EPA's Safer Choice Program
Master Criteria for Safer Ingredients

Version 2.1
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Office of Pollution Prevention & Toxics
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1 Introduction

1.1 Purpose

The Safer Choice Master Criteria for Safer Ingredients (Master Criteria) are comprehensive, science-based criteria designed to ensure that the safest possible ingredients are used in Safer Choice- and Design for the Environment (DfE)-certified products. Safer Choice evaluates every ingredient in a formulation within its functional class context and based on its key, distinguishing human health and environmental characteristics. In this way, potential product ingredients can be viewed as part of a continuum of improved or safer ingredient choices. These criteria also enhance the transparency of the Safer Choice program.

The Master Criteria make it possible to draw a line demarcating the greener or "low-concern" end of the continuum of chemical safety. To define low concern, Safer Choice uses toxicological thresholds established by highly respected health and environmental protection authorities, including the United Nations' Globally Harmonized System (GHS) for the Classification and Labeling of Hazard Substances and the U.S. EPA's New Chemicals Program. For functional classes where no low-concern ingredients currently exist, Safer Choice works with its stakeholders to carefully modify the Master Criteria in a way that allows for ingredient choices while ensuring the safest possible ingredients in that functional class. These criteria were designed for use in distinguishing safer chemicals for the Safer Choice program.

Safer Choice and DfE product review is chemistry and toxicology intensive, calling on the extensive expertise of the EPA's Office of Pollution Prevention and Toxics (OPPT). The Office's depth of expertise helps ensure that chemicals are fully and accurately characterized based on the best available information. Information for the review is drawn from peer-reviewed literature, primary source materials, hazardous chemical lists, Agency databases, and predictive tools which estimate potential human health and environmental concerns based on a chemical's structural and/or biological similarity to known chemicals of concern. EPA will consider all sources of developing information, such as the Endocrine Disruptor Screening Program or enhancements to estimation models such as EPI Suite™ that occur over time.

Per Section 4.3 of this document, EPA has updated the weblinks and references cited in these Criteria to incorporate the most recent version as of October 2024 of each GHS and other testing reference. As part of this update, EPA has removed references to authoritative lists that are no longer in use, including the EU Risk Phrases. For additional information on the removal of the EU Risk Phrases, please see Section 4.4 of this document. Additionally, EPA has incorporated references to the use of New Approach Methods (NAMs), per Section 5.2 of the Safer Choice and Design for the Environment (DfE) Standard (2024) [1]. All thresholds and attributes of concern in the Master Criteria remain unchanged.

1.2 Development

The Master Criteria were developed by the EPA's Safer Choice program. The contents of these criteria, including definitions and toxicological preferences, were developed to facilitate use of safer chemistry under the Safer Choice program.

1.3 Scope

In the Safer Choice program, the Master Criteria serve as the primary tool to advance Green Chemistry in product formulation and to implement Informed Substitution, the reasoned transition from a chemical of particular concern to safer chemicals or non-chemical alternatives. Safer Choice will use the Master Criteria to review all product ingredients (and their chemical components). Where Safer Choice has developed more customized criteria for specific functional classes of chemicals (e.g., surfactants, solvents, etc.), those criteria will apply. All chemicals in products designed for direct release to the environment (e.g., graffiti removers and marine cleaners) must also pass the Criteria for Environmental Toxicity and Fate for Chemicals in Direct Release Products.

2 General Requirements

2.1 Data for all relevant routes of exposure will be evaluated.

2.2 The GHS criteria and data evaluation approach and EPA risk assessment guidance will inform professional judgment in the review of both no observed adverse effect levels/concentrations (NOAEL/NOAEC) and lowest observed adverse effect levels/concentrations (LOAEL/LOAEC). NOAEL/NOAEC and LOAEL/LOAEC values are preferred over no observed effect levels/concentrations (NOEL/NOEC) and lowest observed effect levels/concentrations (LOEL/LOEC). In reviews that include conflicting data, a weight of evidence approach will determine a pass or fail.

2.3 Use of existing data should follow the EPA High Production Volume (HPV) Chemical Challenge Program and OECD HPV Programme data adequacy guidelines: Methodology for Risk-Based Prioritization Under ChAMP [2].

2.4 EPA will perform an additional in-depth review of a chemical under certain conditions. Conflicting data on a chemical, detection in bio- or environmental monitoring studies, or presence on a flagging list will trigger such a review. The additional review will apply GHS criteria and other criteria explained in this document.

3 Terms

3.1 **Acute aquatic toxicity** means the intrinsic property of a substance to be injurious to an organism in a short-term, aquatic exposure to that substance.

3.2 **Acute mammalian toxicity** refers to those adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.

3.3 **Adverse effect:** A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge.

3.4 **Attribute:** The general property of the chemical that is being evaluated (e.g., acute mammalian toxicity, persistence).

3.5 **Bioaccumulation** is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment, e.g., dietary and ambient environment sources. Bioaccumulation is the net result of competing processes of chemical uptake into the organism at the respiratory surface and from the diet and chemical elimination from the organism including respiratory exchange, fecal egestion, metabolic biotransformation of the parent compound and growth dilution.

3.6 **Biodegradation** is a process in which the destruction of the chemical is accomplished by the action of a living organism.

3.7 A chemical is termed **carcinogenic** if it is capable of increasing the incidence of malignant neoplasms, reducing their latency, or increasing their severity or multiplicity.

3.8 A **chemical** (or **compound**) is identified by its Chemical Abstract Service (CAS) number.

3.9 **Chronic aquatic toxicity** means the intrinsic property of a substance to cause adverse effects to aquatic organisms during aquatic exposures which are determined in relation to the life-cycle of the organism.

3.10 A **compound** (or **chemical**) is identified by its Chemical Abstract Service (CAS) number.

3.11 **Criteria:** Endpoints and cutoffs for attribute information. Example: oral acute mammalian toxicity LD50 must be > 50 mg/kg. Data quality requirements (including acceptable test methods and information sources) are developed for all criteria.

3.12 **Degradation product:** Compound resulting from transformation of a chemical substance through chemical, photochemical, and/or biochemical reactions.

3.13 **Dermal sensitizer:** A substance that will lead to an allergic response following skin contact.

3.14 **Developmental toxicity:** Adverse effects in the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.

3.15 **EC50:** The concentration which produces effects in 50% of organisms.

3.16 An **endocrine disruptor** is an external agent that interferes in some way with the role of natural hormones in the body. An agent might disrupt the endocrine system by affecting any of the various stages of hormone production and activity, such as by preventing the synthesis of

hormones, by directly binding to hormone receptors, or by interfering with the natural breakdown of hormones.

3.17 **Estimated concentration three (EC3):** Estimated concentration of a test substance needed to produce a stimulation index of three in the local lymph node assay, a test used to evaluate dermal sensitization.

3.18 **Flagging list:** A publicly available list of chemicals that may have potential hazard concerns as identified by the authors of that list.

3.19 **Genotoxicity:** The more general terms genotoxic and genotoxicity apply to agents or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Genotoxicity test results are usually taken as indicators for mutagenic effects.

3.20 An **ingredient** may be one chemical or a blend of multiple chemicals that are intentionally added.

3.21 **Inorganic phosphate:** This category includes all inorganic soluble forms of phosphates, such as, phosphoric acid [PO_4H_3 or OP(=O)(O)O] and its salts or phosphate salts, pyrophosphates, polyphosphates, and organic and inorganic forms of phosphorous that can be oxidized to phosphates rapidly. Inorganic forms of phosphonic acid (H_2PO_3 or OP(=O)O) are not included in this category because monopotassium phosphonic acid [13977-65-6] has been shown not to be an algal nutrient, not to be a replacement for phosphate in algal growth medium, and not to cause exponential growth of green algae.

3.22 **LC50:** Median lethal concentration.

3.23 **LD50:** Median lethal dose.

3.24 **LOAEL:** Lowest Observed Adverse Effect Level.

3.25 **LOAEC:** Lowest Observed Adverse Effect Concentration.

3.26 **LOEC:** Lowest Observed Effect Concentration.

3.27 **LOEL:** Lowest Observed Effect Level.

3.28 **Metabolite:** Any substance produced by metabolism or by a metabolic process.

3.29 **Mutagen:** The term mutagenic and mutagen will be used for agents which induce permanent, transmissible changes in the amount, chemical properties, or structure of the genetic material. These changes may involve a single gene or gene segment, a block of genes, parts of chromosomes, or whole chromosomes. Mutagenicity differs from genotoxicity in that the change in the former case is transmissible to subsequent cell generations.

3.30 **Neurotoxicity:** An adverse change in the structure or function of the central and/or peripheral nervous system following exposure to a chemical, physical, or biological agent.

3.31 **New Approach Methodologies (NAMs):** Any technology, methodology, approach, or combination thereof that can be used to provide information on chemical hazard and risk assessment that avoids the use of intact animals.

3.32 **NOAEL:** No Observed Adverse Effect Level.

3.33 **NOAEC:** No Observed Adverse Effect Concentration.

3.34 **NOEC:** No Observed Effect Concentration.

3.35 **NOEL:** No Observed Effect Level.

3.36 **Persistence:** The length of time the chemical can exist in the environment before being destroyed (i.e., transformed) by natural processes.

3.37 **Reproductive toxicity:** The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but not be limited to, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems.

3.38 **Respiratory sensitizer:** A substance that will lead to hypersensitivity of the airways following inhalation of the substance.

3.39 **Stimulation Index (SI):** A value calculated to assess the skin sensitization potential of a test substance that is the ratio of the proliferation in treated groups to that in the concurrent vehicle control group.

3.40 **Suitable analog:** Suitable analogs will be based on a chemically (e.g., based on chemical structure) or biologically (e.g., based on metabolic breakdown, or likely mechanistic/mode of action considerations) similar chemical. Guidance for identifying a suitable analog can be found in OECD *Series on Testing and Assessment No. 80 Guidance on Grouping of Chemicals.* The analog used must be appropriate for the attribute being evaluated.

3.41 **Weight-of-evidence:** For the purposes of this document, weight-of-evidence refers to the process of considering the strengths and weaknesses of various pieces of information in reaching and supporting a conclusion concerning a property of the substance.

4 Preferences

4.1 When data are developed to meet the requirements for Repeated Dose Toxicity, EPA requests that a functional observational battery, such as OPPTS 870.6200: Neurotoxicity Screening Battery [3], be added to the test method to provide neurotoxicity information.

4.2 Data for the evaluation of chemicals under these criteria are preferred in the following order: 1) measured data on the specific chemical, 2) measured data from a suitable analog, 3) estimated data from appropriate models. Data requirements specific to each attribute are outlined in Section 4. The majority of measured data are expected to be from laboratory experiments. However, any available human data will be considered, e.g., Human Repeat Insult Patch Tests. Human data may require appropriate review for ethical treatment of the subjects.

4.3 The links and references in this document are current as of the publication date of these Criteria. The reviewer must use the most recent version of each authoritative list, EPA data interpretation guidance, and test protocol when reviewing a chemical against these criteria. In the case where a GHS reference in this document is superseded by a more recent version, EPA may choose to update these Criteria to incorporate that newer version. EPA will consider all sources of developing information that occur over time, such as the EPA Endocrine Disruptor Screening Program[1] [4, 5], enhancements to estimation models such as EPI Suite™ [6], and New Approach Methods (NAMs) identified for use under TSCA (per TSCA Section 4(h)(2)(C)) [7].

4.4 In October 2024, EPA removed references to authoritative lists that are no longer in use, including the EU Risk (R) Phrases. The EU Dangerous Substances Directive (67/548/EEC (DSD)), which outlined the use of R phrases, is no longer in effect as of June 1, 2015 [8]. The EU Classification, Labelling and Packaging (CLP) Regulation ((EC) No 1272/2008) amended the DSD, and is currently the only classification and labeling legislation in force in the EU [9].

[1] The Agency does not consider endocrine disruption to be an adverse endpoint per se, but as a step that could lead to toxic outcomes, such as cancer or adverse reproductive effects…." [5]

5 Attributes of Concern for All Chemicals

Each attribute listed below applies to all chemicals not covered by specific functional class criteria.

5.1 Acute Mammalian Toxicity

Criteria

Applying GHS criteria [10], a chemical does not pass the Criteria if the median lethal dose or concentration is less than or equal to those values listed in Table 1a. For inhalation studies, exposure duration should be at least four hours; the thresholds for inhalation are the same for exposures greater than four hours. Exposures of less than four hours will be evaluated on a case-by-case basis.

Table 1a – GHS Thresholds

Route (units)	Median Lethal Dose/Concentration
Oral, LD50 (mg/kg bw)	2,000
Dermal, LD50 (mg/kg bw)	2,000
Inhalation, LC50 (vapor/gas) (mg/L)	20
Inhalation, LC50 (dust/mist/fumes) (mg/L)	5

Additionally, a chemical does not pass the Criteria if it carries one of the following EU Risk Phrases, which align with the GHS thresholds in Table 1a:

Table 1b – Acute Mammalian Toxicity Authoritative Lists

Authoritative Body	Does not pass Safer Choice Criteria
EU Classification, Labeling, and Packaging (CLP) [11]	H300: Fatal if swallowed H301: Toxic if swallowed H302: Harmful if swallowed H310: Fatal in contact with skin H311: Toxic in contact with skin H312: Harmful in contact with skin H330: Fatal if inhaled H331: Toxic if inhaled H332: Harmful if inhaled

Data Requirements

All available data, measured and/or estimated, for the chemical and/or a suitable analog will be reviewed against the criteria using a weight-of-evidence approach.

Sources for Data Interpretation

- GHS Ch 3.1 Acute Toxicity [10].
- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here:

https://echa.europa.eu/information-on-chemicals/cl-inventory-database.[2]

[2] To access a list or search for substances carrying harmonized H phrases, click on " > CL Inventory" to open the search menu, and under "Discriminator" select "Harmonized C&L". Please note that this database also contains notified classifications, which are not considered part of the Authoritative List specified in this criteria document.

5.2 Carcinogenicity

Criteria

Chemicals considered carcinogens according to the authoritative lists in Table 2 do not pass the Criteria. Chemicals not on those authoritative lists, but that are known or presumed human carcinogens (Category 1), or suspected human carcinogens (Category 2) under GHS [12], do not pass. Chemicals with limited or marginal evidence of carcinogenicity in animals do not pass the Criteria.

Table 2 – Authoritative Lists and GHS Criteria

Authoritative Body	Does not pass Safer Choice Criteria
National Toxicology Program (NTP)	Known to be Human Carcinogen Reasonably Anticipated to be Human Carcinogen
U.S. Environmental Protection Agency (EPA)	(2005/1999) Carcinogenic to humans, Likely to be carcinogenic to humans, or Suggestive evidence of carcinogenic potential[3] (1996) Known/Likely (1986) Group A – Human Carcinogen, Group B – Probable human carcinogen, or Group C – Possible human carcinogen[3]
International Agency for Research on Cancer (IARC)	Group 1 – Carcinogenic to humans Group 2A – Probably carcinogenic to humans Group 2B – Possibly carcinogenic to humans[3]
EU Classification, Labeling, and Packaging (CLP) - Classifications [11]	Category 1A – Known to have carcinogenic potential for humans Category 1B – Presumed to have carcinogenic potential for humans Category 2 – Suspected human carcinogens
EU Classification, Labeling, and Packaging (CLP) - Hazard Statements [11]	H350: May cause cancer H350i: May cause cancer by inhalation H351: Suspected of causing cancer
NIOSH Occupational Carcinogen List	https://www.cdc.gov/niosh/docs/2017-100/pdf/2017-100.pdf?id=10.26616/NIOSHPUB2017100revised
Globally Harmonized System (GHS) [12]	Category 1A – Known to have carcinogenic potential for humans Category 1B – Presumed to have carcinogenic potential for humans Category 2 – Suspected human carcinogens

Data Requirements

All available data will be evaluated. Measured and/or estimated data, for the chemical and/or a suitable analog will be reviewed against GHS criteria using a weight-of-evidence approach.

Flagging Lists

All relevant data and information used to place a chemical on the following flagging lists will be considered when reviewing a listed chemical against the carcinogenicity criteria.

1. Substances flagged for endocrine disruption on the European Chemicals Agency Endocrine Disruptor

[3] Chemicals listed as "possibly carcinogenic to humans" are evaluated largely on animal studies. Safer Choice will consider appropriate data that show cancer concerns are not relevant to humans, e.g., because of an animal specific tissue effect or mode of action. If the data demonstrate that cancer concerns are not relevant to humans, that chemical can be considered under the Safer Choice Criteria.

Assessment List [13],
2. Substances prioritized for testing for endocrine disruption by the US EPA Endocrine Disruptor Screening Program [4],
3. Substances listed on the State of California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA) California Proposition 65 (Safe Drinking Water and Toxic Enforcement Act Of 1986) as Known to the State to Cause Cancer [14].

Sources for Data Interpretation

- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here: https://echa.europa.eu/information-on-chemicals/cl-inventory-database.[2]
- GHS Ch 3.6 Carcinogenicity [12].
- Section 2, Hazard Assessment in Guidelines for Carcinogen Risk Assessment (Risk Assessment Forum) (EPA 2005), https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment [15].
- The following link can be used to identify substances prioritized for testing for endocrine disruption by the European Commission: https://echa.europa.eu/ed-assessment [13].
- EPA Endocrine Disruptors Screening Program, available at: https://www.epa.gov/endocrine-disruption [4].
- Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens, available at: https://www.epa.gov/sites/default/files/2013-09/documents/childrens_supplement_final.pdf [16].

5.3 Genetic Toxicity

Criteria

Chemicals considered mutagens or genetic toxicants according to the authoritative lists in Table 3 do not pass the Criteria. Chemicals not on those authoritative lists, but which are classifiable as to their potential to induce heritable mutations in the germ cells of humans according to GHS [17] do not pass the Criteria. Evidence of mutagenicity in vitro and/or *in vivo* will also cause a chemical to fail the criteria. Effects to be considered include heritable germ cell mutagenicity (including gene mutation and chromosome mutation), germ cell genetic toxicity, and somatic cell mutagenicity or genetic toxicity.

Table 3 – Authoritative Lists and GHS Criteria

Authoritative Body	Does not pass Safer Choice Criteria
EU Classification, Labeling, and Packaging (CLP) - Classifications [11]	Category 1A – Substances known to induce heritable mutations in the germ cells of humans. Category 1B – Substances to be regarded as if they induce heritable mutations in the germ cells of humans. Category 2 – Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans[4]
EU Classification, Labeling, and Packaging (CLP) – Hazard Statements [11]	H340: May cause genetic defects H341: Suspected of causing genetic defects
Globally Harmonized System (GHS) [17]	Category 1A – Chemicals known to induce heritable mutations in germ cells of humans Category 1B – Chemicals which should be regarded as if they induce heritable mutations in the germ cells of humans Category 2 – Chemicals which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans

Data Requirements

All available data, including *in vivo*, *in vitro*, and epidemiological studies, will be evaluated. Measured and/or estimated data, for the chemical and/or a suitable analog will be reviewed against GHS criteria using a weight-of-evidence approach.

Sources for Data Interpretation

- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here: https://echa.europa.eu/information-on-chemicals/cl-inventory-database.[2]
- GHS Ch 3.5 Germ Cell Mutagenicity [17].

[4] Per EU guidance, chemicals classified as Category 3 substances may be placed in that category based on positive results in assays showing (a) mutagenic effects or (b) other cellular interaction relevant to mutagenicity. If a chemical is classified in Category 3(b) only and that classification appears overly conservative, then the submitter may request EPA expert review. In such as case, if EPA determines the data do not support a concern for possible mutagenic effects, then the chemical will pass the criteria.

5.4 Neurotoxicity

Criteria

Chemicals that are considered neurotoxicants under GHS [18] (see GHS guidance values in Table 4) do not pass the screen. Neurotoxicity is evaluated using the GHS chapter called Specific Target Organ Toxicity Repeated Exposure.

Table 4 – GHS Guidance Values

Route of Administration (units)	Guidance Value*
Oral (mg/kg-bw/day)	100
Dermal (mg/kg-bw/day)	200
Inhalation (vapor/gas) (mg/L/6h/day)	1.0
Inhalation (dust/mist) (mg/L/6h/day)	0.2
*The doses provided are for 90-day studies. Guidance values are tripled for chemicals evaluated in 28-day studies.	

Data Requirements

All available data, measured and/or estimated, for the chemical and/or a suitable analog will be reviewed against the criteria using a weight-of-evidence approach.

Sources for Data Interpretation

- Section 3, Hazard Characterization in *Guidelines for Neurotoxicity Risk Assessmen*t [19]; and
- GHS Ch. 3.9 Specific Target Organ Toxicity Repeated Exposure [18].

5.5 Repeated Dose Toxicity

Criteria

Chemicals that are considered repeated dose (systemic) toxicants under GHS [18] (see GHS guidance values in Table 5a) do not pass the Criteria. Repeated dose toxicity is evaluated using the GHS chapter called Specific Target Organ Toxicity Repeated Exposure.

Table 5a – GHS Guidance Values

Route of Administration (units)	Guidance Value*
Oral (mg/kg-bw/day)	100
Dermal (mg/kg-bw/day)	200
Inhalation (vapor/gas) (mg/L/6h/day)	1.0
Inhalation (dust/mist/fume) (mg/L/6h/day)	0.2
*The doses provided are for 90-day studies. Guidance values are tripled for chemicals evaluated in 28-day studies and similarly modified for studies of longer durations.	

Additionally, a chemical does not pass the Criteria if it is present one of the following authoritative lists:

Table 5b – Repeated Dose Toxicity Authoritative Lists

Authoritative Body	Does not pass Safer Choice Criteria
EU Classification, Labeling, and Packaging (CLP) – Hazard Statements [11]	H372: Causes damage to organs H373: May cause damage to organs

Data Requirements

All available data, measured and/or estimated, for the chemical and/or a suitable analog will be reviewed against the criteria using a weight-of-evidence approach.

Flagging Lists

All relevant data and information used to place a chemical on the following flagging lists will be considered when reviewing a listed chemical against the repeated dose toxicity criteria.

1. Substances flagged for endocrine disruption on the European Chemicals Agency Endocrine Disruptor Assessment List [13],
2. Substances prioritized for testing for endocrine disruption by the US EPA Endocrine Disruptor Screening Program [4].

Sources for Data Interpretation

- GHS Ch 3.9 Specific Target Organ Toxicity Repeated Exposure [18],
- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here: https://echa.europa.eu/information-on-chemicals/cl-inventory-database[2]
- The following link can be used to identify substances prioritized for testing for endocrine disruption by

the European Commission: https://echa.europa.eu/ed-assessment [13].
- EPA Endocrine Disruptors Screening Program, available at: https://www.epa.gov/endocrine-disruption [4].

5.6 Reproductive and Developmental Toxicity

Criteria

Chemicals that are considered reproductive or developmental toxicants under GHS criteria [18] and demonstrate adverse effects at doses at or below the values in Table 6a do not pass the Criteria.

Table 6a – TSCA 8(e) Guidance Values [2]

Route of Administration (units)	Guidance Value
Oral (mg/kg-bw/day)	250
Dermal (mg/kg-bw/day)	500
Inhalation (vapor/gas) (mg/L/6h/day)	2.5
Inhalation (dust/mist) (mg/L/6h/day)	0.5

Additionally, a chemical does not pass the Criteria if it carries one of the following EU Risk Phrases:

Table 6b – Reproductive and Developmental Toxicity Authoritative Lists

Authoritative Body	Does not pass Safer Choice Criteria
EU Classification, Labeling, and Packaging (CLP) - Classification 11][5]	Reproductive Toxicant: Category 1A– Known human reproductive toxicant Category 1B – Presumed human reproductive toxicant Category 2 – Suspected human reproductive toxicant
EU Classification, Labeling, and Packaging (CLP) – Hazard Statements [11][5]	H360: May damage fertility or the unborn child H361: Suspected of damaging fertility or the unborn child H362: May cause harm to breast-fed children

Data Requirements

All available data, measured and/or estimated, for the chemical and/or a suitable analog will be reviewed against the criteria using a weight-of-evidence approach. Following the approach in the SIDS Dossier [20], both fertility and developmental effects should be considered.

Flagging Lists

All relevant data and information used to place a chemical on the following flagging lists will be considered when reviewing a listed chemical against the reproductive and developmental toxicity criteria.

1. Substances flagged for endocrine disruption on the European Chemicals Agency Endocrine Disruptor Assessment List [13],
2. Substances prioritized for testing for endocrine disruption by the US EPA Endocrine Disruptor Screening Program [4],
3. Substances listed on the State of California Environmental Protection Agency, Office of

[5] The EU classification criteria do not currently consider a limit dose above which an adverse effect would not trigger classification. EPA will consider evidence demonstrating that a chemical carrying a reproductive/developmental toxicity risk phrase or listed as toxic to reproduction (in Table 6b) did not cause an adverse effect below the TSCA 8(e) Guidance Values listed in Table 6a. Such a chemical may be determined, upon EPA review, to pass the Safer Choice criteria for reproductive/developmental toxicity.

Environmental Health Hazard Assessment (OEHHA) California Proposition 65 (Safe Drinking Water and Toxic Enforcement Act Of 1986) as Known to the State to Cause Reproductive Toxicity [14].

Sources for Data Interpretation

- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here: https://echa.europa.eu/information-on-chemicals/cl-inventory-database.[2]
- GHS Ch 3.7 Reproductive Toxicity [18]
- Part A, Section 3, Hazard Characterization in *Guidelines for Reproductive Toxicity Risk Assessmen*t (EPA 1998), http://www.epa.gov/ncea/raf/pdfs/repro51.pdf [21].
- Part A, Section 3, Hazard Characterization in *Guidelines for Developmental Toxicity Risk Assessmen*t (EPA 1991), http://www.epa.gov/NCEA/raf/pdfs/devtox.pdf [22].
- The following link can be used to identify substances prioritized for testing for endocrine disruption by the European Commission: https://echa.europa.eu/ed-assessment [13]
- EPA Endocrine Disruptors Screening Program, available at: https://www.epa.gov/endocrine-disruption [4].

5.7 Respiratory Sensitization

Criteria

Chemicals considered respiratory sensitizers according to the authoritative list in Table 7 do not pass the Criteria. Chemicals not on that authoritative list, but that are classified under GHS do not pass the Criteria. Chemicals with limited evidence of respiratory sensitization potential including the presence of structural alerts do not pass the Criteria.

Table 7 – Authoritative Lists and GHS Criteria

Authoritative Body	Does not pass Safer Choice Criteria
EU Classification, Labeling, and Packaging (CLP) – Hazard Statements [11]	H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
Globally Harmonized System (GHS) [23]	Category 1A – high frequency of occurrence or sensitization rate in humans Category 1B – low to moderate frequency of occurrence or sensitization rate in humans

Data Requirements

Acknowledging that recognized animal models for the testing of respiratory hypersensitivity are not available at present, data on respiratory sensitization will normally be based on human evidence; all available data will be reviewed. EPA will search public literature and EPA-confidential data to support the review. Chemicals associated with hypersensitivity after appropriate clinical testing may not pass the criteria. See GHS guidance [23] for further details.

Flagging Lists

Chemicals, designated with the following classifications on the Association of Occupational and Environmental Clinics (AOEC) Exposure Code List, require review using all relevant and available data to support GHS classification. These AOEC Exposure Codes include the following:

1. G (generally accepted)
2. Rs (sensitizer-induced asthma)
3. Rr (reactive airway dysfunction syndrome or RADS)
4. Rrs (both Rs and Rr)

Sources for Data Interpretation

- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here: https://echa.europa.eu/information-on-chemicals/cl-inventory-database.[2]
- GHS Ch 3.4 Respiratory and Skin Sensitization [23].
- Association of Occupational and Environmental Clinics Exposure Code List, available from: http://www.aoecdata.org/Default.aspx [24].

5.8 Skin Sensitization

Criteria

Chemicals considered skin sensitizers according to the authoritative list in Table 8 do not pass the Criteria. Chemicals not on that authoritative list, but that are classified under GHS do not pass the Criteria.

Table 8 – Authoritative Lists and GHS Criteria

Authoritative Body	Does not pass Safer Choice Criteria
EU Classification, Labeling, and Packaging (CLP) [11]	H317: May cause an allergic skin reaction
Globally Harmonized System (GHS) [23]	Category 1A – high frequency of occurrence in humans and/or a high potency in animals Category 1B – low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals

Data Requirements

All available data, including *in vivo*, *in vitro*, and epidemiological studies, will be evaluated. Data from estimation models may be considered as part of the weight-of-evidence.

Sources for Data Interpretation

- EU Classification, Labeling, and Packaging (CLP) [11]: A list of substances carrying Hazard (H) Phrases can be found in Annex VI to the CLP regulation, available here: https://echa.europa.eu/information-on-chemicals/annex-vi-to-clp.
- The ECHA Classification & Labelling (C&L) Inventory also contains a searchable database of classification and labeling information on substances under CLP, available here: https://echa.europa.eu/information-on-chemicals/cl-inventory-database.[2]
- GHS Ch 3.4 Respiratory and Skin Sensitization [23].

5.9 Environmental Toxicity and Fate (ET&F)

Criteria

If a chemical is an acute aquatic toxicant (i.e., L/E/IC50 < 100 ppm), then it must biodegrade rapidly and not be bioaccumulative (see Table 12, lines 1-3). If a chemical has low aquatic toxicity (Table 12, line 4), then its half-life must be less than 60 days.

Table 12 – Environmental Toxicity and Fate

	Acute Aquatic Toxicity Value (L/E/IC50)[6,7,8]	Persistence (Measured in terms of level of biodegradation)	Bioaccumulation Potential
1	If ≤1 ppm…	…then may be acceptable if the chemical meets the 10-day window as measured in a ready biodegradation test without degradation products of concern…[9]	…and BCF/BAF <1000.
2	If >1 ppm and ≤10 ppm…	…then the chemical must meet the 10-day window as measured in a ready biodegradation test without degradation products of concern…[9]	
3	If >10 ppm and <100 ppm…	…then the chemical must reach the pass level within 28 days as measured in a ready biodegradation test without degradation products of concern…[9]	
4	If ≥100 ppm…	…then the chemical need not reach the pass level within 28 days as measured in a ready biodegradation test if there are no degradation products of concern[8] and its half-life < 60 days…	

Data Requirements

Acute aquatic toxicity: Measured data are preferred. ECOSAR estimations may be used along with data from a suitable analog(s). Data, whether measured or from analogs, are required for each of the following

[6] In general, there is a predictable relationship between acute aquatic toxicity and chronic aquatic toxicity for organic chemicals, i.e., chemicals that have high acute aquatic toxicity may also have high chronic aquatic toxicity at low concentrations [Rand, G.M., ed. *Fundamentals of Aquatic Toxicology*. 2nd ed. 1995, Taylor & Francis: Washington, DC.]. Since acute aquatic toxicity data are more readily available, the Safer Choice criteria use these data to screen chemicals that may be toxic to aquatic life. Where measured chronic toxicity data is available, it will be assessed with other data and applied in the screen based on the relationship between acute and chronic aquatic toxicity.

[7] A case-by-case approach focusing on rate of biodegradation and degradation products of concern will be implemented for chemicals toxic to aquatic organisms at ≤ 1ppm.

[8] For determining the aquatic toxicity of substances that are not toxic at their solubility limit, see ECOSAR Technical Reference Manual Figure 9, p. 17 (https://www.epa.gov/sites/default/files/2015-09/documents/ecosartechfinal.pdf); When a chemical may have effects at saturation as determined using the guidance in the ECOSAR manual, a weight-of-evidence approach in combination with US EPA expert review will be used. EPA may require additional testing including but not limited to solubility testing, chronic aquatic toxicity testing, or acute aquatic toxicity testing of analogs.

[9] Degradation products of concern are compounds with high acute aquatic toxicity (L/E/IC50 ≤ 10ppm) which mineralize <60% in 28 days.

groups of organisms: algae, aquatic invertebrates and fish (all fresh water). If only estimated data are available, the use of estimated data may be acceptable in combination with EPA expert review. Data for marine species may be added when available.

Bioaccumulation potential: Measured data are preferred. Data from a suitable analog is acceptable, and EPI Suite™ estimations (from the most current version) may be used when those data are unavailable. Results from both the BAF and BCF models should be considered. An estimated BAF is preferred to an estimated BCF for compounds where log $K_{ow} > 5$.

Persistence (measured as level of biodegradation): Measured data are preferred. In the case where measured data are unavailable, data from estimation models or a suitable analog will be accepted as follows:

1. If acute aquatic toxicity ≤ 1ppm: Biodegradability must be measured for the chemical or for a suitable analog. Biodegradability predictions from estimation models, such as EPI Suite™, will be used only to support weight-of-evidence.
2. If acute aquatic toxicity > 1ppm and ≤ 10ppm: Biodegradability must be measured for the chemical or for a suitable analog. Biodegradability predictions from estimation models, such as EPI Suite™, will be used only to support weight-of-evidence.
3. If acute aquatic toxicity > 10ppm and < 100ppm: Biodegradability must be measured for the chemical or for a suitable analog. Biodegradability predictions from estimation models, such as EPI Suite™, will be used only to support weight-of-evidence.
4. If acute aquatic toxicity ≥ 100pm: Biodegradability for the chemical or for a suitable analog are preferred. Biodegradability predictions from estimation models, such as EPI Suite™ (the most current version), may be acceptable.

5.10 Eutrophication

Criteria

The total level of phosphorus in the product will be limited to a maximum level of 0.5 weight % in the product as sold (measured as elemental phosphorus). Inorganic phosphates, as defined by the US EPA New Chemicals Program [25], cannot make up any portion of the 0.5 weight % of phosphorus.

Note: Inorganic phosphates as defined by the US EPA New Chemicals Program [25] will not be allowed in Safer Choice- and DfE-certified products. Eutrophication is a priority concern for EPA scientists, and inorganic phosphates can contribute to eutrophication of fresh water and estuarial ecosystems [25]. Given that the majority of Safer Choice- and DfE-certified products are disposed of down the drain, the likelihood of release to wastewater streams and eventually, water bodies, is high. EPA acknowledges contributions to the phosphorus load from cleaners are relatively small in comparison with other sources [26] and that phosphorus overload may not be an issue in all regions. The EPA policy is consistent with a commitment to reduce contributions of phosphorus, particularly inorganic phosphates, regardless of concentration.

6 Test Methods

The test methods in this section should be used to develop data for conducting chemical reviews based on the criteria in Section 4.

In addition to the tests below, per Section 5.2 of the Safer Choice and DfE Standard (2024), when possible, EPA encourages minimizing the use of new animal testing and instead encourages use of NAMs identified for use under TSCA (per TSCA Section 4(h)(2)(C)). The Safer Choice program may consider additional NAMs that meet EPA's criteria for scientific reliability and relevance on a case-by-case basis. The list and criteria can be found at https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/strategic-plan-reduce-use-vertebrate-animals-chemical.

6.1 Acute Mammalian Toxicity – Test Methods for GHS Review

- OPPTS Harmonized Guideline 870.1100: Acute oral toxicity [27];
- OPPTS Harmonized Guideline 870.1200: Acute dermal toxicity [28];
- OPPTS Harmonized Guideline 870.1300: Acute inhalation toxicity [29];
- OECD Test Guideline 420: Acute Oral Toxicity-Fixed Dose Method [30];
- OECD Test Guideline 423: Acute Oral Toxicity – Acute Toxic Class Method [31];
- OECD Test Guideline 425: Acute Oral Toxicity – Up-and-Down Procedure [32];
- OECD Test Guideline 402: Acute Dermal Toxicity [33]; and
- OECD Test Guideline 403: Acute Inhalation Toxicity [34].

6.2 Carcinogenicity – Test Methods for GHS Review

- OECD Test Guideline 451: Carcinogenicity Studies [35];
- OECD Test Guideline 453: Combined Chronic Toxicity/Carcinogenicity Studies [36];
- OPPTS Harmonized Guidelines 870.4200: Carcinogenicity [37];
- OPPTS Harmonized Guidelines 870.4300: Combined chronic toxicity/carcinogenicity [38]; and
- NTP 2 Year Study Protocol: "Specifications for the Conduct of Toxicity Studies by the Division of Translational Toxicology at the National Institute of Environmental Health Sciences" [39].

6.3 Genetic Toxicity – Test Methods for GHS Review

Per GHS [17], results from multiple, acceptable test methods must be used in conjunction for evaluation of genetic toxicity.

- OECD Test Guideline 471 (OPPTS 870.5100): Bacterial Reverse Mutation Test [40, 41];
- OECD Test Guideline 473 (OPPTS 870.5375): *In vitro* Mammalian Chromosome Aberration Test [42, 43];
- OECD Test Guideline 474 (OPPTS 870.5395): Mammalian Erythrocyte Micronucleus Test [44, 45];
- OECD Test Guideline 475 (OPPTS 870.5385): Mammalian Bone Marrow Chromosome Aberration Test [46, 47];
- OECD Test Guideline 476 (OPPTS 870.5300): *In vitro* Mammalian Cell Gene Mutation Test [48, 49];
- OECD Test Guideline 483 (OPPTS 870.5380): Mammalian Spermatogonial Chromosome Aberration Test [50, 51]; and
- OECD Test Guideline 486: Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *in vivo* [52]. This guideline does **NOT** substitute in the necessary minimum set for either the gene mutation or the chromosome aberration test.

6.4 Neurotoxicity – Preferred Test Methods for GHS Review

- OECD Test Guideline 424: Neurotoxicity Study in Rodents [53] and
- OPPTS Harmonized Guideline 870.6200: Neurotoxicity screening battery [3].

Neurotoxicity – Additional Test Methods for GHS Review

Additional evidence from OECD Test Guideline 426: Developmental Neurotoxicity Study [54] and OPPTS Harmonized Guideline: 870.6300 Developmental neurotoxicity study [55] can be used to screen chemicals for neurotoxicity.

6.5 Repeated Dose Toxicity – Preferred Test Methods for GHS Review

- OECD Test Guideline 408: Repeated Dose 90-Day Oral Toxicity Study in Rodents [56]
- OECD Test Guideline 409: Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents [57]
- OECD Test Guideline 411: Subchronic Dermal Toxicity: 90-day Study [58]
- OECD Test Guideline 413: Subchronic Inhalation Toxicity: 90-day Study [59]
- OPPTS Harmonized Guideline 870.3100: 90-Day oral toxicity in rodents [60]
- OPPTS Harmonized Guideline 870.3150: 90-Day oral toxicity in nonrodents [61]
- OPPTS Harmonized Guideline 870.3250: 90-Day dermal toxicity [62]
- OPPTS Harmonized Guideline 870.3465: 90-Day inhalation toxicity [63]

Repeated Dose Toxicity – Acceptable Test Methods for GHS Review

- OECD Test Guideline 407: Repeated Dose 28-day Oral Toxicity Study in Rodents [64]
- OECD Test Guideline 410: Repeated Dose Dermal Toxicity: 28-day Study [65]
- OECD Test Guideline 412: Repeated Dose Inhalation Toxicity: 28-day Study [66]
- OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test [67]
- OPPTS Harmonized Guideline 870.3050: Repeated dose 28-day oral toxicity study in rodents [68]
- OPPTS Harmonized Guideline 870.3200: 28-Day dermal toxicity [69]

6.6 Reproductive and Developmental Toxicity – Test Methods for GHS Review

Fertility test methods, preferred

- OECD Test Guideline 415: One-Generation Reproduction Toxicity Study [70] and
- OECD Test Guideline 416: Two-Generation Reproduction Toxicity Study [71]

Fertility test methods, acceptable

The following test methods may be used to identify reproductive toxicity, per GHS [18]:

- OPPTS Harmonized Guideline 870.3800: Reproduction and fertility effects [72];
- OECD Test Guideline 421: Reproduction/Developmental Toxicity Screening Test [73];
- OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test [67];
- OPPTS Harmonized Guideline 870.3550: Reproduction/developmental toxicity screening test [74]; and
- OPPTS Harmonized Guideline 870.3650: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [75].

Developmental toxicity test methods, preferred

- OECD Test Guideline 414: Prenatal Developmental Toxicity Study [76]

Developmental toxicity test methods, acceptable

The following test methods may be used to identify developmental toxicity, per GHS [18]:

- OPPTS Harmonized Guideline 870.3800: Reproduction and fertility effects [72];
- OECD Test Guideline 421: Reproduction/Developmental Toxicity Screening Test [73];

- OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test [67];
- OPPTS Harmonized Guideline 870.3550: Reproduction/developmental toxicity screening test [74]; and
- OPPTS Harmonized Guideline 870.3650: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [75].

6.7 Skin Sensitization – Preferred Test Methods for GHS Review

- OECD Test Guideline 406: Skin Sensitization [77]
- OECD Test Guideline 429: Skin Sensitization: Local Lymph Node Assay [78]
- OPPTS Harmonized Guideline 870.2600: Skin Sensitization [79]

6.8 Environmental Fate and Toxicity

6.8.1 Test Methods, Acute Aquatic Toxicity

A baseline data set is required that includes test data in algae, aquatic invertebrates, and fish. Additional aquatic toxicity data in other species or in marine species will also be reviewed if available.

Preferred Test Methods for Fish

- OECD Test Guideline 203: Fish, Acute Toxicity Test [80] and
- OPPTS Harmonized Guideline 850.1075: Fish acute toxicity test, freshwater and marine [81].

NOTE – EPA may request that the test be carried out using semi-static renewal or a flow-through system with mean measured concentration. Any new testing should be done in consultation with EPA.

Preferred Test Methods for Aquatic Invertebrates

- OECD Test Guideline 202, Part 1, Daphnia sp., Acute Immobilisation Test [82];
- OPPTS Harmonized Guideline 850.1010: Aquatic invertebrate acute toxicity test, freshwater daphnids [83]; and
- OPPTS Harmonized Guideline 850.1035: Mysid acute toxicity test [84].

NOTE – EPA may request that the test be carried out using semi-static renewal or a flow-through system with mean measured concentration. Any new testing should be done in consultation with EPA. A 96-hour Mysid shrimp acute toxicity test can be used in place of a daphnid acute toxicity test when the latter is not available.

Preferred Test Methods for Algae

- OECD Test Guideline 201, Alga, Growth Inhibition Test (and biomass) [85] and
- OPPTS Harmonized Guideline 850.4500: Algal toxicity, Tiers I and II (including growth inhibition and biomass) [86].

Alternative Test Methods, Acute Aquatic Toxicity

The following test methods may be considered, when relevant:

- OPPTS Harmonized Guideline 850.1085: Fish acute toxicity mitigated by humic acid [87];
- OPPTS Harmonized Guideline 850.1025: Oyster acute toxicity test (shell deposition) [88];
- OPPTS Harmonized Guideline 850.1045: Penaeid acute toxicity test [89];
- OPPTS Harmonized Guideline 850.1055: Bivalve acute toxicity test (embryo larval) [90]; and
- OPPTS Harmonized Guideline 850.4400: Aquatic plant toxicity test using *Lemna spp.* Tiers I and II [91].

6.8.2 Test Methods, Persistence (measured as biodegradation)

Data from experimental methods are generally preferred over estimations of persistence. For the purposes of screening safer chemicals in Table 12, rows 1-3, ready biodegradation tests are preferred. It is noted that simulation tests are likely to better describe the biodegradability of a chemical in specific environmental conditions, and these tests can provide information to evaluate the half-life of a chemical that is aquatically toxic at ≥100 ppm. Simulation tests may also contribute useful information in a weight-of-evidence evaluation for chemicals aquatically toxic < 100 ppm.

Preferred Test Methods for Persistence

- OECD Test Guideline 301: Ready Biodegradability (sections A-F) [92];
- OECD Test Guideline 310: Ready Biodegradability – CO2 in sealed vessels [93]; and
- OPPTS Harmonized Guideline 835.3110: Ready biodegradability [94].
- For chemicals where acute aquatic toxicity ≥100 ppm (i.e., line 4, Table 12), if the compound degrades by more than 40% in 28 days during one of the Ready Biodegradability tests specified above or by more than 60% in one of the Inherent Biodegradability tests detailed in OECD Test Guidelines 302 (A-C) [95, 96, 97] then the half-life of a chemical is likely to be less than 60 days [98].
- Simulation tests may also be used to determine the half-life of a chemical and may be useful in a weight-of-evidence evaluation for chemicals aquatically toxic at < 100ppm.
  - OECD Test Guideline 303A (OPPTS 835.3240): Aerobic Sewage Treatment: Activated Sludge Units [99, 100],
  - OECD Test Guideline 309 (OPPTS Harmonized Guideline 835.3190): Aerobic Mineralization in Surface Water - Simulation Biodegradation Test [101, 102],
  - OECD Test Guideline 314: Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater (Note: TG 314 uses elements of OECD TG 301, 303A, 309, 310, and 311) [103],
  - OPPTS Harmonized Guideline 835.3280–Simulation Tests to Assess the Primary and Ultimate Biodegradability of Chemicals Discharged to Wastewater [104],
  - OPPTS Harmonized Guideline 835.3170 - Shake Flask Die-Away Test [105], and
  - OPPTS Harmonized Guideline 835.3180 - Sediment/Water Microcosm Biodegradation Test [106].

Other Methods of Degradation

On a case-by-case basis, Safer Choice will consider other routes of degradation in the environment, such as hydrolysis or photolysis, and degradation in other relevant media, for example, soil or sediment. In evaluating such degradation studies, Safer Choice will consider the relevance of that degradation pathway to the chemical in question as well as the significance of the degradation.

6.8.3 Test Methods, Bioaccumulation

A field-measured BAF (located in the literature) is the most preferred data for indicating bioaccumulation.

Alternative Test Methods for Bioaccumulation

When a field-measured BAF is not available, the following test methods may be used:

- OECD Test Guideline 305: Bioconcentration: Flow-through Fish Test [107];
- OPPTS Harmonized Guideline 850.1710: Oyster BCF [108];
- OPPTS Harmonized Guideline 850.1730: Fish BCF [109];

Modeled data from sources such as EPI Suite™ [6] are acceptable when data are unavailable.

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