Using Chemical Hazard Assessment for Alternative Chemical Assessment and Prioritization

Prepared by the Outdoor Industry Association Chemicals Management Working Group and the Zero Discharge of Hazardous Chemicals Programme

Draft Document: Version 1

March 2013

Contents

Acronyms and Abbreviations

ACToR	aggregated computational toxicology resource
ANSI	American National Standards Institute
BOD	biochemical oxygen demand
BOM	Bill of Material
BOP	Bill of Product
BOS	Bill of Substance
CASRN	Chemical Abstract Service Registry Number
CCS	Chemical Compliance Systems
CLP	classification, labeling, and packaging
CCRIS	Chemical Carcinogenesis Research Information System
CHESAR	Chemical Safety Assessment and Reporting
DART	developmental and reproductive toxicology
DfE	Design for the Environment
ECHA	European Chemicals Agency
EHS	environmental, health, and safety
ESIS	European Chemical Substances Information System
EUSES	European Union System for the Evaluation of Substances
GC3	Green Chemistry and Commerce Council
GCI	Green Chemistry Institute
GHS	Globally Harmonized System
GOTS	Global Organic Textiles Standard
HSDB	Hazardous Substances Data Bank
IRIS	Integrated Risk Information System
NGO	nongovernmental organization
NSF	National Science Foundation
OECD	Organisation for Economic Co-operation and Development
PBT	persistent, bioaccumulative, and toxic
POP	persistent organic pollutant(s)
QCAT	Quick Chemical Assessment Tool
QSAR	quantitative structure activity relationship
REACH	registration, evaluation, authorization, and restriction of chemical (substances)
RoHS	restriction of the use of certain hazardous substances
RSL	restricted substances lists

SAR	structure activity relationship
SIDS	Screening Information Dataset
STOT	specific target organ toxicity
TOXNET®	Toxicology Data Network
TOXLINE	Toxicology Information On-Line
UBA	Umweltbundesamt
US EPA	United States Environmental Protection Agency
WHO	World Health Organization

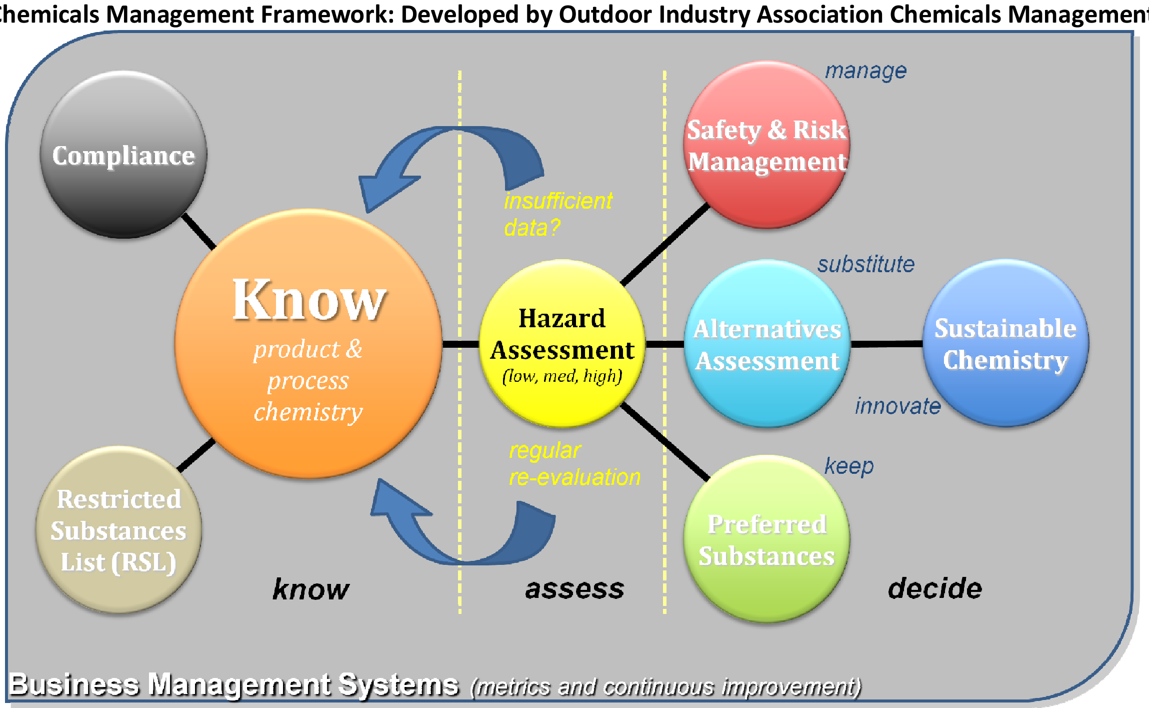
Using Chemical Hazard Assessment for Alternative Chemical Assessment and Prioritization

Purpose

Chemical hazard assessment to identify and prioritize chemical substances for possible replacement with safer alternatives is increasingly required by retailers, brands, and material suppliers in response to both consumer pressure and regulatory requirements. This guidance was developed to support informed chemicals management decisions that will lead to safer chemical choices and proactive management of chemicals in the supply chain. While this guidance is not a substitute for regulatory requirements concerning Alternatives Assessments, it can form the foundation for responding to regulatory requirements. This document also addresses considerations for developing data on new chemicals that are entering the marketplace.

Figure 1 shows how chemical hazard assessments fit into the overall framework logic of a chemicals management system to classify chemicals and make decisions on whether to keep, substitute, or manage the chemical.

FIGURE 1
Chemicals Management Framework: Developed by Outdoor Industry Association Chemicals Management Working Group



The results of chemical hazard and exposure/risk assessments will need to be examined from a life cycle perspective, because substitutions may require trade-offs with other impacts, such as water or energy use or wastewater treatment. For example, there may be a safer alternative, but if the alternative is substituted into a process that does not include adequate wastewater treatment, discharging too much sugar into a waterway could raise the biochemical oxygen demand (BOD) to levels that might result in aquatic toxicity. Another example is that a persistent chemical might be used in a process, which would allow energy savings, thus avoiding greenhouse gas emissions. There may also be socio-economic impacts associated with potential substitution. Evaluation of these trade-offs are outside the scope of this guidance and the reader is referred to other sources[1] for this guidance.

1 http://echa.europa.eu/documents/10162/13637/sea_authorisation_en.pdf, European Chemicals Agency (ECHA), Guidance on the preparation of socio-economic analysis as part of an application for authorisation, January 2011.

Chemical Hazard Assessment

All chemical substances[2] have inherent hazards. The degree to which that hazard poses a risk to humans or the environment is a function of the inherent hazard and the exposure (and resulting dose):

Risk = *f*(Hazard, Exposure)

Chemical hazard assessment can be used in the following ways:

- **Comparative Hazard Assessment** – For chemical substances with similar functional uses, the inherent hazards of chemicals can be compared to identify inherently safer alternatives. In this case, it is assumed that because the application will be the same, all exposures (and the resulting exposure factor in calculating the risk) will be the same, assuming comparable physical properties and usage amounts. Selecting inherently safer chemical substances will result in reduced hazards, and thus reduced overall risk.
- **Prioritization** – Where there are a large number of chemical substances being evaluated, chemical hazard assessments can be used to assess and prioritize chemicals for further evaluation. For example, sorting them into categories of “preferred,” “replace” and “manage” (or low, medium and high priority). Those substances in the “replace” and “manage” groups then can be further prioritized based on potential exposure and risk.
- **Risk Management** – Risk is a function of hazard and exposure; therefore, hazard assessment is a critical first step in risk analysis. Hazard information can support further risk analysis when combined with exposure information. Risk assessment is used to identify overall risk, and thereby determine whether risks are already well managed or require further mitigation.
- **Preferred Substances List** – Hazard assessment can provide the foundation for developing a preferred substances list. Identifying chemicals that are inherently safer (and therefore preferred) helps avoid the unintended consequences of choosing substances that are untested or may be identified as problematic or regulated in the future.

This guidance describes the scientific basis, scope and applicability of several existing chemical hazard assessment decision methodologies and tools for use in comparative hazard assessment and prioritization.

Essential Attributes of the Hazard Assessment Approach

Following are essential attributes of the hazard assessment approach:

- Selected hazard and intrinsic exposure endpoints, such as carcinogenicity or persistence, are derived based on scientifically accepted approaches to characterizing chemicals. These endpoints are common to global chemical regulatory and safety programs and alternative assessment approaches (e.g., European Union [EU] regulations on both the registration, evaluation, authorisation and restriction of chemical [REACH] substances, and the Globally Harmonized System [GHS], along with the United States Environmental Protection Agency [US EPA] Design for the Environment [DfE], Umweltbundesamt [UBA] Sustainable Chemistry Guidance, Organisation for Economic Co-operation and Development [OECD] Screening Information Dataset [SIDS], and National Science Foundation [NSF]/Green Chemistry Institute [GCI], American National Standards Institute [ANSI] 355).
- Toxicological and intrinsic exposure data, such as persistence and bioaccumulation, are gathered from the literature, public databases, and other available sources. (Confidential studies from manufacturers may also be requested.) Data to be considered include those generated from internationally accepted study guidelines (e.g., OECD[3], EU Test Methods Regulation[4]). Because most chemicals do not have a robust dataset, all

2 A chemical element and its compounds in the natural state or obtained by any manufacturing process, including additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition (as defined by REACH)

3 http://www.oecd.org/document/7/0,3343,en_2649_34377_37051368_1_1_1_1,00.html

4 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2008R0440:20101212:EN:PDF

available lines of evidence should be gathered and considered. Data quality standards can be applied to help ensure use of the best available data (e.g., US EPA Data Adequacy Guidelines[5]).

- The toxicological and intrinsic exposure data are then interpreted and classified using internationally accepted criteria (e.g., GHS, classification, labeling, and packaging [CLP], and US EPA). The approach integrates data from multiple endpoints into a simple metric for the chemical that can be used to aid in decision-making. This document does not attempt to determine acceptable criteria for classifying hazards or integrating these classifications into a single benchmark. Rather, the user should understand the criteria available, and determine which criteria best suit their needs.
- A hazard assessment can serve as the basis for other actions, such as comparative hazard assessment, prioritization or risk management. Depending on its use, a chemical hazard assessment may be supplemented with information about the functionality of the chemical, use concentrations or potential exposure pathways.

Benefits of Conducting a Hazard Assessment

Following are the benefits of conducting a hazard assessment:

- The approach can be used to assess and compare alternatives to an incumbent chemical substance. The goal is to identify alternative chemicals that are inherently less hazardous, thereby preventing substitutions that may increase risk to human health and the environment.
- The approach is adaptable to information technology tools, making it capable of screening a large number of chemicals in a relatively short period of time, and providing guidance for more comprehensive profiling of chemicals and materials.
- The approach is readily adaptable to multiple industry sectors and provides a science-based approach to evaluating chemical hazards so that less hazardous alternatives may be identified.

Scientific Basis

Hazard Endpoints

Chemical hazard assessment methodologies and tools evaluate available information on multiple chemical hazard endpoints and use that information to rank the chemical substances using a scoring system of high, medium, or low hazard (sometimes also very high or very low), which allows a single value to be assigned to the chemical to help make informed decisions.

Hazard endpoint data are derived from guideline (or otherwise high quality) mammalian and ecological toxicity, fate, or physicochemical property studies. There are many hazard endpoints that may be selected for use in a chemical hazard assessment; however, a subset of endpoints is common to most regulatory and authoritative bodies.

The hazard endpoints listed in Table 1 are common to multiple authoritative programs and represent the recommended list from which any chemical hazard assessment tool should select endpoints for evaluation.

[5] http://www.epa.gov/HPV/pubs/general/datadfin.htm

TABLE 1
Recommended Hazard Endpoint List

Human Toxicity			Ecotoxicity and Fate
Acute Mammalian Toxicity (oral, dermal, inhalation)	Carcinogenicity	Mutagenicity/Genotoxicity	Persistence
Neurotoxicity	Systemic Toxicity/ Organ Effects Repeated Dose Toxicity (oral, dermal, inhalation)	Respiratory Sensitization	Bioaccumulation
Skin Irritation and Corrosivity	Eye Irritation and Corrosivity	Endocrine Disruption	Chronic and Acute Aquatic Toxicity (on daphnia, algae and fish)
Reproductive and Developmental Toxicity	Skin Sensitization		

These endpoints are selected from the following regulatory or chemical assessment programs:

- *SIDS Manual for the Assessment of Chemicals* (OECD, 2011)
- *Assessment Criteria for Hazard Evaluation* version 2.0 (US EPA DfE, 2011)
- *Guide on Sustainable Chemicals* (UBA, 2011)
- Global Organic Textiles Standard version 3.0 (GOTS, 2010)
- REACH and CLP (European Chemicals Agency, 2012)
- World Health Organization (WHO) Human Health Risk Assessment Toolkit (WHO, 2010)
- The GHS 4th edition (United Nations, 2009)
- Washington State Department of Ecology Quick Chemical Assessment Tool (QCAT) (Washington Department of Ecology, 2013)
- NSF/GCI/ANSI 355 – 2011, Greener Chemicals and Processes Standard (ANSI, 2013)

Appendix A shows the intersection and overlap between the hazard endpoints and those used by the organizations listed in this section.

Recommended Hazard Data Sources

Evaluation of chemicals under these criteria will be based on the best available data. In general, it is recommended that data be used in the following order of preference: 1) measured data on the chemical being evaluated, 2) measured data from a suitable analog, and 3) estimated data from appropriate models.

The following sources are generally considered to be scientifically credible[6] for publically available chemical and toxicology data:

- **EU: European Chemicals Agency (ECHA)** – chemical information/dossiers on REACH registered substances: http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances#search
- **EU: ECHA** – classification and labeling notifications: http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database

[6] No claims are made here regarding the accuracy of the databases listed. It is up to the user to assess accuracy and usability of the data.

- **OECD eChem Portal** – substance search, currently 24 databases available – listed on substance search page: http://www.echemportal.org/echemportal/page.action?pageID=9
- **European Chemical Substances Information System (ESIS)** – includes links to CLP/GHS classifications, persistent, bioaccumulative and toxic (PBT) lists and others: http://esis.jrc.ec.europa.eu/
- **US: Toxicology Data Network (TOXNET)** – Databases on toxicology, hazardous chemicals, environmental health, and toxic releases (ChemIDPlus, Hazardous Substances Data Bank [HSDB], Integrated Risk Information System [IRIS], Toxicology Information On-Line [TOXLINE], Chemical Carcinogenesis Research Information System [CCRIS], Developmental and Reproductive Toxicology [DART] database, and others): http://toxnet.nlm.nih.gov/index.html
- **US EPA Aggregated Computational Toxicology Resource (ACToR)** – online warehouse of all publicly available chemical toxicity data and can be used to find publicly available data regarding potential chemical risks to human health and the environment. ACToR aggregates data from more than 1,000 public sources on more than 500,000 environmental chemicals, searchable by chemical name, structure, and other identifiers: http://actor.epa.gov/actor/faces/ACToRHome.jsp
- **Japan's GHS database:** http://www.safe.nite.go.jp/english/ghs_index.html
- **Japan database with biodegradation data:** http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html

Publicly available databases are not the only sources of hazard data; confidential data held by manufacturers may also be available.

Data Gaps

For many chemicals, available hazard data are limited. In these cases, data from structure activity relationships (SAR) calculations may be useful in filling data gaps. This combination of experimental data followed by SAR analysis is common practice of US EPA, Environment Canada, ECHA, OECD SIDS, and other government agencies. A SAR approach calculates or infers a physical/chemical property, environmental fate attribute, or specific effect on human health or an environmental species of a chemical based on an analysis of its molecular structure. If a calculated value can be determined, this is typically referred to as quantitative structure activity relationships (QSAR).

SAR analysis has the advantage of providing a more complete set of hazard data for a chemical. The drawbacks are that predicted data are generally less preferable than experimental data, the models, and analogs have their limits and it is resource-intensive; SAR strategy depends on the expertise of toxicologists and chemists to properly use and interpret the results of the models.

While the benchmarking chemicals based upon a mixed data set (experimental and SAR) is not ideal, it is often the best that can be achieved given the typically limited publicly available experimental data.

In other cases, data from a suitable analog (read-across data) may be useful in filling in data gaps. For instance, read-across data for Table 1 may be derived from substances that meet criteria of similar chemical composition, mode of action, and biological profile. Read-across is not appropriate when these criteria are not clearly met. Where no hazard data, acute or repeated-dose, are available for a chemical substance, use of read-across in place of actual study data should be documented and substantiated.

Comparative Hazard Assessment Process

Using comparative hazard assessment to identify chemicals with inherent hazards of concern and make informed decisions about possible substitutions (for example, comparing alternative plasticizers for a flexible plastic) requires the following information:

- Knowledge of the identity of the chemical substance(s) in use and proposed alternatives. Typically this involves knowing the Chemical Abstract Service Registry Number (CASRN) or the ECHA equivalent, often referred to as an EC-number. Using a chemical's name or synonym can result in confusion of the chemical's actual identity given how most chemicals have multiple names that are difficult to track.
- Knowledge of the processes in which the chemical substance(s) are used (e.g., chemical function and amount in the mixture, article/material or product, manufacturing process conditions like temperature/process time/other chemicals involved), and knowledge of whether the proposed alternative would be functionally similar (e.g., meet performance and cost requirements).
- Data from appropriate toxicological studies, or, where data gaps exist, data from a suitable analog (so-called "read-across" data), structure activity relationship, or modelling.
- A method to use hazard data to classify chemicals for each endpoint (e.g., high, medium, or low hazard, typically based on GHS or other established classifications).
- A method to weight or combine the individual hazard classifications (e.g., high acute toxicity) to arrive at a single score or benchmark for a chemical that can be used to inform decision-making.
- Knowledge of the relevant potential routes of human and environmental exposure during the life cycle of the chemical so that appropriate hazard data needed for assessment can be identified.

Using a comparative hazard assessment methodology/tool will typically result in one of four possible outcomes:

- The proposed alternative is less hazardous for all relevant hazard endpoints in comparison to the incumbent and therefore would be a more preferable alternative.
- The proposed alternative is less hazardous in some but not all relevant hazard endpoints in comparison to the incumbent and may require further action/evaluation.
- The available hazard data for the proposed alternative are incomplete for relevant endpoints and further data are needed to assess its hazards and draw a conclusion.
- The alternative has a high or unacceptable hazard for relevant endpoints and should be avoided.

When the alternative and the incumbent chemical have equivalent hazard data, the following additional steps will need to be taken to decide on the best alternative until an inherently safer alternative chemical and/or process is found:

- Identify relevant routes of exposure based on use and disposal of the chemical through its life cycle (e.g., if the compound is a volatile solvent, look at the exposure to workers and atmosphere during production).
- Perform a quantitative exposure potential assessment focusing on the relevant routes of exposures identified previously. Among the acceptable exposure estimation tools are ECHA Chemical Safety Assessment and Reporting Tool, Chemical Safety Assessment and Reporting (CHESAR)[7], EU System for the Evaluation of Substances (EUSES) 2.1.2, *Existing Default Values and Recommendations for Exposure Assessment* (Norden, 2012), Exposure and Fate Assessment Screening Tool (E-FAST)[8], and Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER)[9].
- Characterize the health and environmental risk – compare the hazard data to the potential exposures to assess potential risk to human health and the environment and determine whether the alternative presents a lower risk.

---

[7] http://chesar.echa.europa.eu/ (includes ECETOC TRA Tier 1 at least)

[8] http://www.epa.gov/opptintr/exposure/pubs/efast.htm

[9] http://www.epa.gov/opptintr/exposure/pubs/chemsteer.htm

- Examine the use and processes associated with this chemical and decide whether process changes can be used to reduce exposure.
- Evaluate the socioeconomic impact associated with potential substitution with the relevant stakeholders (supply chain, brands, authorities or others)

Relevance and Scoring of Hazard Endpoints

Hazard assessment provides information on a range of human health and environmental hazards and fate properties of chemicals. Some comparative hazard assessment tools provide criteria for classifying the hazards of chemicals (e.g., DfE Alternatives Assessment Criteria), while other tools also add a benchmarking scheme that rolls up these hazard classifications into a single score. These tools can be applied to all types of chemicals, regardless of functionality.

Other tools consider the functionality of a chemical and identify the most relevant endpoints for comparison. For example, the DfE Criteria for Surfactants identifies biodegradation and aquatic toxicity as the most relevant attributes for determining a safer surfactant. That is because these endpoints are distinguishing for surfactants, which have generally similar hazard profiles across other hazard endpoints. Where concern levels for a chemical are similar (e.g., comparing use of a carcinogen to use of a PBT), the use and exposure potential should be considered.

Prioritization

Chemical hazard assessment may also be used for prioritization. For example, a manufacturer may want to evaluate chemicals in their processes and/or products, and categorize them based on their hazards as preferred, to replace and to manage. By conducting this assessment, decisions can be made to prioritize those chemicals to replace with inherently safer chemicals.

The most efficient way to evaluate and prioritize a large list of chemical substances is a 3-step process and is similar to other approaches by US EPA (2012), UBA (2011), National Industrial Chemicals Notification and Assessment Scheme (2012), and the Substitution Support Portal:

1. **Compare to “list of lists”** – The list of chemical substances in use is compared to a list of authoritative lists (“list of lists”) that identify chemicals of concern. Chemicals on these lists have been identified as having hazards of potential high concern. For example, SUBSPORT is a publicly available website that has been developed to assist manufacturers in making decisions on chemical substitutions. It includes a feature that allows for searching of a “list of lists” that includes the following (in addition to several company specific restricted substances lists [RSLs]):

   International Agreement
   Stockholm Convention on Persistent Organic Pollutants (POPs)
   OSPAR List of Substances of Possible Concern
   OSPAR Chemicals for Priority Action

   EU Regulatory Lists
   EU REACH Candidate List
   EU REACH Authorisation List
   EU Water Framework Directive: Priority Substances
   EU Water Framework Directive: Certain Other Pollutants
   EU POPs Regulation
   EU Restriction of the Use of Certain Hazardous Substances (RoHS) Directive

   Governmental Lists
   EU REACH: Member States List
   US EPA
   Massachusetts Toxic Use Reduction Act

KEMI: PRIO Phase-Out Substances
KEMI: PRIO Priority Risk-Reduction Substances
Danish EPA
Finnish Environment Institute
Canadian EPA

Nongovernmental Organization (NGO) or Trade Union List
ChemSec: SIN List
Trade Union Priority List

Chemical substances appearing on one of these lists are then prioritized for further evaluation based on an assessment of their hazards. Another example of a "list of lists" is Clean Production Action's GreenScreen List Translator, which includes substances of very high concern, including CMRs and PBTs, listed on authoritative lists. The List Translator can be readily searched on the Pharos Chemical and Material Library[10].

2. **Chemical by chemical evaluation** – Even though a chemical is not listed on an authoritative list, it may still have some level of inherent hazard. In addition, not all hazardous substances posing a risk have been evaluated or are currently regulated. For these chemicals that are not on the "list of lists," the process for comparative chemical hazard assessment can be used to evaluate and prioritize the chemical. The outcome of this evaluation will be as follows:

   – The proposed alternative is less hazardous for all relevant hazard endpoints in comparison to the incumbent and, therefore, would be a more preferable alternative ("Preferred" list).

   – The proposed alternative is less hazardous in some but not all relevant hazard endpoints in comparison to the incumbent and may require further action/evaluation. The chemical is placed on the "Further Action" list.

   – The available hazard data for the proposed alternative is incomplete for relevant endpoints and further data are needed to assess its hazards and draw a conclusion. The chemical is placed on the "Further Assessment" list.

   – The chemical has a high or unacceptable hazard and should be placed on the "High Priority" list, indicating the need to replace this chemical with a safer alternative.

3. **Evaluation of chemicals identified as needing "Further Action" in Step 2.** For chemical substances identified in Step 2 for further action, the following actions will need to be taken to evaluate potential human and environmental exposures, assess risk, and prioritize actions:

   – Identify relevant routes of exposure based on use and disposal of the chemical through its life cycle (e.g., if the compound is a volatile solvent, look at the exposure to workers and atmosphere during production). Perform a qualitative, and if necessary quantitative, exposure potential assessment using appropriate exposure estimation tools. Among the acceptable exposure estimation tools are ECHA Chemical Safety Assessment and Reporting Tool, CHESAR, EUSES 2.1.2, existing default values, *Existing Default Values and Recommendations for Exposure Assessment* (Norden, 2012), Exposure and Fate Assessment Screening Tool, E-FAST and ChemSTEER.

   – Characterize the health and environmental risk – combine the hazard data with the potential exposures to assess potential risk to human health and the environment and prioritize the chemical for replacement.

   – Examine the use and processes associated with this chemical and decide whether process changes can be used to reduce exposure.

   – Evaluate the socioeconomic impact associated with potential substitution with the relevant stakeholders (supply chain, brands, authorities, and others)

[10] http://www.pharosproject.net/material/

– Conduct an alternatives assessment to find an alternative technology (safer chemical substance or process) that meets or exceeds existing performance requirements.

The BizNGO Chemical Alternatives Assessment Protocol (BizNGO, 2011) provides an example of an alternatives assessment framework that details these steps.

4. **Evaluation of chemicals identified as needing "Further Assessment" in Step 2**

Chemicals identified as needing further assessment have data gaps that make it impossible to determine the relative safety of such chemicals. Further data may need to be developed to fill these gaps. Before testing is conducted, it's valuable to explore whether the manufacturer has any confidential data to fill the gaps and whether models or analogs provide sufficient information.

Considerations for the Development of Data for New Chemicals and Preparations/Mixtures

Hazard assessment is equally important to the selection of chemicals already available in the marketplace, as it is to chemicals newly developed by chemical suppliers. When researching newly synthesized chemicals or preparations/mixtures[11] a stepwise process may be needed to evaluate a small number of hazard endpoints and eliminate unsuitable alternatives early. The appropriateness of testing preparations/mixtures should first be considered. Guidance for this decision-making is provided in *Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures* (OECD, 2000) or the *Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3* (OECD, 2006).

The "First-Tier" endpoints listed in Table 2 can be obtained from tests that can be done simply and less expensively for individual chemicals or formulations (without dilution). First-tier toxicology studies are most commonly conducted to determine the acute (one-time, single exposure) toxicity via a relevant pathway for humans (e.g., oral, dermal, and inhalation), the aquatic environment (e.g., fish), or in vitro test systems (e.g., cell cultures of mammalian cells and microorganisms) that are designed to indicate potential for effects in whole animal systems for a particular endpoint (e.g., mutagenicity).

TABLE 2
Examples of First-Tier Hazard Endpoints for New Chemicals and Preparations/Mixtures

Human Toxicity			**Ecotoxicity**
Acute Mammalian Toxicity (Oral, Dermal and Inhalation)	Mutagenicity/Genotoxicity (in vitro)	Skin irritation and Corrosivity	Acute Aquatic Toxicity (daphnia, algae and fish)
Eye Irritation and Corrosivity	Skin Sensitization		Biodegradation (e.g., OECD 301, 302, 303)

Higher-tier toxicological studies are conducted after acute studies have been completed to develop additional hazard data, when there is potential repeated exposure (Table 3).

11 Preparation means a mixture or solution composed of two or more substances.

TABLE 3
Examples of Higher-Tier Hazard Endpoints for New Chemicals and Preparations/Mixtures

Human Toxicity			Ecotoxicity
Systemic Toxicity/Organ Effects* Repeated Dose Toxicity (Oral, Dermal and Inhalation)	Reproductive and Developmental Toxicity	Carcinogenicity	Persistence
Neurotoxicity	Endocrine Disruption		Bioaccumulation
			Chronic aquatic toxicity (on daphnia, algae and fish)

* Specific target organ toxicity (STOT) – repeated dose

Available Tools

Appendix B lists available tools that follow the general approach outlined above for comparative hazard assessment and prioritization.

Works Cited

American National Standards Institute (ANSI). 2013. *NSF/GCI/ANSI 355-2011, Greener Chemicals and Processes Information Standard*. http://webstore.ansi.org/RecordDetail.aspx?sku=NSF%2FGCI%2FANSI+355-2011. Accessed February 28, 2013.

BizNGO. 2011. *BizNGO Chemical Alternatives Assessment Protocol (v.1.0), How to Select Safer Alternatives to Chemicals of Concern to Human Health or the Environment*. http://www.bizngo.org/pdf/BizNGO_CAAProtocol_ExecSum.pdf. Accessed on February 28, 2013.

European Chemicals Agency. 2012. *Guidance on the application of the CLP criteria*. November. http://www.echa.europa.eu/documents/10162/13562/clp_en.pdf. Accessed February 28, 2013.

Global Organic Textiles Standard. 2010. Version 3.0.

National Industrial Chemicals Notification and Assessment Scheme. 2012. *Inventory Multi-tiered Assessment and Prioritization*.

Norden. 2012. *Existing Default Values and Recommendations for Exposure Assessment*. A Nordic Exposure Group Project 2011. http://www.norden.org/en/publications/publikationer/2012-505. Accessed February 28, 2013.

OECD. 2006. *Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3*. March 23. http://masetto.sourceoecd.org/vl=16030783/cl=17/nw=1/rpsv/cgi-bin/fulltextew.pl?prpsv=/ij/oecdjournals/1607310x/v1n3/s1/p1.idx. Accessed on February 28, 2013.

Organisation for Economic Cooperation and Development (OECD). 2000. *Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures*. http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2000)6&doclanguage=en. Accessed on February 28, 2013.

Organisation for Economic Cooperation and Development (OECD). 2011. *SIDS Manual for the Assessment of Chemicals*.

Umweltbundesamt (UBA). 2011. *Guide on Sustainable Chemicals*.

United Nations. 2009. *Globally Harmonized System of Classification and Labelling of Chemicals*. Fourth edition. http://www.unece.org/trans/danger/publi/ghs/ghs_rev04/04files_e.html. Accessed February 28, 2013.

U.S. Environmental Protection Agency (US EPA). 2012. *TSCA Work Plan for Chemicals*. February.

U.S. Environmental Protection Agency (US EPA) Design for the Environment (DfE). 2011. *Assessment Criteria for Hazard Evaluation* version 2.0.

World Health Organization. 2010. *WHO Human Health Risk Assessment Toolkit: Chemical Hazards*. http://www.who.int/ipcs/publications/methods/harmonization/toolkit.pdf. Accessed February 28, 2013.

Washington Department of Ecology. 2013. *The Quick Chemical Assessment Tool*. http://www.ecy.wa.gov/programs/hwtr/ChemAlternatives/QCAT.html. Accessed February 28, 2013.

Appendix A
Intersection of Hazard Endpoints and Authoritative Programs

Intersection of Hazard Endpoints and Authoritative Programs

Effects			Tie to GHS/CLP		Elements of Authoritative Programs						
	Draft required base dataset in Green shading	OECD test guidelines references	Relevant GHS Hazard Statements	Relevant EU C&L Risk Phrase	NSF/GCI/ANSI 355-2011 (Chemical Characteristics)	OECD SIDS (Dec 2011 Guidance)	EPA DfE Alternatives Assessment (v2.0)	Washington State QCAT (Quick Screen)	UBA Sustainable Chemistry Guidance	GOTS (v3.0) Prohibited if chemical is assigned R-phrase	REACH endpoints (per test #) (endpoints mandatory to be filled with data, i.e. REACH Annexes VII and VIII)
Acute Mammalian Toxicity	Acute Mammalian Toxicity										
	Dermal (if relevant exposure pathway)	402	H310,H311,H312,H313	R21,R24,R27	Tier I	required data	required	required	required	R27	required (8.5.3)
	Oral (if relevant exposure pathway)	401	H300,H301,H302,H303,H304,H305	R22,R25,R28	Tier I	required data	required	required	required	R28	required (8.5.1)
	Inhalation (if relevant exposure pathway)	403	H330,H331,H332,H333	R20,R23,R26,R29,R30,R31,R37	Tier I	required data	required	required	required	R26	required (8.5.2)
	Skin Irritation/Corrosivity	404	H314, H315	R38,R41	Tier I	optional	required		required	no specific reqs.	required (8.1)
	Eye Irritation/Corrosivity	405	H318,H319,H320	R36	Tier I	optional	required		required	no specific reqs.	required (8.2)
Chronic Mammalian Toxicity	Carcinogenicity	451 / 453	H350, H351	R40, R45,R49	Tier I	optional	required	required	required	R40,R45,R49	No specific requirements (test proposal if necessary)
	Mutagenic/ Genotoxic Effects	471 / 473 / 474 / 475 / 476	H340,H341	R46,R47	Tier I	required	required	required	required	R46	required (8.4.1 / 8.4.2 / 8.4.3 / 8.4.4)
	Reproductive Toxicity	415 / 416 / 421 / 422 / 443	H306,H361,H362	R47,R60,R62	Tier I	required	required	required	required	R60,R62	screening required (8.7.1 a)
	Developmental Toxicity	414 / 421 / 422 / 426	H306,H361,H362	R47,R61,R63	Tier I	required data	required	required	required	R61,R63	screening required (8.7.1 a)
	Neurotoxicity	418 / 419 / 424 / 426	*no specific statement*		Tier I	optional	required		no specific reqs.	no specific reqs.	No specific requirements (test proposal if necessary)
	Systemic Tox/Organ Effects (incl. Immune System) Effects/Repeated Dose Toxicity	407 / 410 / 412	H372,H373	R33, R48	Tier I	required data	required		required	no specific reqs.	required (8.6.1.a/b/c - Short-term repeated dose toxicity study in rats (28 days), oral/dermal/inhalation)
	Skin Sensitization	406	H317	R43	Tier I	optional	required		required	no specific reqs.	required (8.3.1)
	Respiratory Sensitization		H334,H335	R42	Tier I	no specific reqs.	required		required	no specific reqs.	No specific requirements
	Endocrine Activity or Endocrine Disruption		*no specific statement*	*no specific phrase*	Tier II	no specific reqs.	evaluated		required	no specific reqs.	No specific requirements

	Assessment of toxicokinetic behavior	**417**									**required (8.8.1)**
	Experience with Human Exposure		*no specific statement*	*no specific phrase*		**if available**	no specific reqs.		no specific reqs.	no specific reqs.	Existing data must be reported
Environmental Toxicology	**Acute Aquatic Toxicity**										
	Fish	**203**	H400,H401,H402	R50,R51,R52	Tier I	**required data**	**required**	**required**	**required**	**R50,R51**	**required (9.1.3)**
	Aquatic Plants (Algae)	**201**	H400,H401,H402	R50,R51,R52	Tier I	**required data**	**required**	**required**	**required**	**R50,R51**	**required (9.1.2)**
	Aquatic Invertebrates (Daphnia)	**202**	H400,H401,H402	R50,R51,R52	Tier I	**required data**	**required**	**required**	**required**	**R50,R51**	**required (9.1.1)**
	Chronic Aquatic Toxicity										
	Fish	**204 / 210 / 212 / 215**	H410,H411,H412,H413	R50,R51,R52	Tier I	**required data**	**required**		**required**	**R50,R51**	No specific requirements (test proposal if necessary)
	Aquatic Plants (Algae)		H410,H411,H412,H413	R50,R51,R52		no specific reqs.	**required**		**required**	**R50,R51**	No specific requirements (test proposal if necessary)
	Aquatic Invertebrates (Daphnia)	**211 ?**	H410,H411,H412,H413	R50,R51,R52	Tier I	**required data**	**required**		**required**	**R50,R51**	No specific requirements (test proposal if necessary)
	Toxicity to microorganisms										
	Aquatic (bacteria in activated sludge)	**209**	*no specific statement*	*no specific phrase*		optional	no specific reqs.		no specific reqs.	no specific reqs.	**required (9.1.4) - Activated sludge respiration inhibition testing**
	Soil	**216 / 217**	*no specific statement*	*no specific phrase*		optional	no specific reqs.		no specific reqs.	no specific reqs.	No specific requirements(test proposal if necessary)
	Terrestrial										
	Plants	**208 / 227 ?**	*no specific statement*	*no specific phrase*		optional	no specific reqs.		no specific reqs.	**R54**	No specific requirements(test proposal if necessary)
	Earthworms	**207 / 222**	*no specific statement*	*no specific phrase*	Tier I (subchronic)	optional	no specific reqs.		no specific reqs.	**R56**	No specific requirements (test proposal if necessary)
	Toxicity to Sediment Dwelling Organisms										
	Chironamid toxicity	**218 / 219**	*no specific statement*	*no specific phrase*		optional	no specific reqs.		no specific reqs.	no specific reqs.	No specific requirements (test proposal if necessary)
Environmental Fate	**Persistence**	**301 and followings**	*no specific statement*	*no specific phrase*	Tier I	**required data**	**required**	**required**	**required**	**specific POPs banned**	**required (9.2.1.1.a / b) - ready biodegradability**
	Bioaccumulation	**305 / 315 / 317**	*no specific statement*	*no specific phrase*	Tier I	optional	**required**	**required**	**required**	required	**required (PBT assessment)**
	Hydrolysis as a function of ph and identification of degradation products	**111**									**required (9.2.2.1)**

	Adsorption/desorption screening study (hPLc method)	**121**									**required (9.3.1)**
	Partition coefficient n-octanol/water, flask shake method	**107**									**required (7.8)**
Chemical Reactivity	**Reactivity (e.g. explosive properties / auto-ignition temperature for liquids and gases)[1]**	**113 / EU methods A.14 / A.15 and A.16**	H200-H205, H240-H242,H250-H252, H260-H261, H270-H272, H280,H290	R1-R6, R14-R16,R19,R29,R44	Tier I	no specific reqs.	if relevant to chemicals evaluated		**required**	no specific reqs.	**required (7.11 and 7.12)**
	Flammability (e.g. flash point for liquids)	**EU test method A.9**	H220-H228	R7-R12, R17-R18,R30	Tier I	no specific reqs.	if relevant to chemicals evaluated		**required**	no specific reqs.	**required (7.9 - flash point and 7.10 flammability, liquids)**
Other	**VOC Content**		*no specific statement*	*no specific phrase*		no specific reqs.	no specific reqs.		no specific reqs.	**specific solvents banned**	No specific requirements

1) Other physico-chemical properties may be required for exposure pathway evaluations

Appendix B
Comparative Hazard Assessment and Prioritization – Methodologies and Tools

APPENDIX B

Comparative Hazard Assessment and Prioritization - Methodologies and Tools

The following methodologies and tools are among those that could be used for assessment. Other methodologies and tools following the guidelines described in this document may also be available. If there are a large number of chemicals, the ability to link the approach with a software tool for automated data analysis will be important.

Government-developed Tools

Following are government-developed tools that can be used for assessment:

- **US EPA DfE Alternatives Assessment Criteria for Hazard Evaluation** – The DfE Alternatives Assessment Criteria are toxicological definitions of high, moderate, and low (and sometimes very high or very low) hazard across most of the endpoints described in Table 1 of *Using Chemical Hazard Assessment for Alternative Chemical Assessment and Prioritization*. The criteria are largely based on the GHS classifications, though DfE does draw from EU criteria for very bioaccumulative substances and US EPA's acute toxicity categories. DfE uses the Alternatives Assessment criteria in its own comparative hazard assessments.
- **German Federal Agency Approach, Guide on Sustainable Chemicals (2011)** – This guide assists the selection of sustainable chemicals by providing criteria to distinguish between sustainable and non-sustainable substances. It can also support a more sustainable use of chemicals by highlighting single aspects of the evaluation. The guide is not specific to certain industry sectors, but the criteria can be used across all fields of economy. Substance-specific criteria, which only depend on the substance properties, are differentiated from use-specific criteria, which depend on the type of its application and use.
- **Washington State QCAT** – QCAT is a simplified assessment tool used to evaluate hazards associated with alternatives to toxic chemicals. The Washington Department of Ecology developed the QCAT to help small and medium businesses that are concerned about the alternative assessment process. It is not intended as a replacement for more thorough assessment methods like the GreenScreen but as an introduction to the hazard assessment process. The QCAT is based upon the GreenScreen methodology. It is neither as complete nor as complicated as the GreenScreen. The QCAT user should understand that a QCAT assessment is not as thorough an evaluation of the hazards posed by alternatives to a toxic chemical as the GreenScreen method; however, if a chemical is found to be a poor alternative using the QCAT methodology, it will also be rejected by the GreenScreen methodology. There remains a chance that a chemical not rejected by QCAT could still prove to be unsatisfactory if a more complete review is done using methods like the GreenScreen. QCAT does show the benefits of conducting a hazard assessment and provides a good introduction to the hazard assessment process (Washington Department of Ecology, 2013).

Nongovernmental Organizations/Private Sector Tools

- **GreenScreen** – The GreenScreen for Safer Chemicals is a transparent, freely accessible, health-protective, and science-based method to compare and rank chemicals along a hazard index developed by Clean Production Action. The GreenScreen uses internationally recognized criteria, hazard lists and scientific literature to assess the inherent hazards of a chemical against individual human health and environmental endpoints. The GreenScreen hazard classifications harmonize with GHS and the US EPA DfE Alternatives Assessment Criteria for Hazard Assessment. The method then goes beyond DfE by providing four overall benchmarks: Benchmark 1 (red) through Benchmark 4 (green). Companies use the GreenScreen to identify chemicals of concern to human health and the environment as well as safer alternatives. The List Translator is a portion of the full GreenScreen method that facilitates the quick review of chemicals based on authoritative and hazard screening lists, and GHS country classifications. Software tools developed by Pharos and GreenWERCS facilitate the rapid use of the List Translator.

- **GreenWERCS** – This tool uses user defined hazard endpoints (e.g., GreenScreen) to quickly and automatically screen single chemicals or formulations against a particular set of categories (i.e., known carcinogens, mutagenic hazards, or acute toxicity). The program also allows screening against a "list of lists" database that incorporates more than 4,000 global regulatory lists. GreenWERCS allows complete user configurability of all models used including changing any endpoint and using as few or as many endpoint as desired. The database is updated every 3 months and is currently comprised of more than 4,000 different regulations and sources of data from all over the world.
- **SciVera Lens** – SciVera Lens is a cloud-based "software as a service" tool that provides the following three key functionalities: 1) it enables users to collect chemical/material/product data from suppliers electronically, 2) these data are then used to generate automated chemical hazard assessments and 3) for chemicals/materials/products with high hazards, exposure and risk assessments can be generated for further prioritization. The hazard endpoints are based on GHS and US EPA DfE criteria, which can be customized to meet the needs of specific customers or industry sectors. Bill of Product (BOP)/Bill of Material (BOM)/Bill of Substance (BOS) data can be uploaded into SciVera Lens and assessments generated on all substances concurrently following overnight processing.
- **Chemical Compliance Systems (CCS)** – CCS, via secure web-based platforms, provide rapid risk assessments of chemicals, chemical products, and manufacturing processes through integration of the individual chemical attribute information. CCS's methodology is definitive and fully embodies the NSF/ GC)/ANSI 355 Standard for Greener Chemicals and Processes Information, applying all prescribed 44 endpoints for numerically calculating determinations. CCS's chemical risk assessment methodology has alignment with decision-making logic set forth in the Chemical Management Framework by assuring global regulatory compliance across hundreds of regulatory restricted substance Lists and proscribed substances. CCS's secure supply chain communication systems can free the flow of chemical information, even CBI, for purposes of risk determinations of chemical products and processes. CCS generates risk assessments using a "Green Scoring" technology based on the combined hazard of a chemical composition and endpoint factor weightings customizable for areas of concerns specific to the customer or industry. CCS can screen large numbers of chemical entities for purposes of identification of candidates for prioritization and "greening" chemical management or replacement. CCS provides tools for aiding decision-making for "greener" and safer alternatives by documented and transparent quantitative analysis.
- **bluesign** – Specific to the textile supply chain, bluesign offers a holistic approach which includes evaluation of the chemical hazard. The bluesign standard is described as "a comprehensive Input-Stream-Management-System that covers all Environmental, Health, and Safety (EHS) aspects along the textile manufacturing chain."[1] The bluesign standard is built around five principles: resource productivity, consumer safety, air emission, water emission, and occupational health and safety. The basic idea behind the bluesign standard is to combine aspects of consumer safety, water, and air emission as well as occupational health into a single standard under the general objective of resource productivity. To improve the EHS aspects and resource efficiency along the whole textile supply chain is therefore the main critical focus of the bluesign standard. In other words, the bluesign standard can be understood as a highly efficient tool to optimize the sustainability of the manufacturing process along the textile chain. The bluesign standard brings together the entire textile manufacturing chain to jointly reduce the ecological footprint of a responsibly acting textile industry. All input streams are analyzed – from raw materials to chemical components to resources – with sophisticated tools. Prior to production, components are assessed based on their toxicological and ecological properties and risks. Potentially harmful substances can hence be eliminated before production even begins (bluesign, 2013).

[1] bluesign. 2013. http://www.bluesign.com/index.php?id=57. Accessed February 28, 2013.

- **Green Chemistry and Commerce Council (GC3)** – GC3 offers a summary of tools relevant to evaluation of chemicals some of which may be applicable (GC3, 2013).

Works Cited

bluesign. 2013. http://www.bluesign.com/index.php?id=57. Accessed February 28, 2013.

Green Chemistry and Commerce Council (GC3). 2013. Retailer Portal Database: Tools to Evaluate Chemical Ingredients in Products. http://www.greenchemistryandcommerce.org/retailer.portal.php. Accessed February 28, 2013.

Washington Department of Ecology. 2013. *The Quick Chemical Assessment Tool*. http://www.ecy.wa.gov/programs/hwtr/ChemAlternatives/QCAT.html. Accessed February 28, 2013