SECTION V — ANNEX 2

GreenScreen Hazard Endpoint Classification Guidance

GreenScreen Hazard Endpoint Classification Guidance

A2.1 GreenScreen Hazard Endpoints

There are 18 GreenScreen Hazard Endpoints—Human Health, Environmental Toxicity, Fate, and Physical Hazard Endpoints—that must be evaluated for each chemical. The endpoints are grouped as shown in Table A2.1 below. This Annex outlines supplementary guidance for classifying the hazard level for Reproductive Toxicity, Developmental Toxicity, Endocrine Activity, and Systemic Toxicity.

Group I Human Health endpoints reflect priorities that are consistent with national and international governmental regulations, and cover hazards that can lead to chronic or life-threatening effects or adverse impacts that are potentially induced at low doses and transferred between generations. They are built on international and national criteria for identifying chemicals with hazardous properties of high concern.

Group II and II* Human Health endpoints reflect hazards that are also important for understanding and classifying chemicals. Typically, Group II hazards may be mitigated. Group II and II* are differentiated from one another in the Benchmarking system because Group II endpoints have 4 hazard levels (i.e., vH, H, M and L) while Group II* endpoints have 3 hazard levels (i.e., H, M and L) and are evaluated based on repeated exposure.

Environmental Toxicity and Fate endpoints include Acute and Chronic Aquatic Toxicity, Persistence and Bioaccumulation potential. Additional Ecotoxicity endpoints such as Avian or Bee Toxicity may be included when data are available and the endpoints are relevant.[1]

Physical hazard endpoints include Flammability and Reactivity and are based on GHS criteria.

TABLE A2.1: **Groupings of GreenScreen Hazard Endpoints**

Human Health Group I	Human Health Group II	Human Health Group II*	Environmental Toxicity & Fate	Physical Hazards
Carcinogenicity (C)	Acute Mammalian Toxicity (AT)	Systemic Toxicity & Organ Effects – Repeated Exposure sub-endpoint (ST-repeated)	Acute Aquatic Toxicity (AA)	Reactivity (Rx)
Mutagenicity & Genotoxicity (M)	Systemic Toxicity & Organ Effects (ST-single)	Neurotoxicity – Repeated Exposure sub-endpoint (N-repeated)	Chronic Aquatic Toxicity (CA)	Flammability (F)
Reproductive Toxicity (R)	Neurotoxicity (N-single)	Skin Sensitization (SnS)	Other Ecotoxicity studies when available	
		Respiratory Sensitization (SnR)		
Developmental Toxicity including Neurodevelop-mental Toxicity (D)	Skin Irritation (IrS)		Persistence (P)	
	Eye Irritation (IrE)		Bioaccumulation (B)	
Endocrine Activity (E)				

1 Refer to EPA's Design for the Environment (DfE) Program Alternatives Assessment Criteria for Hazard Evaluation, Office of Pollution Prevention & Toxics, U.S. Environmental Protection Agency (Version 2.0, August 2011); http://www.epa.gov/sites/production/files/2014-01/documents/aa_criteria_v2.pdf, accessed 12/5/17.

A2.2 Hazard Classification Guidance

The following endpoint-specific guidance should be followed in conjunction with the GreenScreen Chemical Hazard Criteria in Annex 1 to assign hazard levels for the endpoints indicated.

A2.2.1 Reproductive and Developmental Toxicity

Reproductive and Developmental Toxicity are separate endpoints in GreenScreen. If a study includes both reproductive and developmental effects, they should be evaluated and reported in the respective section of the GreenScreen assessment. Effects on or via lactation are included under Developmental Toxicity. Although presence of data indicating effects on or via lactation must be reported and considered in the assessment, lack of negative data for effects on or via lactation does not result in a Data Gap.

A2.2.2 Endocrine Activity

A preliminary hazard level or range is assigned by determining whether the chemical is endocrine active. This is done by searching all GreenScreen Specified Lists and available data. For chemicals that are endocrine active, determine whether there is a plausibly related adverse human health effect, and identify the associated level of hazard. Assigning the final hazard level for Endocrine Activity will use expert judgment and a strength of evidence approach.[1]

A2.2.2.1 Low Hazard

1. Low hazard classification requires data for multiple endocrine pathways. Negative data on at least the following five pathways is required to assign a low hazard classification for endocrine activity: androgenicity, anti-androgenicity, thyroid effects, estrogenicity, and anti-estrogenicity.

A2.2.2.2 Moderate Hazard

1. Endocrine Activity is classified as Moderate if there is indication of Endocrine Activity in the scientific literature.
   a. All chemicals with data suggesting Endocrine Activity associated with adverse effects are initially assigned as Moderate. It is also acceptable to assign a range (Moderate or High) to indicate preliminary classification.
   b. For chemicals listed on GreenScreen Specified Lists for Endocrine Activity, other than EU – SVHC Authorisation List, classify them initially as Moderate. It is also acceptable to assign a range (Moderate or High) to indicate preliminary classification.
   c. Chemicals initially classified as Moderate using GreenScreen Specified Lists should be further reviewed using the scientific literature to confirm classification.

A2.2.2.3 High Hazard

1. If the chemical being assessed is present on the EU – SVHC Authorization List for Endocrine Activity, classify it as High hazard for Endocrine Activity.
2. Where Endocrine activity is plausibly[2] related to an adverse effect such as Carcinogenicity, Reproductive Toxicity, Developmental Toxicity and/or Systemic Toxicity (Repeated dose, typically, thyroid) and the hazard endpoint for the plausibly related adverse effect has been classified as High or very High, modify the hazard level for Endocrine Activity from Moderate to High. Where the adverse effect is not plausibly related or the hazard endpoint for the plausibly related adverse effect has been classified as Moderate, do not modify the Endocrine Activity level. See Table A2.2.

1 The science associated with testing for endocrine activity and associated adverse effects continues to evolve rapidly and will be incorporated into future revisions of GreenScreen.

2 Plausibly related means that the adverse effect is likely to be due to the endocrine mode of action. For example, an increase in T3 along with thyroid tumors would be plausibly related, but an increase in T3 would have no obvious connection to a skin cancer.

TABLE A2.2: **Modified Endocrine Activity Classifications for Select Endpoints**

Endpoint	Initial Endocrine Activity Classification	Plausibly Related Hazard Endpoint Classification	Modified Endocrine Activity Classification
Carcinogenicity	M	H	H
Carcinogenicity	M	M	M
Reproductive Toxicity	M	H	H
Reproductive Toxicity	M	M	M
Developmental Toxicity	M	H	H
Developmental Toxicity	M	M	M
Systemic Toxicity—repeated dose (Thyroid)	M	vH	H
Systemic Toxicity—-repeated dose (Thyroid)	M	H	H
Systemic Toxicity—-single dose (Thyroid)	M	M	M

A2.2.2.4 Data Gaps

1. A chemical that is not listed on any GreenScreen Specified Lists for Endocrine Activity and for which test data do not exist shall be assigned Data Gap.

2. Data Gaps are assigned using expert judgment: 1) if there is no evidence of Endocrine Activity, but data are incomplete for one or more of the five required endocrine mediated pathway, and/or 2) when a study demonstrating Endocrine Activity is judged to be inadequate.

A2.2.3 Systemic Toxicity/Organ Effects and Neurotoxicity

These two endpoints can belong in either Group II or Group II* depending on whether the data are generated from single exposure (acute) or repeated exposure (sub-chronic or chronic) studies. Results from single and repeated exposures are not considered as separate endpoints but rather sub-endpoints.

A2.2.3.1 When classifying hazard for Systemic Toxicity/Organ Effects and Neurotoxicity endpoints, repeated exposure results are required. Lacking repeated exposure data results in a Data Gap.

A2.2.3.2 If data from both single and repeated exposure studies are available, then both hazard classifications shall be included in the GreenScreen Hazard Summary Table and the more conservative value will drive the hazard classification Benchmark score. If the less conservative value is used, include the rationale for why it was chosen in the assessment report.

A2.2.3.3 Lacking single exposure data, including data for aspiration hazards, does not result in a Data Gap when repeated exposure data are available. Enter the repeated exposure hazard classification in the GreenScreen Hazard Summary Table and shade out the single exposure sub-endpoint cell.

A2.2.3.4 If single exposure data are available for both systemic toxicity/organ effects generally and aspiration hazards specifically, use the most conservative value to fill in the Hazard Summary Table for Systemic Toxicity/Organ Effects – single exposure.