



CHEMFORWARD Guidance: Chemical Hazard Rating Version 2.1

FEBRUARY 2024

# Table of Contents

Table of Contents	.2
Introduction	. 3
Scores which do not require a full CHA	.4
F Hazard Band Chemicals	4
D Hazard Band Chemicals	. 5
Scores which require a full CHA	. 7
Endpoint Adjustments and Exemptions	.7
F Hazard Band Chemicals	8
D Hazard Band Chemicals	. 9
Data Gap Rules and U Hazard Band Chemicals1	10
C Hazard Band Chemicals1	10
B Hazard Band Chemicals1	11
A Hazard Band Chemicals1	11
Appendix A: List-based x* Exemptions	12
Candidate List of SVHC: Respiratory Sensitizing Properties	13
Candidate List of SVHC: Equivalent Concern	13
Per and polyfluoroalkyl Substances (PFAS)	14
PFAS x* Exemptions	14
Chlorinated Organic and Brominated Organic Compounds	15
Chlorinated and Brominated Organic Compounds Exemptions	15
Climatic relevance	16
Appendix B: Endpoint Adjustments and Exemptions1	18
Universal Exemptions for Endpoints that do not Influence Chemical Rating1	19
Adjusted Hazard Scores	19
Endpoint Data Gap Exemptions1	19
Appendix C: Data Gap Rules	21
Appendix D: Deriving Adjusted Hazard Classifications via Limited Exposure Assessment &	
Combined Scoring	23
Appendix E: Chemical Rating Assignment Flowchart	25

# Introduction

The Cradle to Cradle Certified (C2CC) Material Health Methodology was developed to assign ratings to individual chemicals and homogeneous materials that are subject to further review as part of the C2CC certification process. While ChemFORWARD provides a C2CC hazard table view, ChemFORWARD Chemical Ratings are hazard-based ratings and *do not represent* the full C2CC Material Health Methodology. ChemFORWARD Chemical Ratings do not not consider product use and associated exposure as is done in the full C2CC Material Health Methodology.

ChemFORWARD has prepared this concise Chemical Hazard Rating Guidance document, which provides qualification criteria for each of the ChemFORWARD Chemical Ratings and Hazard Bands, including hazard endpoint adjustments, exemptions, and minimum data requirements. The ChemFORWARD Harmonized Hazard Bands and corresponding Chemical Ratings are provided in **Figure 1** below.

These individual Chemical Ratings are useful in informing chemical suppliers and product manufacturers about the hazard profiles of the chemicals used in products. Chem*FORWARD* is committed to creating a database of chemical hazard assessments of safer alternative chemicals. We believe that providing Chemical Ratings for safer alternative chemicals will expedite green formulation, safe and circular product design, and meaningful product certification, including C2CC product certification.

Harmonized Hazard Band	Implications	Chemical Rating
Α	Low hazard and low risk	а
В	Some moderate hazards, low risk	b or c/b
С	Moderate hazard and moderate risk; or uncertainty that could result in moderate risk	x/c, x/c-CMR(2), grey/C, c/b-CRE
D	Moderate to high hazard; emerging regulatory risk (may be chemical-class based with uncertain hazard)	x/c-CMR(2)-E, x*, x-PMT, x-vPvM
F	High hazards and high risk in most scenarios	x-Reg, x-PBT, x-vPvB, x-PB, x-vPT, x/c-CMR(1), x/c-E
U	CHA completed with excessive data gaps, rating is not possible	grey
;	Request a CHA to inform a decision	No CHA

Figure 1. Summary of ChemFORWARD Harmonized Hazard Bands

# Scores which do not require a full CHA

Certain Chemical Ratings and Hazard Bands are assigned using list screening via Pharos API. List screening can be utilized to assign Hazard Bands associated with authoritative and/or well documented higher hazards (D & F) but not for safer chemistry Hazard Bands (A, B, C).

## F Hazard Band Chemicals

Chemicals of Regulatory Concern are assigned the Chemical Rating of x-Reg. Lists that trigger the x-Reg Chemical Rating and F Hazard Band include national and international regulations and treaties, and restricted substances lists restricting chemicals with a high level of human or environmental hazard (Table 1). Chemicals found on the following lists are commonly explicitly restricted in certification programs and are not expected to meet minimum criteria for "safer" definitions, such as EPA's Safer Choice Program and OECD's Minimum Criteria for Safer.

List & Link	Chemical Rating	Hazard Band
Annex XIV for CMR/Ds and PBTs	x-Reg	F
Candidate List of SVHCs: CMR/Ds		
Candidate List of SVHCs: PBTs		
Candidate List of SVHCs: vPvBs		
<u>Candidate List of SVHCs:</u> Endocrine Disrupting Properties (human health & environment)		
<u>Candidate list of SVHCs: Specific</u> <u>Target Organ Toxicity After</u> <u>Repeated Exposure (STOT-RE)</u>		
Annex XVII Entries 28-30 (CMR/Ds)		
Annex VI Carc. 1 or Muta. 1		
Stockholm POPs		
C2CC RSL for All Products Listed as NON-USE		
<u>Toxic metals and their</u> <u>compounds</u>		

#### Table 1. Lists qualifying for x-Reg Chemical Rating

## D Hazard Band Chemicals

Chemicals which can be identified as moderate to high human or environmental hazard either as a discrete chemical or as a member of a chemical class and those of emerging regulatory risk are automatically assigned the Chemical Rating of **x**\* during screening (Table 2). Chemicals meeting the following criteria are flagged in the x\* Chemical Rating and D hazard band; these chemicals may not meet minimum criteria for "safer" definitions, and may be targets for phase-out and innovation.

Exemptions may apply for x\* Chemical Ratings of chemicals in a representative chemical class (i.e. an individual PFAS) at the screening level. To qualify for an exemption, the chemical must undergo a full CHA in the ChemFORWARD repository. To qualify for an exemption, a chemical from the x\* Chemical Rating must have a full hazard table that will be evaluated to determine whether or not the hazards largely associated with the entire chemical class are applicable to the chemical in question.

See <u>Appendix A</u> for more information on x\* Exemptions.

### Table 2. Lists qualifying for x\* Chemical Rating

List & Link	Chemical Rating	Basis for listing	Eligible for exemption? (See <u>Appendix A</u> )	Hazard Band
PFAS - listed on OECD Comprehensive Global Database of PFASs	x*	Chemical class of concern	Yes	D
PFAS - listed on PFASIEPA: ToxCast Chemical Inventory		Chemical class of concern	Yes	
Chlorinated Organic Compound		Chemical class of concern	Yes	
Brominated Organic Compound		Chemical class of concern	Yes	
<u>US EPA- Ozone</u> Depleting <u>Substances</u>		Climatic Relevance of concern	No	
IPCC - Global Warming Chemicals (Third Report)		Climatic Relevance of concern	No	
<u>Candidate list of</u> <u>SVHCs: Respiratory</u> <u>Sensitising</u> <u>Properties</u>		Hazard of concern	No	
Candidate list of SVHCs: Equivalent Level of Concern Having Probable Serious Effects to Human Health or the Environment		Hazard of concern	No	

# Scores which require a full CHA

Most Chemical Ratings and Hazard Bands require a full CHA to determine the hazards relevant for the chemical in question. Chemical Ratings are assigned by evaluating the individual hazard endpoint scores using a tiered model which allows for appropriate adjustments and exemptions.

## **Endpoint Adjustments and Exemptions**

Individual endpoint classifications (e.g. oral carcinogenicity, dermal neurotoxicity, mutagenicity, fish toxicity, etc.) may be assigned an "adjusted" hazard classification by considering available information across all exposure routes for that hazard endpoint or by deriving combined hazard scores for closely related hazard endpoints; referred to as "adjusted hazard classifications."

Certain endpoints may be exempt from contributing to the minimum data requirements and/or influencing a chemical's final Chemical Rating or Hazard Band. Careful consideration of inherent potential for exposure, expected data availability, and the purpose of the endpoint (i.e. informational) is critical to assign exemptions.

See Appendix B for Endpoint Adjustment and Exemption Rules.

# F Hazard Band Chemicals

Table 3. CHA-based Chemical Ra	atings for F Hazard Band
--------------------------------	--------------------------

Chemical Rating	Hazard Band	Endpoint Criteria
x-PBT	F	Chemical's combined Persistence & Bioaccumulation score is RED or PURPLE and any adjusted human or environmental hazard classification is RED (except irritation or sensitization)
x-vPvB	F	Chemical's combined Persistence & Bioaccumulation classification is PURPLE.
x-PB	F	Chemical's combined Persistence & Bioaccumulation classification is RED.
x-vPT	F	Chemical's Persistence score is PURPLE and any adjusted human or environmental hazard classification is RED (except irritation or sensitization)
x/c-CMR(1)	F	Chemical has a RED adjusted hazard classification for at least one of the three CMR (Carcinogenicity, Mutagenicity, Reproductive/Developmental Toxicity) endpoints and the RED classification is associated with Category 1 <sup>1</sup> .
x/c-E	F	Chemical has a RED adjusted hazard classification for Endocrine Activity/Disruption.

<sup>&</sup>lt;sup>1</sup> GHS and C2CC diverge for Reproductive/Developmental Classification. C2CC allows for threshold values (e.g. NOAEL/LOAEL) to drive classification. ChemFORWARD relies on the C2CC guidance values for the purpose of scoring.

# D Hazard Band Chemicals

Table 4. CHA-based Chemical I	Ratings for D Hazard Band
-------------------------------	---------------------------

Chemical Rating	Hazard Band	Endpoint Criteria
x/c-CMR(2)-E	D	Chemical has a RED adjusted hazard classification for Reproductive/Developmental Toxicity where the RED classification is associated with Category 2 <sup>1</sup> in addition to a YELLOW adjusted hazard classification for Endocrine Activity/Disruption.
x*	D	See below
PFAS	D	Assessor-verified PFAS that do NOT meet exemption criteria
Chlorinated Organic Substances	D	Assessor-verified Chlorinated Organic Substances that do NOT meet exemption criteria
Brominated Organic Substances	D	Assessor-verified Brominated Organic Substances that do NOT meet exemption criteria
Climatically Relevant Substances	D	Assessor-verified RED for Climatic Relevance
x-PMT	D	Criteria under development for Persistent, Mobile & Toxic Chemicals
x-vPvM	D	Criteria under development for Very Persistent & Very Mobile Chemicals

## Data Gap Rules and U Hazard Band Chemicals

The remainder of Chemical Ratings and Hazard Bands are assigned to chemicals which are considered safer alternatives (C, B, and A) and can only be assigned if the minimum data requirements are met. Chemicals that do not meet F or D hazard band criteria nor the criteria below must be scored a grey Chemical Rating and U Hazard Band.

A, B, and C Hazard Band chemicals may contain exempt data gaps that do not influence the final scoring. The Chemical Rating "grey/c" contains non-exempt data gaps.

See <u>Appendix C</u> for Data Gap Rules.

Table 5. CHA-b	based Chemical	Ratings for U	Hazard Band
----------------	----------------	---------------	-------------

Chemical Rating	Hazard Band	Endpoint Criteria
grey	U	Chemical has multiple GREY adjusted hazard classifications, with insufficient information on human and environmental health endpoints to assign a hazard band.

## C Hazard Band Chemicals

#### Table 6. CHA-based Chemical Ratings for C Hazard Band

Chemical Rating	Hazard Band	Endpoint Criteria
x/c	С	Chemical has one or more RED adjusted hazard classifications.
x/c-CMR(2)	С	Chemical has a RED adjusted hazard classification for at least one of the three CMR endpoints and the RED classification is associated with Category 2 <sup>1</sup> .
grey/c	С	Chemical has one or more GREY adjusted hazard classifications.
c/b-CRE	С	Chemical has one or more YELLOW adjusted hazard classifications in Carcinogenicity, Reproductive or

		Developmental Toxicity, or Endocrine Activity/Disruption endpoints.
--	--	------------------------------------------------------------------------

## **B** Hazard Band Chemicals

B Hazard Band Chemicals capture both endpoint criteria and maximum score criteria for certain EXEMPT data gaps of concern (Carcinogenicity and Endocrine Activity/Disruption).

#### Table 7. CHA-based Chemical Ratings for B Hazard Band

Chemical Rating	Hazard Band	Endpoint Criteria
b	В	Chemical has no YELLOW adjusted hazard classifications but lacks long-term cancer studies and/or data regarding potential Endocrine Activity/Disruption.
c/b	В	Chemical has one or more YELLOW adjusted hazard classifications.

### A Hazard Band Chemicals

#### Table 8. CHA-based Chemical Ratings for A Hazard Band

Chemical Rating	Hazard Band	Endpoint Criteria
a	A	Chemical has no YELLOW or RED adjusted hazard classifications nor Cancer and/or Endocrine Activity/ Disruption data gaps.

For more information on how final endpoint classifications are assigned, see <u>Appendix D</u>: Deriving Adjusted Hazard Classifications via Limited Exposure Assessment & Combined Scoring

For more information on how final Chemical Ratings are assigned, see <u>Appendix E:</u> Chemical Rating Assignment Flowchart

# Appendix A: List-based x\* Exemptions

## Candidate List of SVHC: Respiratory Sensitizing Properties

Chemicals listed on ECHA's Candidate List of substances of very high concern (SVHC) for Authorisation with "reason for inclusion" cited as Respiratory Sensitising Properties (Article 57 (f) - human health) meet criteria in (EC) No 1907/2006 Article 57 as having "...scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e)...)" with regard to their hazard potential with regard to respiratory sensitization.

The Cradle to Cradle Material Health Assessment Methodology (MHAM) v4.0 lists all chemicals on the REACH Candidate List of SVHC as "chemicals of regulatory concern," and therefore will always receive a risk flag equal to the hazard flag.

<u>ECHA</u> defines a respiratory sensitiser as "an agent that will lead to hypersensitivity of the airways following inhalation exposure to that agent," and respiratory sensitisation/ hypersensitivity as "a term that is used to describe asthma and other related respiratory conditions (rhinitis, extrinsic allergic alveolitis), irrespective of the mechanism (immunological or non-immunological) by which they are caused."

Respiratory sensitization is a route-specific concern which may not be relevant for all product forms (i.e. liquids and non-respirable particles) for which the risk may not be applicable or may be further managed using exposure control measures for workers.

Given the potential regulatory risk associated with chemicals on the candidate list of SVHC, this chemical class meets ChemFORWARD's x\* criteria.

## Candidate List of SVHC: Equivalent Concern

Chemicals listed on ECHA's Candidate List of substances of very high concern (SVHC) for Authorisation with "reason for inclusion" cited as Equivalent Level of Concern Having Probable Series Effects to Human Health (Article 57 (f) - human health) and Equivalent Level of Concern Having Probable Series Effects to the Environment (Article 57 (f) - environment) meet criteria in (EC) No 1907/2006 Article 57 as "substances – such as those having endocrine disrupting properties or those having persistent, bioaccumulative and toxic properties or very persistent and very bioaccumulative properties, scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e)...)."

The Cradle to Cradle Material Health Assessment Methodology (MHAM) v4.0 lists all chemicals on the REACH Candidate List of SVHC as "chemicals of regulatory concern," and therefore will always receive a risk flag equal to the hazard flag.

"Equivalent concern" may be engaged to identify chemicals with considerations regarding various hazard endpoints, some of which may be route-specific, acute in nature, or of mixed severity. Classification based on form-specific hazards and exposure control measures cannot be done at the group level.

Given the potential regulatory risk associated with chemicals on the candidate list of SVHC, this chemical class meets ChemFORWARD's x\* criteria.

### Per and polyfluoroalkyl Substances (PFAS)

PFAS chemicals are a group of chemicals for which no consensus definition exists. The <u>OECD</u> provides the generic definition: "PFASs consist of a fully (per) or partly (poly) fluorinated carbon chain connected to different functional groups." This class of chemicals has been used for decades due to their water and grease-proofing and other properties and have applications in countless industries and across the supply chain from industrial use to consumer products.

Studies on certain PFAS chemicals show ubiquitous presence in environmental media, biota, and biological samples from human and animals and indication of long-range transport. Studies show that exposure to some PFAS chemicals (particularly PFAS and PFOA) may cause health effects, such as: reduced immune system response, reproductive impacts, developmental impacts or delays, increased risk of certain cancers, liver damage, increased cholesterol levels and/or obesity risk, impacts to the endocrine system, and more (European Environment Agency, EPA 2023).

Given widespread use of PFAS and emerging hazard concerns, several global regulatory bodies have passed or proposed legislation restricting or banning the entire class of chemicals for use across the supply chain.

Definitions of PFAS determine how chemicals that fall under these classifications are monitored and regulated. For example, the OECD definition of PFASs may not necessarily align with those of several US states or other jurisdictions. ChemFORWARD is committed to ongoing research to identify potential PFAS chemicals that may be of regulatory concern, and intends to align to the x\* hazard band to the most inclusive interpretation of the definition of PFAS to best capture regulatory risk for users. Currently, chemicals listed on the OECD Comprehensive Global Database of PFASs and EPA's ToxCast Chemical Inventory meet ChemFORWARD's x\* criteria.

### PFAS x\* Exemptions

Given the vast number of PFAS chemicals, high frequency of data gaps in the class, and known hazards for certain data-rich PFAS chemicals, the entirety of the chemical class of PFAS is often considered to be of potential concern. Certain PFAS chemicals have been shown to demonstrate a high concern for one or more of the following hazards: Carcinogenicity, Reproductive Toxicity, Developmental Toxicity, Endocrine Disruption, Persistence, Bioaccumulation, and Mobility.

If a chemical demonstrates a lack of concern (i.e receives a GREEN endpoint hazard classification) for all of these associated Group I Human endpoints (Carcinogenicity, Mutagenicity, Reproductive/Developmental Toxicity, Endocrine Disruption), and either a GREEN or YELLOW endpoint hazard classification for Priority Environmental endpoints of Persistence and Bioaccumulation) the chemical would be exempted from x\* criteria as low concern is clearly

demonstrated for the endpoints of concern. Presence of data gaps (GREY endpoints) renders a chemical ineligible from the exemption as valid data must clearly prove a lack of effect. Note that mobility criteria are not yet a part of ChemFORWARD Chemical Ratings, but will be in the future; exemption criteria will also be developed that apply to the mobility endpoint.

Any exempted PFAS chemical is subject to the remainder of scoring exercise outlined in this guidance; the final Chemical Rating will be reflective of the totality of the hazards as is the case for most chemicals in the repository. For combined final hazard endpoint scores (i.e. Aquatic Toxicity and Persistence & Bioaccumulation) the presence of one individual endpoint score of REDor PURPLE disqualifies the chemical from this exemption; since P&B hazards are well documented for the class, combined scores are not sufficiently health-protective for the purposes of an exception.

Note: x-Reg status and all other x\* criteria still apply and cannot be overridden unless explicitly mentioned in this Guidance. It is common that PFAS chemicals receive a RED for climatic relevance, and may still receive an x\* rating on this basis.

## Chlorinated Organic and Brominated Organic Compounds

Chlorinated organic and brominated organic compounds refers to classes of chemicals with a carbon to chlorine or bromine bond, respectively.

The widespread use of chlorinated, brominated (and fluorinated, addressed under "PFAS") organic substances, and their persistent nature have resulted in global environmental contamination. Increasing levels of these compounds in environmental media (i.e., air, water, soil, sediment) and in human tissues including adipose tissue, breast milk, and placenta continue to be a cause of ecological and human health concern

Exposure to this class of chemicals has been implicated in a wide variety of health effects including reproductive, neurological, immunological, endocrine, behavioral, and carcinogenic effects in both wildlife and humans. In addition, recent studies indicate that exposure to chlorinated and brominated organic compounds contribute to obesity and type 2 diabetes. Several regulatory agencies either banned or placed severe restrictions on their production and usage due to these demonstrated adverse effects of exposure (EPA 2023). Chemicals listed in the Pharos Brominated Organic Compounds or Chlorinated Organic Compounds lists, defined by the SMILES string C[Br] or C[CI], respectively, or is otherwise assigned this classification by a ChemFORWARD assessor meet ChemFORWARD x\* criteria.

### Chlorinated and Brominated Organic Compounds Exemptions

It is documented that the hazards associated with many well-studied chlorinated and brominated organic substances are not the same across this chemical class. However, their similarities allow for a grouping approach to be applied for the x\* Chemical Rating for which exemptions apply. Certain chlorinated organic and/or brominated organic substances have been shown to demonstrate a high concern for one or more of the following hazards: Carcinogenicity, Mutagenicity, Reproductive Toxicity, Developmental Toxicity, Persistence, Mobility, and Bioaccumulation (WA Department of Ecology Draft Priority Chemical Report 2023).

If a chemical demonstrates a lack of concern (i.e receives a GREEN endpoint hazard classification) for all of these associated Group I Human endpoints (Carcinogenicity, Mutagenicity, and Reproductive/Developmental Toxicity), and either a GREEN or YELLOW endpoint hazard classification for Priority Environmental endpoints of Persistence and Bioaccumulation) the chemical would be exempted from x\* criteria as low concern is clearly demonstrated for the endpoints of concern. Presence of data gaps (GREY endpoints) renders a chemical ineligible from the exemption as valid data must clearly prove a lack of effect. Note that mobility criteria are not yet a part of ChemFORWARD Chemical Ratings, but will be in the future; exemption criteria will also be developed that apply to the mobility endpoint.

Any exempted chlorinated or brominated organic chemical is subject to the remainder of scoring exercise outlined in this guidance; the final Chemical Rating will be reflective of the totality of the hazards as is the case for most chemicals in the repository. For combined final hazard endpoint scores (i.e. Aquatic Toxicity and Persistence & Bioaccumulation,) the presence of one individual endpoint score of RED, or PURPLE disqualifies the chemical from this exemption; since P&B hazards are well documented for the class, combined scores are not sufficiently health-protective for the purposes of an exception.

Note: x-Reg status and all other x\* criteria still apply and cannot be overridden unless explicitly mentioned in this Guidance. It is common that PFAS chemicals receive a RED for climatic relevance, and may still receive an x\* rating on this basis.

### **Climatic relevance**

Chemicals of climatic relevance are defined as those listed by the USEPA as being an ozone depleting substance as defined by the Montreal Protocol. The Montreal Protocol is a landmark multilateral environmental agreement that regulates the production and consumption of nearly 100 man-made chemicals referred to as ozone depleting substances. When released into the atmosphere, those chemicals damage the stratospheric ozone layer, Earth's protective shield that protects humans and the environment from harmful levels of ultraviolet radiation from the sun.

The Intergovernmental Panel for Climate Change (IPCC) offers a definition of Global Warming Potential (IPCC, 1999): "Global warming potential is an index that attempts to integrate the overall climate impacts of a specific action (e.g., emissions of CH4, NOx or aerosols). It relates the impact of emissions of a gas to that of emission of an equivalent mass of CO2. The duration of the perturbation is included by integrating radiative forcing over a time horizon (e.g., standard horizons for IPCC have been 20, 100, and 500 years). The time horizon thus includes the cumulative climate change and the decay of the perturbation."

GHS offers a definition of Ozone Depleting Potential (UNECE, 2009): "Ozone Depleting Potential (ODP) is an integrative quality, distinct for each halocarbon source species, that represents the extent of ozone depletion in the stratosphere expected from the halocarbon on a mass-for-mass basis relative to CFC11. The formal definition of ODP is the ratio of integrated perturbations to total ozone, for differential mass emission of a particular compound relative to an equal

emission of CFC-11."

A RED rating is assigned if the chemical is included among the known greenhouse gases in Table 6.7 of the IPCC Third Assessment Report, is on the EPA's list of Ozone Depleting Substance substitutes with global warming potential, or is otherwise assigned this classification by a ChemForward assessor, and thus meets ChemFORWARD x\* criteria.

# Appendix B: Endpoint Adjustments and Exemptions

### Universal Exemptions for Endpoints that do not Influence Chemical Rating

Some hazard endpoints are universally exempt from impacting the chemical's final chemical rating since they are informational and/or broad in nature:

- Other (Human Health & Physical Properties)
- Other (Environmental Health)

### Adjusted Hazard Scores

For the purpose of scoring, certain exposure-route divided endpoints are subject to "roll-up" scores and environmental endpoints are subject to combined scoring. These scores are considered adjusted hazard scores because the endpoint classification(s) may differ from the final representative score used in the scoring exercise. Adjusted scores streamlined scoring in situations where:

- 1. Data gaps exist for some exposure routes for a given endpoint
- 2. Where closely related endpoints influence the overall hazard profile of a chemical (e.g. persistence & bioaccumulation.)

Endpoints eligible for adjusted hazard classifications:

- Carcinogenicity (Oral, Dermal, Inhalation)
- Reproductive & Developmental Toxicity (Oral, Dermal, Inhalation)
- Neurotoxicity (Oral, Dermal, Inhalation)
- Combined Aquatic Toxicity (Algae, Daphnia, Fish, Persistence, Bioaccumulation)
- Combined Persistence & Bioaccumulation (Persistence, Bioaccumulation)

### Endpoint Data Gap Exemptions

Certain data gaps are exempt from impacting the final score. Minimum data requirements still apply, see <u>Appendix C</u>. Data gaps may be exempt for various reasons, including: negligible/no intrinsic exposure potential for that exposure route, the endpoint is informational, or generating data sufficient to classify is technically challenging, and therefore scarce.

Endpoint with GREY Classification	Criteria for Exemption
Carcinogenicity	Roll-up score across three exposure routes is GREY
Endocrine Activity/Disruption	Endpoint score is GREY
Neurotoxicity	Roll-up score across three exposure routes is GREY

#### Table A1. Data Gap Endpoint Exemptions

Terrestrial Toxicity	Endpoint score is GREY
Oral Toxicity	Endpoint score is GREY and one of the following are true: 1. Highly volatile chemicals: BP<0°C 2. High molecular weight (>1000 g/mol) & known not to undergo hydrolysis or cleave under acidic conditions 3. If 3+ of the following criteria are met: a. Molecular weight >500 g/mol b. Octanol-water partition coefficient (log Kow) >5 c. >5 hydrogen bond donors (defined as the total # of N-H and O-H bonds) d. >10 hydrogen bond acceptors (defined as all nitrogen and oxygen atoms)
Dermal Toxicity	Endpoint score is GREY and one of the following are true: 1. Molecular weight >1000 g/mol 2. Molecular weight is >500 g/mol AND the log Kow >4.
Inhalation Toxicity	Endpoint score is GREY and one of the following are true: 1. Boiling point > 240°C 2. Vapor pressure < 10-6 mm Hg. 3. Particulates and aerosols: aerodynamic diameter >100 μm.

Appendix C: Data Gap Rules

## Data Gap Rules and U Hazard Band Chemicals

A minimum dataset must be available to assign a Chemical Rating and associated Hazard Band for chemicals not assigned a D or F Hazard Band. If data are missing for too many endpoints, a chemical will be assigned a Chemical Rating of grey and a Hazard Band of U.

#### Table A2. Data Gap Rules

Endpoint Category	Data Gap Rules triggering a grey Chemical Rating/ U Hazard Band
Chronic Human Health Hazards (C,M,R/D, E)	Data are missing for 3+
Other Human Health Hazards (O, D, I, N, SnS/SnR, C/I)	Data are missing (GREY and not exempt) for 3+
Environmental Hazards (Algae, Daphnia, Fish,) Persistence & Bioaccumulation	Data are missing for all 5 endpoints

Appendix D: Deriving Adjusted Hazard Classifications via Limited Exposure Assessment & Combined Scoring



Appendix E: Chemical Rating Assignment Flowchart



Appendix E: Chemical Rating Assignment Flowchart

Note: for brevity, "flag" is used interchangeably with "classification" for the purpose of this flowchart.

Hazard Classification = Hazard Flag

