsequent transfer of technology and results for practical application by the water utility community.

WRF's purpose in this cooperative program is to provide a communication link with the water utilities throughout North America and serve as the focal point for identification of research needs of the water supply industry with respect to the additives program.

The Association of State Drinking Water Administrators

The Association of State Drinking Water Administrators (ASDWA) is a non-profit organization whose eligible membership is comprised of drinking water program administrators in each of the 50 states and seven U.S. territories. Through the organization, representatives speak with a collective voice to Congressional committees, the United States Environmental Protection Agency, professional and trade associations, water utilities, and the general public on issues related to state drinking water programs. With its mission of protecting the public health through assurance of high quality drinking water, and promoting responsible, reasonable, and feasible drinking water programs at the state and federal levels, the Association is a valued contributor to the consortium and to the program. It provides the link between the additives program and the state drinking water programs.

The Conference of State Health and Environmental Managers

The Conference of State Health and Environmental Managers (COSHEM), known formerly as the Conference of State Sanitary Engineers (CSSE), is currently inactive as an organization. It brought to the consortium expertise and involvement of state health and environmental program managers. The Conference was the focal point for health concerns of all state environmental programs, including drinking water, wastewater, air, solid and hazardous wastes, radiological, occupational, health, and food. A standing committee on water supply focused on drinking water issues and kept the membership informed. The Conference played an important role early in the program through two-way communication with state health and environmental program decision makers.

American Water Works Association

The purpose for which the American Water Works Association (AWWA) is formed is to promote public health, safety, and welfare through the improvement of the quality and quantity of water delivered to the public and the development and furtherance of understanding of the problems relating thereto by:

- advancing the knowledge of the design, construction, operation, water treatment and management of water utilities, and developing standards for procedures, equipment, and materials used by public water supply systems;

- advancing the knowledge of problems involved in the development of resources, production, and distribution of safe and adequate water supplies;

- educating the public on the problems of water supply and promoting a spirit of cooperation between consumers and suppliers in solving these problems; and

- conducting research to determine the causes of problems of providing a safe and adequate water supply and proposing solutions thereto in an effort to improve the quality and quantity of the water supply provided to the public.

AWWA brings to the Consortium its established position as the largest public drinking water association in North America, with a broad range of membership, including utilities, consultants, manufacturers/ distributors/ agents, contractors, and other organizations with a direct interest in drinking water.

NSF/ANSI Standard
for Drinking Water Additives —

Drinking water treatment chemicals — Health effects

1 Purpose, scope, and normative references

1.1 Purpose

This Standard establishes minimum health effects requirements for the chemicals, the chemical contaminants, and the impurities that are directly added to drinking water from drinking water treatment chemicals. This Standard does not establish performance or taste and odor requirements for drinking water treatment chemicals.

1.2 Scope

This Standard contains health effects requirements for drinking water treatment chemicals that are directly added to water and are intended to be present in the finished water. This Standard also contains health effects requirements for other chemical products that are directly added to water but are not intended to be present in the finished water. Chemicals covered by this Standard include, but are not limited to, coagulation and flocculation chemicals, softening, precipitation, sequestering, pH adjustment, and corrosion/scale control chemicals, disinfection and oxidation chemicals, miscellaneous treatment chemicals, and miscellaneous water supply chemicals.

Contaminants produced as by-products through reaction of the treatment chemical with a constituent of the treated water are not covered by this Standard.

1.3 Normative references

The following documents contain requirements, which by reference in this text, constitute requirements of this Standard.

APHA, *Standard Methods for the Examination of Water and Wastewater*, twentieth edition[3]

ASTM E29-02. *Standard Practice for Using Significant Digits in Test Data to Determine Conformance with Specifications*[4]

ASTM E506-98. *Standard Test Method for Mercury in Liquid Chlorine*[4]

ASTM G22-76 (1996). *Standard Practice for Determining Resistance of Plastics to Bacteria*[4]

CGA, G-6.2-1994. *Commodity Specification for Carbon Dioxide*[5]

[3] American Public Health Association, 800 I Street NW, Washington, DC 20001 www.apha.org

[4] ASTM International, 100 Barr Harbor Drive, West Conshohocken, PA 19428-2859 www.astm.org

[5] Compressed Gas Association, 1725 Jefferson Davis Highway, Suite 1004, Arlington, VA 22202-4102 www.cganet.com

OECD, Guidelines for the Testing of Chemicals, May 1996[6]

USEPA-600/4-79-020. *Methods for the Chemical Analysis of Water and Wastes*, March 1983[7]

USEPA-600/4-80-032. *Prescribed Procedures for Measurement of Radioactivity in Drinking Water*[7]

USEPA, *Health Effects Testing Guidelines*, 40 CFR Part 798[8]

USEPA, *Good Laboratory Practice Standards*, 40 CFR Part 160[8]

USFDA, *Good Laboratory Practice for Non-Clinical Laboratory Studies*, 21 CFR 587[9]

USFDA, Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives in Food[9]

1.4 Alternate chemicals

Chemicals or mixtures of chemicals used for the various purposes discussed in this Standard, but not specifically referenced, shall be acceptable provided they meet the requirements of this Standard.

1.5 Significant figures

When determining conformance with the specifications in this standard, the Absolute Method in ASTM E29 (*Standard Practice for Using Significant Digits in Test Data to Determine Conformance With Specifications*) shall be used.

2 Definitions

2.1 analytical summary: A list of the analytical procedures, both chemical and microbiological, which are selected to determine whether a product is compliant to the requirements of the Standard.

2.2 at-the-tap: Referring to the point of delivery of potable water.

2.3 blend: A treatment product composed of two or more individual chemicals that do not react with one another.

2.4 by-product: A contaminant produced secondarily to the production of a principal compound.

2.5 contaminant: Any physical, chemical, biological, or radiological substance or matter in water.

NOTE – Consistent with the definition in the federal Safe Drinking Water Act, a contaminant can have either a beneficial or detrimental effect on the potability of water.

2.6 direct additive: A drinking water treatment chemical and any of its contaminants added directly to water during the production of drinking water.

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[6] Organization for Economic Cooperation and Development, 2 Rue Andre-Pascal, 75775 Paris Cedex 16, France www.oecd.org

[7] USEPA, Environmental Monitoring and Support Laboratory, Cincinnati, OH 45268 www.epa.gov

[8] Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402 www.gpo.gov

[9] USFDA, 5600 Fishers Lane, Rockville, MD 20857 www.fda.gov

2.7 drinking water: Water intended for human consumption.

2.8 evaluation dose: The concentration of a direct additive used to evaluate the impurities imparted to drinking water.

2.9 good manufacturing practice: The practice of maximizing the purity of the product by maintaining and practicing appropriate quality control and quality assurance procedures.

2.10 indirect additive: A contaminant that is extracted into drinking water through contact with surfaces of materials or products used for drinking water treatment, storage, transmission, or distribution.

2.11 manufacturer: A corporation, company, or individual that produces, formulates, packages, relabels, or repackages direct additives.

2.12 maximum contaminant level (MCL): The maximum concentration of a contaminant permitted in a public drinking water supply as defined by the federal Safe Drinking Water Act.

NOTE – If the manufacturer requests review relevant to alternate regulatory requirements, the certifying agency can consider alternative regulatory levels, e.g. Canadian Maximum Acceptable Concentrations (MACs).

2.13 maximum use level: The maximum concentration of a direct additive that has been found to be acceptable under this Standard.

2.14 normalization: The process of adjusting laboratory results to account for differences between laboratory and at-the-tap exposures.

2.15 normalized concentration: A value for a contaminant concentration from a laboratory evaluation that has been adjusted to reflect the contaminant concentration at-the-tap.

2.16 single product allowable concentration (SPAC): The maximum concentration of a contaminant in drinking water that a single product is allowed to contribute under annex A of this Standard.

2.17 total allowable concentration (TAC): The maximum concentration of a non-regulated contaminant permitted in a public drinking water supply as defined by annex A of this Standard.

3 General requirements

3.1 General

Direct additives shall be evaluated and tested in accordance with annexes A and B. The SPAC of a contaminant shall be calculated as outlined in annex A. Under the provisions of this Standard, a product shall not contribute any contaminant to drinking water in excess of the contaminant's SPAC.

Direct additives under this Standard shall be:

- the treatment or water supply product itself;
- the product-specific contaminants listed in each of the product sections of this Standard; and
- other constituents as identified in the formulation review.

Figure 3.1 provides an overview of the evaluation process.

3.2 Formulation submission and review

3.2.1 The manufacturer shall submit, at a minimum, the following information for each product:

– a proposed maximum use level for the product, which is consistent with the requirements of annex A;

– 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 abstract number (CAS number), chemical name, and supplier for each chemical present in the formulation; and

– a list of known or 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;

– selected spectra (e.g. UV/visible, infrared) shall be required for some additive products or their principle constituents; and

– when available, a list of published and unpublished toxicological studies relevant to the treatment chemical and the chemicals and impurities present in the treatment chemical.

3.2.2 The formulation information provided by the manufacturer shall be reviewed, and this review shall determine any formulation-dependent contaminants to be evaluated in addition to the product-specific analytes identified in each product section (see 4 through 8).

3.3 Sampling, preparation, and analysis of samples

Sample collection, preparation, and analysis shall be done in accordance with methods outlined in annex B.

3.4 Contaminant concentrations

3.4.1 Individual treatment chemicals

Contaminant concentrations for individual treatment chemicals shall be no greater than the limits established in accordance with annex A.

3.4.2 Blends of treatment chemicals

For products which are blended entirely of treatment chemicals which have met the requirements of this Standard as individual treatment chemicals, contaminant concentrations from the individual treatment chemicals shall be no greater than the limits established in accordance with annex A.

For products which are blended using one or more treatment chemical(s) which have not met the requirements of this Standard, contaminant concentrations of the blended product shall be no greater than the limits established in accordance with annex A.

Evaluation of products that are blends shall also consider whether contaminant concentrations from the individual chemicals are changed by the use of the chemicals in combination.

3.5 Product labeling

The product container shall be clearly identified with the manufacturer's name and address, product identification, net weight, and lot number. When applicable, the manufacturer shall specify any special precautions for handling, storage, and use.

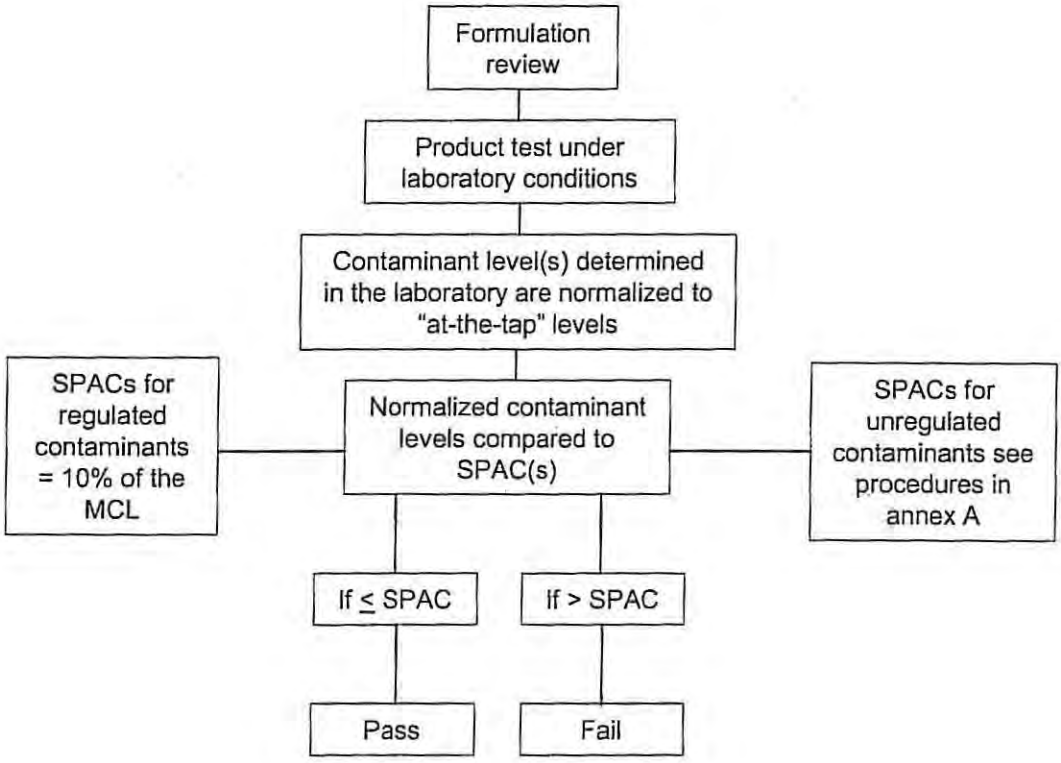

Figure 3.1 – Product evaluation overview

Annex A
(normative)

Toxicology review and evaluation procedures

A.1 General requirements

This annex defines the toxicological review and evaluation procedures for the evaluation of substances imparted to drinking water through contact with drinking water system components. It is intended to establish the human health risk, if any, of the substances imparted to drinking water under the anticipated use conditions of the product. Annex D (normative) of this Standard contains evaluation criteria that have been determined according to the requirements of this annex.

The following general procedure shall be used to evaluate drinking water substances under this Standard:

a) 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 substance is available.

b) When a quantitative risk assessment is available, the reviewer shall determine whether the assessment is currently used in the promulgation of a drinking water regulation or published health advisory for the substance (see the requirements of annex A, section A.3).

– If the assessment is used in the promulgation of a drinking water regulation, the Single Product Allowable Concentration (SPAC) shall be derived from the regulatory value(s); or

– If the assessment is not the basis of a drinking water regulation, the assessment and its corresponding reference dose shall be reviewed for its appropriateness in evaluating the human health risk of the drinking water substance.

NOTE – When reviewing an assessment used in the promulgation of a drinking water regulation, it is recommended that the regulatory authority be contacted to verify the currency of the assessment under consideration.

c) If a published and peer reviewed quantitative risk assessment is not currently available for the substance, the Total Allowable Concentration (TAC) and SPAC shall be derived after review of the available toxicology data for the substance (see annex A, section A.4).

– When the data requirements for qualitative risk assessment are satisfied (see annex A, section A.4.2 and table A1), a qualitative risk assessment shall be performed according to annex A, section A.7; or

– When the data requirements for quantitative risk assessment are satisfied (see annex A, section A.4.3 and table A2), a quantitative risk assessment shall be performed according to annex A, section A.7.

Annex A, figure A1 provides an overview of the toxicity data review requirements of this annex.

A.2 Definitions

A.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 BMD_X (adapted from Barnes et al., 1995).

NOTE – For the purposes of this Standard, the benchmark dose shall be calculated at the 10% response level.

A.2.2 continuous data: A measurement of effect that is expressed on a continuous scale, e.g., body weight or serum enzyme levels (USEPA, 1995).

A.2.3 critical effect: The first adverse effect, or its known precursor, that occurs as the dose rate increases (USEPA, 1994).

A.2.4 ED_{10}: Effective dose 10; a dose estimated to cause a 10% response in a test population (USEPA, 1996a).

A.2.5 genetic toxicity: Direct interaction with DNA that has the potential to cause heritable changes to the cell.

A.2.6 health hazards (types of) (USEPA, 1994 and 1999)

A.2.6.1 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.

A.2.6.2 allergic reaction: Adverse reaction to a chemical resulting from previous sensitization to that chemical or to a structurally similar one.

A.2.6.3 chronic effect: An effect that occurs as a result of repeated or long-term (chronic) exposures.

A.2.6.4 chronic exposure: Multiple exposures occurring over an extended period of time or a significant fraction of the animal's or the individual's lifetime.

A.2.6.5 chronic toxicity: The capability of a substance to cause adverse human health effects as a result of chronic exposure.

A.2.6.6 irreversible toxicity: Toxic effects to a tissue that cannot be repaired.

A.2.6.7 local toxicity: Effects that occur at the site of first contact between the biological system and the toxicant.

A.2.6.8 reversible toxicity: Toxic effects which can be repaired, usually by a specific tissue's ability to regenerate or mend itself after chemical exposure.

A.2.6.9 systemic toxicity: Effects that are elicited after absorption and distribution of a toxicant from its entry point to its target tissue.

A.2.7 LED_{10}: Lowest effective dose 10; the lower 95% confidence limit on a dose estimated to cause a 10% response in a test population (USEPA, 1996a).

A.2.8 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 (USEPA, 1994).

A.2.9 margin of exposure (MOE): The LED_{10} or other point of departure, such as a NOAEL, divided by the environmental dose of interest (USEPA, 1996a).

A.2.10 model: A mathematical function with parameters that can be adjusted so that the function closely describes a set of empirical data. A mathematical or mechanistic model is usually based on biological or physical mechanisms, and has model parameters that have real world interpretation. Statistical or empirical models are curve-fitted to data where the math function used is selected for its numerical

properties and accuracy. Extrapolation from mechanistic models (e.g., pharmacokinetic equations) usually carries higher confidence than extrapolation using empirical models (e.g., logit) (USEPA, 1994).

A.2.11 no observed adverse effect level (NOAEL): An exposure concentration at which no statistically or biologically significant increases in the frequency or severity of adverse effects are observed between an exposed population and its appropriate control. Some physiological effects may be produced at this concentration, but they are not considered as toxicologically significant or adverse, or as precursors to adverse effects (USEPA, 1994).

A.2.12 nonregulated substance: A substance for which a statutory concentration limit does not exist.

A.2.13 peer review: A documented critical review of a scientific or technical work product conducted by qualified individuals or organizations who 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 satisfies established requirements (USEPA, 1998).

A.2.14 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 LED_{10}, which is the lower 95% confidence limit on a dose associated with 10% extra risk (adapted from Barnes et al., 1995).

A.2.15 qualitative risk assessment: An estimation of the risk associated with the exposure to a substance using a non-quantitative methodology.

A.2.16 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 (USEPA, 1995).

A.2.17 quantitative risk assessment: An estimation of the risk associated with the exposure to a substance using a methodology that employs evaluation of dose response relationships.

A.2.18 range of extrapolation: Doses that are outside of the range of empirical observation in animal studies, human studies, or both (adapted from Barnes et al., 1995).

A.2.19 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).

A.2.20 reference dose (RfD): An estimate (with uncertainty spanning approximately an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (USEPA, 1994).

A.2.21 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.

A.2.22 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).

A.2.23 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).

A.2.24 treatment technique: A technology or one or more procedures used to control the concentration of a substance in a drinking water supply when it is neither technically nor economically feasible to ascertain the concentration of the substance (U.S. Safe Drinking Water Act, 1996).

A.2.25 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 USEPA, 1994).

A.3 Data requirements for published risk assessments

A.3.1 General requirements

Evaluation of all published risk assessments shall include review of the written risk assessment document and a determination of whether additional toxicity data exist that were 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 annex A, section A.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 annex A, section A.4 with respect to selection of uncertainty factors or other assumptions.

A.3.2 Substances regulated by USEPA or Health Canada

If a substance is regulated under the USEPA's National Primary Drinking Water Regulations and USEPA has finalized a Maximum Contaminant Level (MCL) or other means of regulation such as a treatment technique (see annex A, section A.2.18), no additional collection of toxicological data shall be required prior to performance of the risk estimation (see annex A, section A.6.1). Where Health Canada has finalized a Maximum Allowable Concentration (MAC), no additional toxicological evaluation shall be required prior to performance of the risk estimation (see annex A, section A.6.1). Annex D contains a list of regulatory values (MCL or MAC) and their corresponding SPACs. This list includes consensus evaluation criteria for those substances that are regulated by both countries.

A.3.3 Substances regulated by other agencies

If a substance is regulated by agencies including the U.S. Food and Drug Administration (Code of Federal Regulations, Title 21 Food and Drug Regulations), or state, national, or international regulatory bodies other than those specified in annex A, section A.3.2, the relevance of the regulation to drinking water shall be evaluated. This evaluation shall include a review of the quantitative risk assessment that supports the regulation, and a determination of whether additional toxicity data exist that have not been considered in the current assessment. No additional collection of toxicological data shall be required when the regulation provides sufficient information for performance of the risk estimation (see annex A, section A.6.1). If additional toxicity data are identified which were not considered in the current risk assessment, a revised risk assessment incorporating those data shall be performed as indicated in annex A, sections A.4 and A.7.

A.3.4 Evaluation of multiple published risk assessments

When multiple published assessments are available for a specific substance, 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 through drinking water. 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) which 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:

- USEPA;
- Health Canada;
- international bodies such as the World Health Organization (WHO) or the International Programme on Chemical Safety (IPCS);
- European bodies such as the Drinking Water Inspectorate (DWI) and KIWA; and
- entities such as other federal or state regulatory agencies, private corporations, industry associations, or individuals.

A.4 Data requirements for new or updated risk assessments

A.4.1 General requirements

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. To more fully understand 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, as well as studies using routes of exposure other than ingestion. 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 recent adopted toxicity testing protocols such as those described by the Organization For Economic Cooperation and Development (OECD), U.S. Environmental Protection Agency, and U.S. Food and Drug Administration (FDA). All studies shall be reviewed for compliance with Good Laboratory Practice (21 CFR, Pt 58/40 CFR, Pt 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 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. The quality and quantity of toxicity data available for the substance shall determine whether the evaluation is performed using a qualitative risk assessment approach (see annex A, section A.4.2) or a quantitative risk assessment approach (see annex A, section A.4.3).

A.4.2 Data requirements for qualitative risk assessment

Toxicity testing requirements for the qualitative risk assessment procedure are defined in annex A, table A1. A minimum data set consisting of a gene mutation assay and a chromosomal aberration assay shall be required for the performance of a qualitative risk assessment. Modifications in the specified toxicity testing requirements (inclusions or exclusions) shall be permitted when well supported by peer reviewed scientific judgment and rationale.

NOTE – Modifications may include, but are not limited to, the following types of considerations: alternate assays of genetic toxicity, and supplemental toxicity studies other than those specified.

Required studies and available supplemental studies shall be reviewed in order to perform a qualitative risk estimation in accordance with annex A, section A.7.2.

A.4.3 Data requirements for quantitative risk assessment

Toxicity testing requirements for the quantitative risk assessment procedure are defined in annex A, table A2. 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 annex A, table A2. 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 toxicity 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 annex A, section A.7.3.

Additional studies for the evaluation of reproductive and developmental toxicity (as specified in annex A, table A2) 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.

A.5 Data requirements for evaluating short-term exposures

Extractants from products used in contact with drinking water may be elevated initially, but rapidly decline with continued product contact with water. Examples include, but are not limited to, solvent-containing coatings and solvent cements. 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. The short-term exposure period shall be defined as the first 14 d of in-service life of the product.

Sound scientific judgment shall be used to determine whether calculation of a Short-term Exposure Level (STEL) is appropriate for a 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 14-d post-treatment observation period, clinical observations, hematology and clinical chemistry, and gross pathology (preferably an oral study in rodents);

– reproduction or developmental assays (for substances having 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 annex A, section A.8.

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. The STEL shall be calculated using assumptions to protect for a child's exposure to the contaminant in the absence of data that demonstrate adults are more sensitive than children. In the absence of appropriate data to calculate a STEL, see annex A, section A.7.1.2.

A.6 Risk estimation for published assessments

Calculation of the SPAC is intended to account for the potential contribution of a single substance by multiple products or materials in the drinking water treatment and distribution system. In any given drinking water treatment and distribution system, a variety of products and materials may be added to or contact the treated water prior to ingestion. The SPAC calculation is intended to ensure that the total contribution of a single substance from all potential sources in the drinking water treatment and distribution system does not exceed its acceptable concentration.

A.6.1 SPAC calculation for regulated substances

To calculate the SPAC, an estimate of the number of potential sources of the substance from all products in the drinking water treatment and distribution system shall be determined. The SPAC shall be calculated as follows:

$$\text{SPAC (mg/L)} = \frac{\text{promulgated regulatory value (mg/L)}}{\text{estimated number of drinking water sources}}$$

In the absence of specific data regarding the number of potential sources of the substance in the drinking water treatment and distribution system, the SPAC shall be calculated as 10% of the promulgated regulatory value.

A.6.2 SPAC calculation for other published risk assessments

Review of the risk assessment shall include evaluation of the risk estimation, if one is provided. If the existing risk estimation has been performed in a manner consistent with the procedures in annex A, section A.7.3 for non-carcinogenic or carcinogenic endpoints, the SPAC shall be calculated as follows:

$$\text{SPAC (mg/L)} = \frac{\text{existing risk estimation (mg/L)}}{\text{estimated number of drinking water sources}}$$

In the absence of specific data regarding the number of potential sources of the substance in the drinking water treatment and distribution system, the SPAC shall be calculated as 10% of the existing risk estimation.

If the existing risk estimation is not consistent with annex A, section A.7.3, or a risk estimation is not provided, a TAC and SPAC shall be calculated for the substance according to the procedures in annex A, section A.7.3.

A.7 Risk estimation using new and 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 annex A, section A.4). When available toxicity data are insufficient to perform the qualitative or quantitative risk assessments, or when toxicity data are available, but the normalized contaminant concentration does not exceed the applicable threshold of evaluation value, a threshold of evaluation shall be determined for the substance according to annex A, section A.7.1 if applicable. For all other data sets, the risk estimation shall be performed according to annex A, sections A.7.2 or A.7.3.

A.7.1 Threshold of evaluation

The following thresholds of evaluation shall be considered when available toxicity data do not meet the minimum requirements to perform a risk estimation using either the qualitative or quantitative approaches. Application of the threshold of evaluation shall also be considered for the evaluation of normalized contaminant concentrations which do not have existing risk assessments, and which do not exceed the defined threshold of evaluation concentrations. In this case, a qualitative review of the available data shall be performed to determine whether adverse health effects can result at the threshold of evaluation exposure concentrations defined in annex A, section A.7.1.1.

A.7.1.1 Threshold of evaluation for chronic exposure

Performance of a risk assessment shall not be required for an individual substance having a normalized concentration less than or equal to the following threshold of evaluation values:

- static normalization conditions:

  toxicity testing shall not be required for an individual substance having a normalized concentration less than or equal to the threshold of evaluation value of 3 µg/L.

- flowing normalization conditions:

  toxicity testing shall not be required for an individual substance having a normalized concentration less than or equal to the threshold of evaluation value of 0.3 µg/L.

These threshold of evaluation values shall not apply to any substance for which available toxicity data and sound scientific judgment such as structure activity relationships indicate that an adverse health effect results at these exposure concentrations.

A.7.1.2 Threshold of evaluation for short-term exposure

If an appropriate short-term toxic effect is not identified by the available data, the initial (D 1) laboratory concentration shall not exceed 10 µg/L. This threshold of evaluation value shall not apply to any chemical for which available toxicity data and sound scientific judgment, such as structure activity relationships, indicate that an adverse health effect can result at the 10 µg/L concentration upon short-term exposure to the chemical.

A.7.2 TAC determination for qualitative risk assessment

TACs for qualitative risk assessments shall be determined as indicated in annex A, table A3.