Washington State PFAS in Food Packaging AA – Hazard Assessment Approach

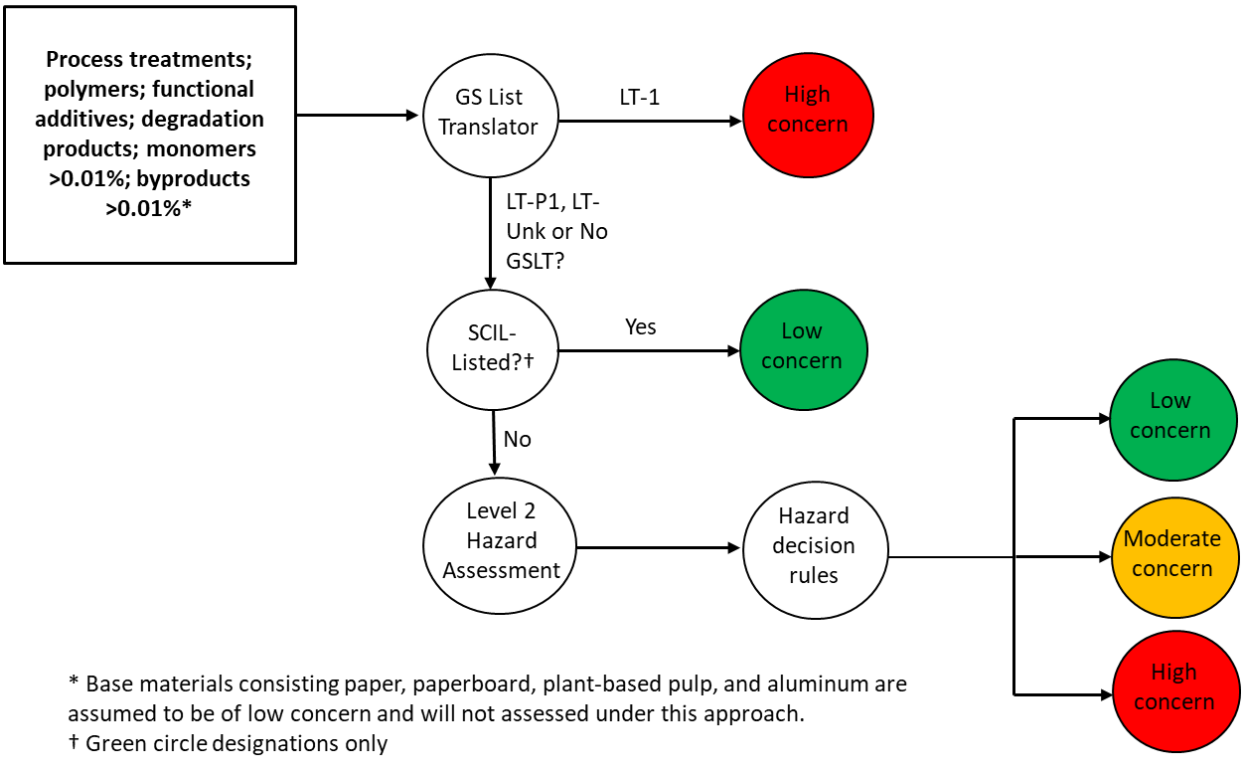
1. Tiered Approach to Hazard Assessment

As mentioned in the May 2019 Stakeholder Webinar, alternatives can be roughly categorized into 3 groups: process treatments, base materials, system alternatives. For the purposes of this project, these are defined as:

- Process treatments: dry-end coatings or wet-end additives that are applied to the base material to provide oil and grease repellent properties to the product.
- Base materials: the primary substrate (paper, paperboard, fiber pulp, plastics, and aluminum), treated (including mechanical densification) or untreated.
- System alternatives: alternatives that provide the desired function but are not process treatments or base material alternatives. The primary system alternative for the PFAS in Food Packaging AA is reusable packaging and service ware.

SRC is recommending a tiered approach to assess these substances in a way that will ensure efficiency of project resources, reduction of redundancy, and consistency with IC2 Guidelines. This approach incorporates previous assessments and methods such as the GreenScreen® List Translator, the Safer Chemical Ingredients List (SCIL), and other publicly available, high-quality assessments. This tiered assessment approach is outlined in Figure 1.

Figure 1. Tiered Hazard Assessment Approach for Substances Undergoing Hazard Evaluation



* Base materials consisting paper, paperboard, plant-based pulp, and aluminum are assumed to be of low concern and will not assessed under this approach.
† Green circle designations only

The GreenScreen® List Translator calculates a hazard score based on a set of authoritative lists that identify chemicals known to have human and ecological hazard concerns. These designations correspond to GreenScreen® criteria, and for the purposes of this assessment, any process treatment, base material, polymer, functional additive, and byproduct or monomer present at >0.01% with a List Translator score of "LT-1" will be designated a high concern and will not proceed to a Level 2 hazard assessment.

The Safer Chemical Ingredients List (SCIL) contains chemicals that meet the Safer Choice standard criteria, which is a hazard-based standard that is very similar to GreenScreen®. These designations are based on data-driven assessments that are verified by the U.S. EPA. To be conservative, only SCIL designations of "green circle" will be used in this assessment. SCIL chemicals designated as "half-green circle" or "yellow triangle," having specified use-restrictions, or those listed under Specialized Industrial Products (SIP) *will not* be considered supportive of low concern designation and will be assessed via Level 2 hazard assessment methodology.

Base materials consisting of paper, paperboard, and pulp sourced from plant materials will not be evaluated under a Level 2 hazard characterization as these substances are cellulosic materials that are of generally low concern. Aluminum is another alternative base material that will not be evaluated under a Level 2 hazard characterization. Aluminum metal has been studied extensively in humans and animals and is generally considered to be of low concern to the general population. There has been a weak association of aluminum with Alzheimer's disease, but this association is "highly controversial and there is little consensus regarding current evidence" (ATSDR, 2008). Gastrointestinal absorption is generally low, ranging of 0.1-0.4% in humans, although this varies depending on the chemical form (ATSDR, 2008).

2. Level 2 Hazard Assessment Methodology

The hazard assessment portion of this AA will comply with a Level 2 assessment under IC2 guidelines. The approach used for this AA combines the U.S. EPA DfE AA criteria v2.0 (2011) (*herein DfE AA Criteria*) and Sustainable Futures Interpretative Assistance Document for Assessment of Polymers (2013) (*herein SF Polymer Guidance*) to meet the criteria of a Level 2 hazard assessment. All target substances, including the base-case and candidate alternatives, will be evaluated against the hazard assessment methodology, as well as their potential breakdown products. As per IC2 guidelines, the endpoints required for a Level 2 assessment include the following:

IC2 Hazard Assessment Level 2 Endpoints		
Human Health	Carcinogenicity	*DfE AA Criteria (discrete substance and polymers MW<1000; polymers MW>1000 supplemented with SF Polymer Guidance)*
	Mutagenicity & Genotoxicity	
	Reproductive toxicity	
	Developmental toxicity (including developmental neurotoxicity)	
	Endocrine activity	
	Acute mammalian toxicity	
	Systemic toxicity (repeat dose toxicity, including immunotoxicity)	
	Neurotoxicity	
	Skin sensitization	
	Respiratory sensitization	

Ecological	Acute aquatic toxicity	
	Chronic aquatic toxicity	
Environmental Fate	Persistence	
	Bioaccumulation	
Physical*	Flammability	
	Reactivity	

*Corresponding to GHS hazards for explosives, self-reactive substances, substances which on contact with water emit flammable gases, oxidizing gases, oxidizing liquids & solids, organic peroxides, self-heating substances, and substances corrosive to metal.

The DfE AA criteria clearly defines the cut-off criteria for categorizing (assigning severity) the chemical hazards as either:

- Very High/High
- Moderate
- High/Very High

SF Polymer Guidance will be used to supplement the assessment of polymeric materials with a MW of >1,000. This guidance categorizes polymers into 3 groups:

- Category 1 – polymers with low MW (MWn <1000)
- Category 2 – polymers with high MW (MWn >1000) and large low MW (LMW) material composition
- Category 3 – polymers with high MW (MWn >1000) and minimal LMW

Polymers with low molecular weight (MW <1000; SF Category 1) are expected to be bioavailable and will be evaluated using the same methods and approaches as for discrete substances, including the evaluation of any experimental toxicity data or reliable estimation methods (read across, QSAR models, etc.).

The SF Polymer Guidance will be used to address the special considerations associated with evaluating polymers with high MW (MW >1000; SF Category 2 & 3). Many of these substances are of variable composition and lack adequate data sets, making it difficult to evaluate these substances under the established hazard assessment paradigms like the DfE AA criteria. Various approaches for assessing physical/chemical properties, ecological hazards, and human health hazards are summarized in the SF Polymer Guidance. SRC will be sure to highlight cases where the SF Polymer Criteria were applied, including any relevant justifications for the hazard endpoint calls. Any qualitative assessments of the endpoints will be applied within the context of the DfE AA criteria.

In cases of where the data set for an endpoint contains limited or conflicting data, a weight of evidence (WoE) may be used. A WoE approach may consider factors such as data quality, consistency, nature and severity of effects, and general relevance (ECHA, 2019). Data hierarchy, described below, may also be used to inform a WoE approach. Hazard severity that is based on WoE will be supported by adequate scientific justification.

3. Data Hierarchy

To assign a hazard severity for each endpoint we will evaluate supporting data in the following order of preference::

1. Reliable experimental data for the target substance based on:
    a. Preferred guideline test methods highlighted by endpoint in the DfE AA criteria.
    b. Non-guideline studies evaluated for adequate study design using SRC professional judgement.
    c. Studies published in the peer-reviewed literature, reliable toxicological or chemistry databases, government assessments, or unpublished laboratory reports or summaries. The data sources consulted will comply with IC2 Guidelines.
2. Experimental data for a reliable analog:
    a. The analog is structurally similar to and operates with a similar mechanism of action to the target substance. Analog data may be used to make qualitative assessments against the endpoint criteria.
        i. Appropriate justifications for the use of analogs will be provided by SRC in the final report.
        ii. Any analog data provided by stakeholders will be critically evaluated for appropriateness and relevance.
3. Estimated data using suitable computational models or methods (i.e., QSAR's) including:
    a. EPISuite v4.11
    b. ECOSAR v2.0
    c. OECD QSAR Toolbox v.4.3
    d. Oncologic v. 8.0

4. Data Needs (for Stakeholders)

1. Substance identification (including the base-case and candidate alternatives):
    a. Product formulation disclosure, including:
        i. Active ingredient (substance providing oil/grease-proofing function)
        ii. Functional additives
        iii. Known residual monomers or oligomers
        iv. Known byproducts
    b. Should include at a minimum a CAS RN and systematic chemical name for each formulation component.
    c. Chemical structure (SMILES, image). At the very least, one that could be easily derived from a CAS RN and chemical name.
    d. Composition of each component by wt%
    e. For polymeric substances, the following additional information are also required:
        i. Representative structure
        ii. Mole ratios of monomers
        iii. Indication as to whether the monomers are blocked
        iv. MW_n (molecular weight average)
2. Experimental studies that address the endpoints for the hazard assessment (see table above Section 1).
    a. The substance evaluated in these studies should be sufficiently characterized as per Section 3.1.

3. **A special note about Safety Data Sheets (SDS):** SDS's submitted by stakeholders will be reviewed for data adequacy and relevancy. These documents may be helpful in characterizing test substance identity, physical hazards associated with product handling, and accidental poisoning concerns. SDS's typically lack the necessary details to evaluate hazard endpoints in accord with IC2 Level 2 guidelines.

5. Data Reporting

The available data will be compiled and presented at multiple levels that will include the supporting study summaries, endpoint analysis, and a hazard call table that aids in cross-comparison of the endpoint calls. In cases where WoE or analog approaches are used, adequate justification will also be provided.

1. Study summaries will feature:
    a. High level overview of the critical study details including test substance details, test conditions, test methods, outcomes.
    b. Reference citation
    c. Disclosure of the study type:
        i. Experimental
        ii. Analog (read across)
        iii. Estimated
    d. Any limitations or deviations of the study method
2. Endpoint analysis:
    a. Each endpoint will be summarized by highlighting the available information, including the relative quality and how the available data set informs the designated endpoint hazard call.
3. Summary table will contain high-level overview of the test substance evaluated and the designated endpoint calls. This table will aid in the comparison of evaluated substances. The summary table will contain:
    a. Test substance identification
    b. Function in the formulation (active ingredient, additive, monomer, byproduct, or breakdown product)
    c. Designation of the study type (experimental, estimated, or read across)
    d. Summary table template (see Appendix 1)

6. Decision Rules

High concern (Red):

- CMR endpoints: H or VH
    - Carcinogenicity
    - Reproductive toxicity
    - Developmental toxicity (including developmental neurotoxicity)
    - Genotoxicity
- Acute toxicity, Repeat dose toxicity or Neurotoxicity: H or VH

- Endocrine activity indicating high concern, based on WoE and/or professional judgment
- VH Aquatic toxicity
- VH/H Persistence AND VH/H Bioaccumulation AND VH/H Aquatic toxicity
- VH Persistence AND VH Toxicity
- VH Bioaccumulation AND VH Toxicity
- VH or H Physical Hazard

Moderate concern (Orange):

- CMR endpoints (see above): M
- Acute toxicity, Repeat dose toxicity, neurotoxicity: M or L (low if CMR endpoints are moderate)
- Endocrine activity indicating moderate concern, based on WoE and/or professional judgment
- H Aquatic toxicity AND M Persistence
- M Aquatic toxicity AND M Persistence
- M Bioaccumulation
- M Physical Hazard

Low concern (Green):

- CMR Endpoints (see above): L or VL
- Acute toxicity, Repeat dose toxicity, or Neurotoxicity: L (if CMR endpoints are low)
- Endocrine activity indicating low concern, based on WoE and/or professional judgment
- H Aquatic toxicity AND VL/L Persistence
- M Aquatic toxicity AND VL/L Persistence
- L Bioaccumulation
- L Physical Hazard

Identification of Improved Hazard or Exposure Potential for Equivalent Characterizations

In cases where the alternative is assigned the same hazard or exposure potential as the base-case, SRC will determine if there are sufficient data to designate the alternative substance's score as "improved". For example, an "improved" hazard annotation may be warranted if an alternative is designated a high concern due to a physical hazard such as flammability, while the base-case is high due to CMR data. An "improved" hazard designation may be justified, particularly if the exposure assessment supports a reasonable assumption that the physical hazard could be properly mitigated. In cases where both substance's scores are driven by the same endpoint, then SRC may compare severity and potency of the effects in order to designate a score as "improved". A narrative approach will be taken and all hazard concerns that are annotated as being "improved" will be supported by adequate justification.

References:

ATSDR (2008) Toxicological profile for aluminum. Atlanta, GA. Agency for Toxic Substances and Disease Registry. Available at: https://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=191&tid=34

ECHA (2019) Weight of Evidence: How to avoid unnecessary testing on animals. Available at: https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/weight-of-evidence

Appendix 1 – Template for Hazard Calls Table

			Human Health Effects												Aquatic Toxicity		Environmental Fate		Physical Hazards	
Chemical	**CAS RN**	**Function**	**Acute Toxicity**	**Carcinogenicity**	**Genotoxicity**	**Reproductive**	**Developmental**	**Neurotoxicity**	**Repeat Dose**	**Skin Sensitization**	**Respiratory Sensitization**	**Eye Irritation**	**Skin Irritation**	**Endocrine activity**	**Acute**	**Chronic**	**Persistence**	**Bioaccumulation**	**Flammability**	**Reactivity**