Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternatives

Series on Risk Management
No. 60

OECD
BETTER POLICIES FOR BETTER LIVES

Series on Risk Management
No. 60

Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternatives

Please cite this publication as:

OECD (2021), *Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternative,* OECD Series on Risk Management, No. 60, Environment, Health and Safety, Environment Directorate, OECD.

About the OECD

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation in which representatives of 37 industrialised countries in North and South America, Europe and the Asia and Pacific region, as well as the European Commission, meet to co-ordinate and harmonise policies, discuss issues of mutual concern, and work together to respond to international problems. Most of the OECD's work is carried out by more than 200 specialised committees and working groups composed of member country delegates. Observers from several countries with special status at the OECD, and from interested international organisations, attend many of the OECD's workshops and other meetings. Committees and working groups are served by the OECD Secretariat, located in Paris, France, which is organised into directorates and divisions.

The Environment, Health and Safety Division publishes free-of-charge documents in twelve different series: **Testing and Assessment**; **Good Laboratory Practice and Compliance Monitoring**; **Pesticides**; **Biocides**; **Risk Management**; **Harmonisation of Regulatory Oversight in Biotechnology**; **Safety of Novel Foods and Feeds; Chemical Accidents; Pollutant Release and Transfer Registers; Emission Scenario Documents; Safety of Manufactured Nanomaterials;** and **Adverse Outcome Pathways.** More information about the Environment, Health and Safety Programme and EHS publications is available on the OECD's World Wide Web site (www.oecd.org/chemicalsafety/).

This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among **FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

Foreword

This guidance was developed with the aim to advance broader agreement on a general approach and criteria for the selection of safer alternatives, with a focus on chemical substitution. It is intended to advance a consistent understanding of the minimum requirements needed to determine whether a chemical alternative is safer than the priority chemical, product, or technology for substitution, independent of the entity performing the assessment or the alternatives assessment framework being used.

The guidance was developed within the framework of the OECD Ad Hoc Group on the Substitution of Harmful Chemicals. An initial draft was developed by Abt Associates to which Ad Hoc Group members contributed text and provided review comments. It is published under the responsibility of the OECD Chemicals and Biotechnology Committee.

Table of Contents

1. Background

As the demand for safer chemicals and technologies grows, the field of alternatives assessment is becoming increasingly important in guiding the transition towards safer, less toxic alternatives. Throughout Organisation for Economic Co-operation and Development (OECD) delegations, alternatives assessments are being used to respond to government regulations, including the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) in the European Union (EU) and state-level regulations in the United States (U.S.), as well as industry, retailer, and consumer demands for products that do not contain harmful chemicals. The U.S. National Research Council (NRC) defines alternatives assessment as a "process for identifying and comparing potential chemical and non-chemical alternatives that could replace chemicals of concern on the basis of their hazards, comparative exposure, performance, and economic viability" (National Research Council 2014). Alternatives assessment generally takes place after a decision to substitute occurs and helps guide that process.

The use and practice of alternatives assessment approaches have advanced considerably in the last decade. Alternatives assessment frameworks, guidance documents, tools, and data sources have been developed by governments and other organizations to assist practitioners in selecting safer alternatives. Businesses have successfully replaced chemicals with known hazards for human health and the environment with lower concern alternatives. Leaders in industry, academia, and the research community continue to drive innovation towards chemicals, products, and processes that are "safer by design." In addition, new research and professional networks are advancing dialogue on best practices in the field. Initiatives are underway to document and disseminate these tools and real-world examples of informed substitution, including the case study repository in the OECD Substitution and Alternatives Assessment Toolbox (SAAToolbox),[1] SUBSPORTplus,[2] the European Chemical Agency's (ECHA) Repository of Analyses of Alternatives (performed both in the context of REACH applications for authorization[3] and restriction proposals),[4] ECHA's Substitution to Safer Chemicals website,[5] U.S. OSHA's Transitioning to Safer Chemicals Toolkit,[6] and Ontario's Toxics Reduction Program - Reference Tool for Assessing Safer Chemical Alternatives.[7] Resources including the Interstate Chemicals Clearinghouse's (IC2) Chemical Hazard Assessment Database[8] and GreenScreen® Library[9] provide access to completed chemical hazard assessments. Additionally, U.S. Environmental Protection Agency (EPA)'s Safer Chemical Ingredients List (SCIL)[10] provides a list of chemical ingredients, arranged by functional-use class, that the EPA's Safer Choice Program has evaluated and determined to be safer than traditional chemical ingredients.

Despite this progress, important gaps in alternatives assessment approaches remain. These include limitations and differences in hazard and comparative exposure evaluation approaches, missing data on chemicals, lack of training and expertise in conducting alternatives assessments, and inadequate time and/or resources to perform careful, transparent analyses. An important limitation that can hinder efforts to evaluate and adopt alternatives for priority chemicals is the lack of consistent criteria for defining "safer." Practitioners face challenges on what constitutes "safer" when evaluating alternatives from both a hazard and exposure perspective – especially in instances of incomplete, uncertain data on human health and environmental endpoints. The workshop of the OECD Ad Hoc Group on the Substitution of Harmful Chemicals in May 2018 highlighted this complexity, with members citing the need for guidance for defining safer chemicals and technologies. A recent report commissioned by the EU, called the "Chemicals Innovation Action Agenda: Transition to Safer Chemicals and Technologies," echoed this need for criteria for safer alternatives, citing it as one of four key priority actions needed to "scale investment and innovation in safer chemicals and technologies to accelerate their adoption" (Wood Environment & Infrastructure Solutions 2019). Similarly, the European Green Deal (European Commission 2019), which includes "eliminating pollution" as one of the key policy areas for making the EU's economy sustainable by 2050, calls for improving "rules on assessment of substances launched on the market," developing "more sustainable chemical alternatives," and protecting "citizens against dangerous chemicals with a new chemicals strategy for sustainability for a toxic-free environment."[11]

This guidance responds to these calls by identifying and outlining key considerations for the identification and selection of safer alternatives. The remainder of this report is organized as follows:

- ***Section 2 (Purpose and Key Principles)***: This section describes the purpose and scope of this guidance, as well as the key principles on which this guidance is based.
- ***Section 3 (Minimum Criteria and Recommended Assessment Practices for Safer to Support Substitution Processes)***: This section outlines minimum requirements (criteria) and recommended assessment practices for determining whether alternatives are safer within the context of substitution decisions, as well as suggested approaches for moving beyond the minimum requirements.
- ***Section 4 (Self-Assessment Checklist)***: This section provides a self-assessment checklist of the recommended assessment practices and criteria discussed in Section 3.
- ***Section 5 (Beyond Safer to More Sustainable Substitution)***: This section discusses broader sustainability considerations (beyond chemical safety) that can be used to select more sustainable chemical alternatives.

Notes

1 http://www.oecdsaatoolbox.org/

2 https://www.subsportplus.eu/

3 https://echa.europa.eu/regulations/reach/authorisation/applications-for-authorisation

4 https://echa.europa.eu/registry-of-restriction-intentions

5 https://echa.europa.eu/substitution-to-safer-chemicals

6 https://www.osha.gov/dsg/safer_chemicals/

[7] https://www.ontario.ca/document/ontario-toxics-reduction-program-reference-tool-assessing-safer-chemical-alternatives-0

[8] http://theic2.org/hazard-assessment

[9] https://store.greenscreenchemicals.org/gs-assessments

[10] https://www.epa.gov/saferchoice/safer-ingredients

[11] https://ec.europa.eu/commission/presscorner/detail/en/fs_19_6729

2. Purpose and Key Principles and Definitions

2.1. Purpose and Scope of this Guidance

This guidance was developed by the OECD Ad Hoc Group on Substitution of Harmful Chemicals to advance broader agreement on a general approach and criteria for the selection of safer alternatives, with a focus on chemical substitution. It is intended to advance a consistent understanding of the *minimum requirements* needed to determine whether a chemical alternative is safer than the priority chemical, product, or technology for substitution, independent of the entity performing the assessment or the alternatives assessment framework being used. The guidance focuses on minimum assessment criteria and recommended assessment practices for four core areas of alternatives assessments: (1) determining the assessment's scope, (2) comparative hazard assessment, (3) comparative exposure assessment, and (4) the integration of hazard and exposure results to select a safer alternative. The guidance also includes recommendations for moving beyond the minimum criteria and assessment practices. Future activities on substitution at the OECD could be focused on refining these minimum criteria based on evolving knowledge and practice, establishing additional criteria that go beyond these minimum requirements, and examining how these criteria can more effectively influence the design of new chemicals.

Factors such as performance, cost, and commercial availability are critical assessment components in determining if an alternative is viable, but they are not the focus of this guidance. For example, an alternative that does not perform as well, reduces the lifespan of a product (requiring more material), or requires additional inputs to achieve an acceptable level of performance may not be considered an acceptable alternative. This guidance also does not define or establish criteria for the broader suite of sustainability considerations discussed in Section 5, yet it is meant to complement ongoing efforts within the EU and other OECD delegations focused on sustainable chemistry.

Additionally, this guidance is focused primarily on single chemical substitutions and not "functional substitution" where the alternative could include technology, product, or service changes (Tickner et al., 2015). A functional substitution approach is recommended in any alternatives assessment not only to broaden the scope of possible alternatives, but also to identify safer alternatives when drop-in chemical substitutes are not significantly safer or more sustainable than the original substances of concern. In the case of functional substitution, use of other tools and criteria to evaluate trade-offs at a mixture, product, or technology level may be needed. However, in principle, the processes and criteria contained in this guidance can be useful in evaluating mixture, product, or technology level assessments.

2.2. Key Definitions and Principles

Informed substitution is defined as "replacing hazardous substances with safer alternatives, [and] is the goal of a solutions-oriented approach to chemical management. It involves identifying alternatives and evaluating their health and safety hazards, potential trade-offs, and technical and economic feasibility" (U.S. Occupational Safety and Health Administration (OSHA)). Within this substitution context, and for the purpose of this guidance, a "safer alternative" is meant to denote a chemical, product, or technology that is preferable, in terms of both hazard and potential for exposure to humans and the environment, than the existing option. Evaluating comparative hazard and exposure is an element of the process. Use of the term "safer" in this guidance reflects its common usage across OECD delegations (including in regulatory guidance and the scientific literature), as well as the way it has been formally defined by authoritative bodies (see **Exhibit 1**).

Exhibit 1. Example Definitions of "Safer" within a Substitution Context

U.S. National Research Council (National Research Council 2014, p. 13) – *A safer alternative represents an option that is less hazardous to humans and the environment than the existing chemical or chemical process.*

California Safer Consumer Products regulation (California Code of Regulations 2013, p. 13) – *"Safer alternative" means an alternative that, in comparison with another product or product manufacturing process, has reduced potential adverse impacts and/or potential exposures associated with one or more Candidate Chemicals, Chemicals of Concern, and/or replacement chemicals, whichever is/are applicable.*

U.S. Occupational Safety and Health Administration – *A safer alternative is an option that is less hazardous for workers than the existing means of meeting that need.*

European Council, Chemical Agents Directive (Council of the European Union 1998) – *The employer must ensure that the risk is eliminated or reduced to a minimum, preferably by substitution (replacing a hazardous chemical agent with a chemical agent or process which is not hazardous or less hazardous).*

Additional guiding principles for this guidance are the concepts of green and sustainable chemistry[1] and continuous improvement. As noted by the U.S. NRC, in many cases – for specific chemical functions and applications, safer alternatives may not exist for priority chemicals and need to be developed through green and sustainable chemistry methods. Less hazardous substances can be adopted now, where they are available, while efforts to speed the pace of new, green and sustainable chemistry innovations will provide future opportunities to move to safer chemistry. The transition to safer chemicals and technologies is a continuous improvement process. Even though the present guidance focuses on identifying safer substances in the context of an alternatives assessment, the general principles remain applicable in the context of developing new, green or sustainable chemistry solutions.

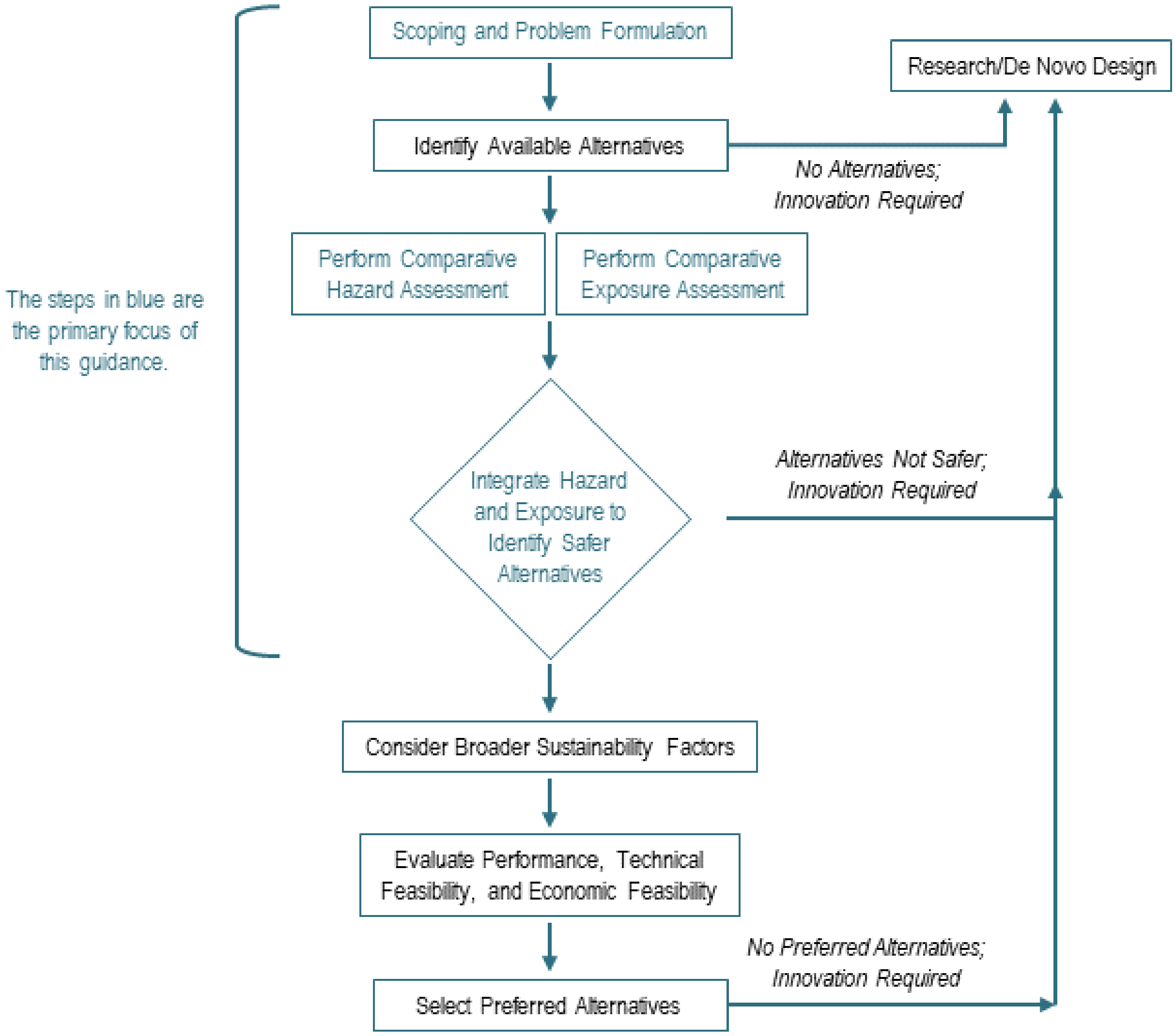
Notes

[1] As defined by OECD, sustainable chemistry "encompasses the design, manufacture and use of efficient, effective, safe and more environmentally benign chemical products and processes." http://www.oecd.org/chemicalsafety/risk-management/sustainablechemistry.htm

3. Minimum Criteria and Assessment Practices for Safer Alternatives to Support Substitution Processes

The minimum criteria, recommended assessment practices, and the practices that go beyond the minimum criteria proposed in this section are informed by a review of the literature, including alternatives assessment frameworks, safer product/material certification processes, and published alternatives assessments. Based on this review, the process of determining whether a chemical, product, or technology is "safer," for the purpose of this guidance, consists of three key steps: comparative hazard assessment, comparative exposure assessment, and integration of hazard and exposure information (as shown in Exhibit 2 below). The initial step of scoping and problem formulation is also covered by this guidance given its importance in identifying and documenting the goals and principles that will guide the assessment. Because this guidance is designed to complement any alternatives assessment framework or decision-making context (not serve as a standalone approach), it does not prescribe a step-wise process a practitioner should take when performing an alternatives assessment.

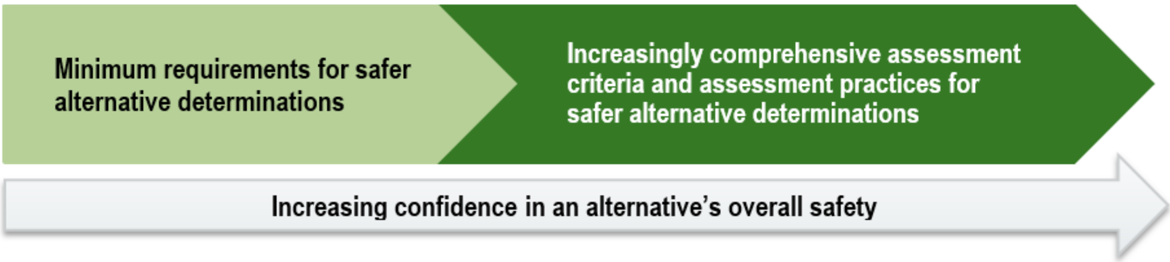
Exhibit 2. Generic Alternatives Assessment Framework Showing What's Covered by this Guidance



Although this guidance focuses on a minimum set of requirements (criteria and recommended practices) for determining if an alternative is safer, these requirements may evolve as understanding and agreement on them changes. For example, the ability to develop a more comprehensive set of requirements is currently hindered by factors that include a lack of agreement on criteria used to determine hazard and/or exposure potential, a lack of agreed upon methods and decision rules to integrate quantitative and qualitative information, as well as a lack of accepted approaches to address uncertainty in safer alternatives determinations. Additionally, there is a need for any minimum set of requirements to be adaptable to different assessment contexts and levels in knowledge of the assessor (from academic or government contexts to those in the range of industries that might use them).

Minimum requirements should be seen as the *baseline level* in a spectrum or hierarchy of an increasingly comprehensive set of criteria and assessment practices that may ultimately be needed to support broad stakeholder confidence that a given alternative is safer. This minimum set of criteria and practices should not preclude assessors from including more comprehensive approaches in their alternatives assessments. Assessments that go beyond these minimum requirements will reduce the likelihood of a substitution decision leading to unintended consequences to the environment, workers, and the public more broadly. Specific assessment contexts, availability of resources, and expertise will dictate the ability to address additional assessment criteria. In addition, data gaps remain a significant challenge in the ability to conduct assessments that are more comprehensive. As science advances, certain criteria, endpoints, or practices may become more generally used and the minimum requirements may change. An extension in the minimum criteria should balance the need to make timely decisions in the face of imperfect information with the benefit of that extra knowledge in improving decisions. To support more comprehensive approaches, criteria and recommended practices for going beyond the minimum have been suggested as a supplement to minimum requirements.

Exhibit 3. Spectrum of Safer Criteria for the Selection of Alternatives to Priority Substances



In cases where a safer alternative cannot be identified for a particular chemical function or application, these minimum criteria as well as criteria for going beyond the minimum can be useful in helping to direct the development of green chemistry solutions. Traditionally, many health and safety impacts are not considered in the design-stage of new chemistry development/innovation. Use of these minimum requirements for evaluating and comparing hazard and exposure potential can help to advance aligned efforts focused on safer or green chemistry.

It should be noted that cases could arise where all alternatives present intrinsic hazard concerns, and while awaiting green chemistry solutions, assessors could choose to use exposure information (e.g., whether the alternatives are hazardous via dermal, inhalation, and/or oral routes, and the likelihood of exposure via each route) to identify the *relatively* safer option. However, for the purposes of this guidance, these alternatives should only be considered "safer" from a relative perspective and green chemistry solutions should be pursued for a more ideal solution.

Minimum criteria for establishing the scope of the assessment, comparative hazard assessment, comparative exposure assessment, and the integration of both assessments to make a safer alternative determination are outlined below in Sections 3.1-3.4, and are key considerations for helping assessors move beyond the minimum criteria. At the end of Section 3 a case example of a hypothetical solvent manufacturer seeking to replace a solvent with potential concerns for several human health endpoints with a safer alternative for use in high-performing cleaning products is included to demonstrate how these minimum requirements and considerations for moving beyond the minimum can be applied in practice. This solvent example is also referenced throughout Section 3 to illustrate how the criteria apply to the components of an alternatives assessment that are within the scope of this Guidance. It does not illustrate how to perform other elements that make up an alternatives assessment, such as performance, technical feasibility, or economic viability

3.1. Determining the Assessment Scope

Scoping is an important initial step of an alternatives assessment and sets the stage for subsequent steps. This step is important because it not only defines and documents the goals and principles that will guide the assessment, it can also help to screen out alternatives that are clearly infeasible or unacceptable from a functional, legal, economic, market, or corporate policy standpoint, thus saving time and resources in the assessment by focusing on a smaller range of viable options. The performance needs for alternatives are often defined during scoping. The following recommended assessment practices should be included in the scoping step to support a safer alternative determination:

A. Include appropriate stakeholder input in determining the scope of the assessment; and

B. Clearly document the goals, principles, and decision rules used.

A. Include appropriate stakeholder input in determining the scope of the assessment

Careful consideration of which stakeholders to engage and how will make the assessment more efficient, robust, and beneficial with regards to acceptance of the results, no matter whether the assessment is conducted by industry, a government authority, or other entity. For example, if a manufacturer of cleaning products is seeking to identify a safer solvent for use in a new line of cleaning products, production workers, research and development, regulatory, and Environment, Health, and Safety (EHS) departments within the company may have insights into what options may be most viable, market trends, and concerns about alternatives that could result in regrettable substitutions. Including external stakeholders, such as suppliers, purchasers, scientists, non-governmental organizations (NGOs), and other professionals, can help identify critical concerns with the incumbent option as well as potential trade-offs that could occur with alternatives. Bounding the assessment is an important role for stakeholders. Identifying potential human health effects (and endpoints to consider), reasonably foreseeable exposure scenarios and pathways, life cycle segments, and environmental impacts of greatest concern for the chemical prioritized for substitution can help to focus the assessment. The narrower the scope, the more streamlined the assessment can be. However, such streamlined assessments run the risk of missing potential trade-offs. Including stakeholder input and concerns can help ensure that the assessment is designed to reveal and consider trade-offs. For example, environmental justice issues, such as effects on vulnerable populations, can be identified through stakeholder engagement[1].

At a minimum, stakeholder concerns should be based on informal discussions, conducting research or listening to presentations in meetings/conferences. Beyond this minimum requirement is the direct engagement of stakeholders using more structured and formal approaches, such as a formal project team with external stakeholders to inform a specific step of the assessment or the entire assessment process. For the latter, stakeholders should be included from the scoping step through the review of the entire assessment in order to provide input into which alternatives are safer and feasible.

B. Document the goals, principles and decision criteria/rules used

Developing clear goals, principles and decision rules for the assessment will improve the assessment and help focus its scope. Goals should reflect why the assessment is being conducted – *what is driving the organization to identify a safer alternative?* Is it to go beyond regulatory compliance or respond to customer demands? Is it an innovation strategy to help unlock new markets? Is it to reach a corporate sustainability goal? Goals include "using renewable feedstocks" or "achieving zero discharge of hazardous substances." Principles help guide the assessment process, such as "ensure transparent information" and "take a precautionary approach when faced with uncertain information."[2] Assessment criteria and decision rules are derived from the goals and principles and implemented during subsequent assessment steps. To the extent possible, it is important to involve stakeholders in helping to help establish these assessment criteria and decision rules during the scoping step, as this will help ensure clarity and transparency in how the assessment will be carried out. A clear decision-rule may be "avoid SIN (Substitute It Now!) list chemicals," "avoid chemicals on my clients' restricted substances lists," or "consider only chemicals with data for my key endpoints."

Exhibit 4. Scoping and Problem Formulation

Recommended Assessment Practice

- **At a minimum, include stakeholder input and concerns.** Establish an understanding of stakeholder concerns through informal discussions, conducting research (literature and document reviews), attending conferences and listening to stakeholder presentations.
- **Use stakeholder input to help bound the assessment** by including those assessment criteria that are most relevant.
- **Clarify goals, associated principles, assessment criteria and decision rules** to focus the scope of the assessment using stakeholder input to the extent possible.

3.2. Comparative Hazard Assessment

The purpose of a comparative hazard assessment is to compare the hazards of alternatives to the chemical prioritized for substitution (termed "priority chemical" in this guidance) for a specific functional use and application. This step of an alternatives assessment seeks to answer: *Do specific alternatives present a higher or lower hazard to human health and/or the environment considering an array of human and environmental health endpoints/criteria?*

To identify safer alternatives, minimum requirements for the comparative hazard assessment step include:

A. Use Authoritative Lists to quickly screen out problematic alternatives from consideration before a full hazard evaluation is performed;

B. Select endpoints and apply criteria/thresholds using the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals;

C. Establish transparent decision rules to organize and prioritize information; and

D. Consider data gaps and uncertainty.

A. Use Authoritative Lists to quickly screen out problematic alternatives from further consideration before a full comparative hazard evaluation is performed

Authoritative lists (i.e., lists developed by government bodies or government-recognized expert bodies that include substances of concern for human health and/or the environment) are used extensively in the hazard assessment element of alternatives assessment regardless of the specific framework used. Using these lists to screen out unacceptable alternatives saves time and resources as other bodies have identified them as a problematic, meaning that *substances on these lists should generally not be considered safer alternatives.* These lists serve multiple purposes—from lists of restricted chemicals to lists of chemicals that have known or suspected hazardous properties of concern. They are often established based on results from expert reviews of the scientific literature and stakeholder engagement. Many companies and sectors use authoritative lists to create Restricted Substances Lists (RSLs) that may include additional substances that have raised concern based on review processes established by industry sectors or NGOs, or are under increased scientific or market scrutiny. Many, often overlapping, authoritative lists and RSLs exist. If two authoritative bodies publish conflicting conclusions on the hazard of a substance, further understanding of the underlying data and time of publication may be needed. This approach is considered moving beyond the minimum criteria. In general, presence on an authoritative list signals an inherent hazard, with divergences on authoritative lists resulting either from differences in expert interpretation and weight of scientific evidence decisions or from differences in regulatory schemes. As a general rule, a chemical in this situation should be handled with care in accordance with the regulatory system in place or the goal of the alternatives assessment.

Exhibit 5 is a minimum set of authoritative lists to use for screening out potentially problematic alternatives. These lists are frequently aligned with regulatory programs restricting priority chemicals or requiring consideration of alternatives for priority chemicals; they include endpoints that are identified as minimum requirements during the assessment of comparative hazards (see below); and they are routinely incorporated into automated hazard assessment screening tools. **Exhibit 5** also includes additional lists and information sources to consult for supporting decision making when going beyond the minimum, as resources allow. Unlike authoritative lists, these additional lists will not provide an automatic screen-out of unacceptable alternatives. (Note: a list of tools and approaches for conducting hazard assessments can be found in the OECD SAAToolbox's Tool Selector.)[3] It should be noted that absence of a chemical from a list is not an indication of safety.

Exhibit 5. Use of Authoritative Lists

MINIMUM CRITERIA: Use the following Authoritative Lists to screen out unacceptable alternatives based on environmental and human health concerns.	
Montreal Protocol	• List of Controlled Ozone-depleting Substances
Stockholm Convention	• List of Persistent Organic Pollutants (POPs)
World Health Organization's International Agency for Research on Cancer	• List of Classified Carcinogens
Canada	• Toxic Substances List and the Virtual Elimination List
European Chemicals Agency (ECHA)	• Candidate List of Substances of Very High Concern for Authorization • Substances classified as substances with carcinogenic, mutagenic or reproductive toxicity properties (CMR) 1a or 1b under Annex VI of CLP
U.S. Environmental Protection Agency	• Toxics Release Inventory's Persistent, Bioaccumulative and Toxic (PBT) Chemicals List and PBT Chemicals under the Toxic Substances Control Act (TSCA) Section 6(h)
U.S. National Toxicology Program	• Report on Carcinogens
State of California	• Proposition 65 List
	•

MOVING BEYOND THE MINIMUM: Consult additional lists (from authorities and stakeholders) as resources allow and as they align with your goals. Examples of such lists are provided below (there are 200+ restrictive substance lists).		
Authorities	European Union	• Priority List of Suspected Endocrine Disruptors
	ECHA	• Information on chemicals" Webpages: Hazardous properties and regulatory status of substances in several pieces of EU legislation, including REACH, CLP, BPR, etc. • List of Restrictions under REACH • List of Harmonized Classifications in Annex VI of CLP • C&L Inventory: Contains basic classification and labelling information on notified and registered substances received from manufacturers and importers • Public Activities Coordination Tool (PACT): Substances considered for further assessment – RMOA and informal hazard assessment (PBT/vPvB and endocrine disruptors) • REACH: Annex III Inventory
	OECD	• eChemPortal: Information on the properties of chemicals
NGOs	European Environmental Bureau	• RISCTOX: A database on toxic and hazardous substances
	European Trade Unon Institute	• Trade Union Priority List for REACH Authorisation
	AOEC	• List of Respiratory Sensitization Substances
	SINLIST	• The "Substitute it Now" list from environmental organisations
	TEDX*	• List of potential endocrine disruptors
Industry Sectors	Textiles	• ZDHC Manufacturing Restricted Substance List • American Apparel and Footware Association's Restricted Substance List
	Automotive	• Global Automotive Stakeholders Group's (GASG's) Global Automotive Declarable Substance List (GADSL)
	Furniture	• Business and Institutional Furniture Manufacturers' (BIFMA's) ANSI/BIFMA e3-2012 Furniture Sustainability Standard Annex B – Chemicals of Concern List
	Grandjean and Landrigan	• *List of 201 chemicals known to be neurotoxic in humans

***From 2003 to 2019, TEDX produced and shared scientific evidence of endocrine disruption. The TEDX list was last updated in September 2018; the website will remain available until September 2022.**

B. Use Globally Harmonized System (GHS) of Classification and Labeling of Chemicals methods – for both selecting endpoints and applying classification criteria/thresholds for those endpoints

Only a subset of chemicals have been evaluated for placement on authoritative government lists. Absence of a chemical from a list is not an indication of safety. This fact points to the value of a comparative hazard assessment. Hazard assessment methods used in alternatives assessments, as well as safer product certification assessments, consistently use criteria from the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals. GHS provides internationally standardized criteria for classifying chemicals, according to their health, physical, and environmental hazards. Applying GHS criteria for a given endpoint allows assessors to review available hazard data and categorize an alternative as Low, Moderate, or High concern for a specific hazard (or some similar ranking scheme).

A review by Jacobs et al. (2016) of 20+ alternatives assessment frameworks found that carcinogenicity, reproductive toxicity, mutagenicity, acute toxicity, and skin irritation are the most frequently included human health endpoints. Most frequently included ecological endpoints are acute and chronic aquatic toxicity, persistence, and bioaccumulation. It is important to note that there are endpoints that are not included in the GHS, but which are included in many comparative hazard assessment methodologies, including endocrine activity/disruption. The review found that ecological endpoints such as wildlife toxicity are more infrequently classified than human health endpoints.

Alternatives assessments should address the broadest range of endpoints that resources, capacity and data availability allow to minimize the possibility of regrettable substitution. **Exhibit 6** includes a subset of GHS endpoints that are considered minimum criteria for a safer alternative determination, as well as additional endpoints that can be assessed as time, expertise, and resources allow. Data availability may differ for various endpoints and assessors may need to go beyond traditional sources and types of data, such as in-vitro and in-vivo testing compiled in government databases or scientific journals to using read across, structure activity, and high-throughput data to inform a weight-of-evidence-based decision – an important strategy for addressing data uncertainty as described in Section 3.2.D. below. Stakeholder engagement processes and core knowledge of a chemical and its uses can help prioritize endpoints to include. Based on the hypothetical case example of a solvent manufacturer seeking to identify a safer solvent for use in high-performing cleaning products the assessor may choose to add skin irritation as an additional endpoint, based on skin irritation observed for the priority chemical in workers during manufacturing processes.

There may be a need to include additional hazard criteria – beyond toxicological endpoints to address worker health and safety. Although GHS includes a number of safety hazard endpoints, such as explosivity and corrosivity as outlined in **Exhibit 6,** other factors such as noise, vibration, or ergonomics may be relevant factors to consider to ensure the health and safety of workers with regards to alternatives. Some alternatives assessment tools, such as the Massachusetts Toxics Use Reduction Institute’s P2OASyS,[4] include consideration of worker health and safety trade-offs of alternatives.

Exhibit 6. Use of GHS Hazard Endpoints: Minimum Hazard Criteria

MINIMUM CRITERIA: Evaluate endpoints shown below, using GHS criteria to ascribe level of concern/classification for a given hazard.[1]		
Human Health Hazards	**Environmental Hazards**	**Physical Hazards**
• Carcinogenicity • Germ cell mutagenicity • Reproductive toxicity[2] • Acute toxicity • Specific target organ toxicity – repeated exposure[3]	• Acute aquatic toxicity • Chronic aquatic toxicity • Bioaccumulation potential • Biodegradability[4]	• Flammability

Notes:

[1]An assessor may need to go beyond traditional sources and types of data, such as in-vitro and in-vivo testing compiled in government databases or scientific journals to using read across, structure activity, and high-throughput data to inform a weight-of-evidence-based decision.

[2]Considers the potential for developmental toxicity

[3]Referred to as Repeated Dose Toxicity in this paper

[4]Referred to as Persistence in this paper

Please see UNECE, 2019 for GHS classification criteria for the above endpoints.

MOVING BEYOND THE MINIMUM: Consider additional GHS and other priority endpoints based on stakeholder engagement, expertise, and data availability.		
Human Health Hazards	**Environmental Hazards**	**Physical Hazards**
• Neurotoxicity • Specific target organ toxicity – single exposure • Skin corrosion/irritation • Serious eye damage/eye irritation • Respiratory or skin sensitization • Aspiration hazard • Endocrine disruption*	• Mobility • Wildlife toxicity* • Eutrophication* • Greenhouse gas emissions, ozone depletion potential, waste generation, and other sustainability endpoints**	• Corrosivity • Explosivity • Oxidizing properties • Pyrophoric properties • Self-reactivity • Self-heating properties • Emission of flammable gases in contact with water • Other physical hazards: aerosols, gases under pressure, organic peroxides, ergonomics, vibration, noise

**Not included in GHS criteria*

***Please see Section 5 for more discussion on sustainability considerations.*

C. Use transparent decision rules to help organize and prioritize information needed to determine safer alternatives

Decision rules provide a systematic and transparent means to support the determination of a safer alternative. For example, authoritative lists are the result of specific decisions to limit or control priority chemicals. Decisions are made throughout the assessment process, yet few alternatives assessment frameworks detail specific decision rules that should be followed, leaving value-based judgments up to assessors and stakeholders involved in the assessment. Some hazard assessment methods and safer product certifications do have such rules built in. The creation of harmonized decision rules or criteria is an important step in creating a consistent definition of a “safer” alternative.

“Avoiding CMRs, PBTs and vPvBs (very persistent, very bioaccumulative substances)” is a decision rule that is consistent with most regulatory program priorities, for example authorization under REACH (Article 57), whereby substances characterized by these hazard traits are prioritized for substitution. This is also consistent with U.S. EPA’s Safer Choice criteria, in which – among other more stringent criteria – products labelled with EPA’s Safer Choice label cannot contain chemicals that are CMRs or PBTs or contain chemicals that release, degrade to, or form by-products that are CMRs or PBTs (U.S. EPA 2015). Where there is evidence of high concern for CMR, PBT, vPvB or other well-established toxicity endpoints for a given potential alternative, the alternative should not be considered safer.

Exhibit 7 outlines the minimum criteria for decision rules to aid in the selection of a “safer” alternative, as well as considerations for going beyond the minimum. For example, in the case of the hypothetical solvent manufacturer seeking to add a safer solvent to its product line (See Case Example at the end of Section 3), the assessor may choose to establish decision rules that exclude alternatives that are flammable and skin irritants.

D. Consider uncertainties and data gaps related to hazard data

Data gaps or uncertainty in the existing data can complicate decisions about which alternative is safer, particularly if multiple options have similar hazards. An important consideration in alternatives assessment is to minimize the potential for regrettable substitutes. Assessors should avoid replacing a priority chemical for which there is significant evidence of hazards with one for which the hazards may not be adequately understood.

Many existing hazard assessment methodologies include notations and descriptions in the hazard assessment summary regarding the quality of the evidence used in determining specific endpoint classifications or overall hazard assessment scores or classifications. The process and level of complexity for determining data quality is context dependent. Many regulatory agencies provide guidance on approaches that can be used to assess data quality as part of the weight of evidence approach to chemical assessment (OECD, 2019; ECHA, 2011a, b). The selected approach for data quality assessment should be applied consistently across all lines of evidence and transparently communicated so that stakeholders can understand the impact of data quality on reliability. Endpoints with data gaps or high levels of uncertainty are a key focus in the consideration of exposure potential and trade-offs later in the assessment. **Exhibit 8** outlines an example data quality hierarchy for data sources. Quality, sufficiency, and consistency all contribute to data reliability for predicting human and ecological hazards.

Exhibit 7. Use of Specific Decision Rules to Select a Safer Alternative

MINIMUM CRITERIA
Exclude alternatives that are classified as **"High" concern** based on GHS criteria for: • Carcinogenicity • Germ Cell Mutagenicity • Reproductive/Developmental Toxicity • PBT • vPvB
Please see UNECE, 2019 for classification criteria for the above endpoints.

MOVING BEYOND THE MINIMUM
Level 1: **Exclude** alternatives with a classification of **"High" concern** for the remaining minimum endpoints in Exhibit 6 based on the results of a hazard evaluation using GHS criteria for: • Acute mammalian toxicity • Specific target organ toxicity from repeated exposure • Flammability Level 2: **Exclude** alternatives with **"High" concern** associated with the other priority endpoints listed in Exhibit 6, including: • Human health hazards, such as neurotoxicity, irritation, sensitization, and other human health endpoints • Environmental hazards, such as wildlife toxicity, eutrophication, mobility and other environmental endpoints • Physical hazards, such as corrosivity, explosivity, and others
Please see UNECE, 2019 for classification criteria for the above endpoints.

Exhibit 8. Data Source Hierarchy for Chemical Hazard Information

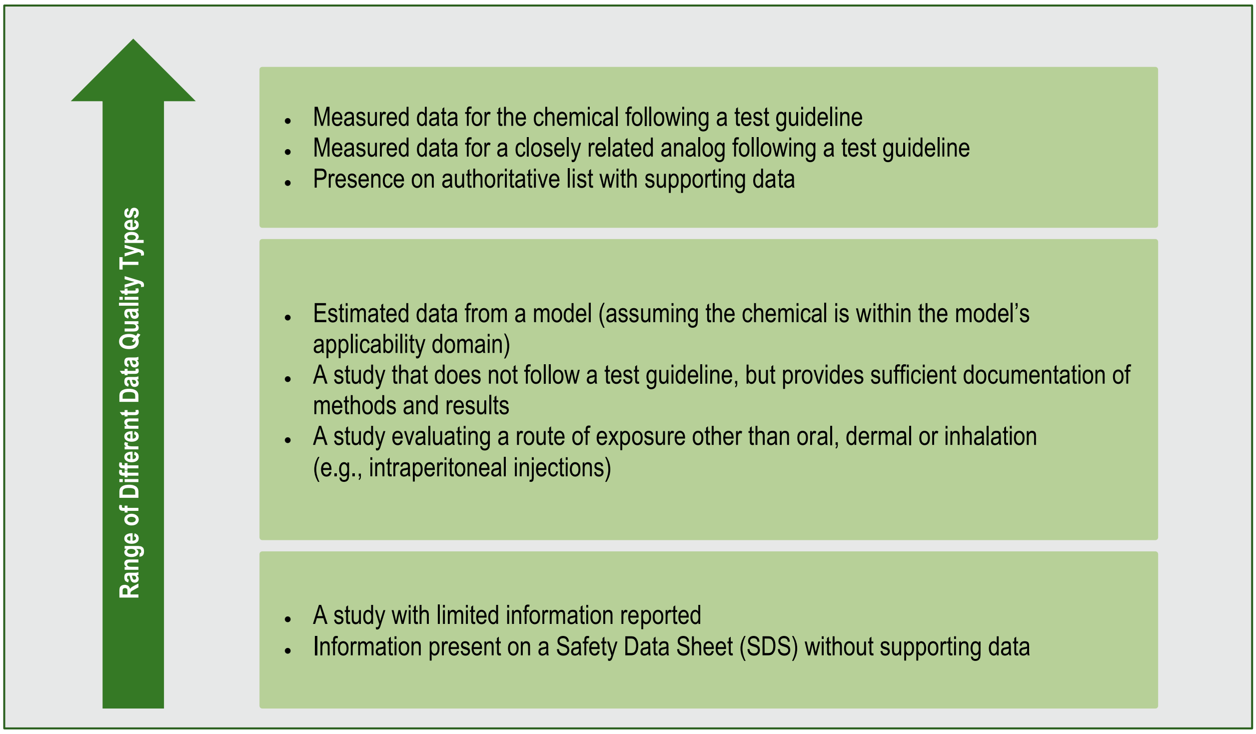


Exhibit 9 outlines a range of strategies and their pros/cons for addressing uncertainty during a comparative hazard assessment, as outlined in the U.S. NRC framework (National Research Council 2014). None of the presented strategies are considered a best practice. This guidance recommends that as a minimum assessment practice, practitioners select and follow a specific strategy that best meets the scope and goals of the assessment, and then transparently document the data gaps, the strategy and decision-making approach used to resolve them. Data for alternatives for which hazards are not fully characterized should be regularly reviewed to identify any emerging information. To better characterize a given hazard, an assessor can use information beyond traditional sources and types of data, such as in-vitro and in-vivo testing compiled in government databases or scientific journals. Such information can be drawn from read across, structure activity and high-throughput data, and can inform a weight-of-evidence-based decision for a given endpoint or an alternative. In the case of the hypothetical solvent, data gaps and endpoint classifications based on lower confidence data could be clearly ascribed as shown in the case study example below. Data gaps and hazard levels classified based on low confidence are important considerations during the navigation of trade-offs, thus transparency is key for such issues to be considered in final decisions about which alternative is safer.

Exhibit 9. Strategies for Considering Uncertainties in the Hazard Data

RECOMMENDED ASSESSMENT PRACTICES: At a minimum, use one or more of the practices listed below to address data gaps and provide explicit documentation on the practice/method used.	
Tier 1 Practices: Lower Level of Expertise and Resources Required	
Provide descriptions of the confidence level in the data associated with a specific hazard classification: Considers the sources and quality of the data used for characterizing the hazard level for a given endpoint and assigns a corresponding confidence level (e.g., high, moderate, or low confidence).	**Pros:** Assists with transparency and is useful when considering trade-offs across the full assessment **Cons:** Requires professional judgement. Not all assessors will describe confidence levels in the same set of data the same way.
Use external expert knowledge: An expert review panel can enhance understanding whether uncertainty is problematic and can advise on the best course of action given the potential consequences of data being wrong.	**Pros**: Deliberation among experts can reveal useful insights about specific data uncertainties. **Cons:** May be time consuming to convene and there may no clear answer or course of action.
Exclude alternatives with missing data: Only alternatives with data for priority endpoints are considered, and alternatives with unknown toxicity for critical hazard endpoints are excluded.	**Pros:** Evidence of safety is necessary to be considered a safer alternative. **Cons:** May discriminate against newer safer chemicals that have less available data.
Penalize data gaps: Uncertainty for a given hazard endpoint or is penalized/weighted less favorably in the overall evaluation.	**Pros:** Evidence of safety is necessary to be considered a safer alternative. **Cons:** May discriminate against newer safer chemicals that have less available data.
Remain neutral about uncertainty and missing data: In this strategy, the presence of uncertainty and missing data are simply noted, but no alternative is excluded or penalized as a result.	**Pros:** Avoids prematurely removing potentially safer alternatives from the evaluation process – important if other attributes such as economic and technical feasibility also need to be considered. **Cons:** May result in regrettable substitution since alternatives with missing data may appear preferable even if they are not. Requires near-term testing and monitoring to protect against a regrettable substitution.
Tier 2 Practices: Higher Level of Expertise and Resources Required	
Use additional tools: Use tools such as structure-activity relationships models and read-across approaches to fill data gaps.	**Pros:** Structurally similar chemicals for which data are available are used as surrogates to fill data gaps. **Cons:** Requires additional expertise than many assessors may not have.
Use quantitative uncertainty analysis: Uncertainty in toxicity values, for example; could be expressed quantitatively or illustrated graphically – expressed as a probability distribution, among other options.	**Pros:** Easier to see that one alternative is preferable to another if shown in a clear illustration. **Cons:** Requires additional expertise than many assessors may not have.

3.3. Comparative Exposure Assessment

The purpose of a qualitative comparative exposure assessment is to determine the differences in the intrinsic exposure potential of alternatives relative to a priority chemical for humans and ecosystems, regardless of external exposure controls in place (such as gloves), over the life cycle of the substance and its potential alternatives. This component of the assessment will help answer the question: *Is the alternative preferable, equivalent to, or potentially worse than the priority chemical given the potential for exposure?*

Conducting a comparative exposure assessment may not be necessary if the alternatives have similar forms, use patterns, and physical-chemical properties. In the more likely case, where alternatives' physical-chemical properties vary, it is important to know whether these properties will impact a determination about which alternative is safer. A qualitative exposure assessment can help determine whether properties of the substance or its use characteristics can increase or decrease specific hazards. Chemicals and their alternatives can then be compared across hazards using the potential for exposure.

Exposure assessments that are conducted as part of an alternatives assessment are comparative and consider the potential for exposure based on inherent or intrinsic chemical and physical properties as well as expected use scenarios and do not, necessarily, attempt to quantify those exposures, except where necessary to understand potential exposure trade-offs. A quantitative assessment is typically used in conducting risk assessments. The U.S. National Research Council's (NRC) alternatives assessment framework established the use of the term *intrinsic potential for exposure* because it focuses on the use of physical-chemical properties and qualitative exposure considerations such as use conditions and plausible routes of exposure (National Research Council 2014). This guidance lays out the steps by which a qualitative exposure assessment should be carried out by identifying exposure pathways and comparing exposure potential.

The main components for a qualitative exposure assessment are:

A. Identifying exposure pathways and reasonably foreseeable exposure scenarios throughout the lifecycle; and

B. Comparing exposure potential

A. Identify exposure pathways and reasonably foreseeable exposure scenarios throughout the lifecycle

Identifying reasonably foreseeable exposure scenarios throughout the lifecycle, includes considering how the chemical is used (including conditions of use) or potentially disposed of during its lifecycle, allowing the assessor to consider the potential for human and environmental exposures. Stakeholders can be helpful in identifying these exposure scenarios by providing information on how chemicals are used in a process and/or where they end up in finished products or at the end of their lives. Conceptual site models and exposure maps can also be used to help assessors systematically define and identify potential routes of exposure and relevant receptors, especially in cases of environmental exposure where there may be many downstream receptors. Examples of conceptual maps for use in alternatives assessment were created by Greggs et al. (2019).

Exhibit 10 outlines minimum assessment practices for this component of the assessment.

Exhibit 10. Exposure Pathways and Reasonable Use Scenarios

RECOMMENDED ASSESSMENT PRACTICE
Identify potential routes of exposure (such as dermal, inhalation, and ingestion pathways for human health and air, water, and soil pathways for the environment) for the substance that needs to be substituted and each alternative given conditions of use. **Step 1**: Based on the scope of the assessment, identify the life cycle stage(s) where concerns for exposure trade-offs may occur. Examples include: Chemical manufacturing Product manufacturing Product use End of life Reuse in a recycled form **Step 2:** Within each life cycle stage, identify potential routes of exposure and receptors given conditions of use and conditions of potential misuse of the substance. This could be accomplished by: Engagement with stakeholders (relevant worker, consumer or environmental stakeholders) Review of the literature Use of conceptual exposure maps (See Greggs et al. 2019 for examples)

B. Compare exposure potential

Once potential exposure pathways are determined, the next step is to compare exposure potential between alternatives. As **Exhibit 11** indicates, there are several sources of exposure information, both from indirect as well as direct measurements. For less-studied chemical alternatives, exposure information will be more difficult to find. In such cases, and even where measured exposure information is available for one or more chemicals, an analysis of physical-chemical properties can give valuable insight into the potential for exposure.

Exhibit 11. Data Sources for Evaluating Exposure

Direct exposure measurement data sources:

- Exposure monitoring (e.g., biomarkers of exposure, use of personal monitors, environmental monitoring)
- Experimental emissions data (e.g., chamber tests)

Indirect exposure measurement data sources:

- Physical-chemical properties
- Modeling
- Observational information
- Questionnaires
- Classification, Labeling and Packaging of substances and mixtures (CLP) compliant (or analogous) safety data sheets

Evaluating physical-chemical properties of each chemical under consideration is a primary method in alternatives assessment to help assessors compare exposure potential, including environmental fate. The results of this comparison may pave a clear path to identifying a safer alternative and eliminating the need to continue further with the qualitative exposure assessment. Some alternatives may have a significantly lower log K_{ow} or higher water solubility compared to the priority chemical, creating differences in bioavailability and increased exposure potential to ecological receptors. Critical physical-chemical properties used to estimate and compare exposure potential for both human and ecological receptors are detailed in Greggs et al. 2019 as well as the 2014 US National Research Council's framework (Chapter 5). Because of the general availability of physical-chemical properties, this information can also be used to identify routes of exposure to potential alternatives as well as reasonably foreseeable exposure pathways given conditions for how the chemical will be used and potentially misused.

In cases where physical-chemical properties are unavailable, assessors can use tools such as EPI Suite, a U.S. EPA program that estimates physical-chemical properties. The exposure scenario and route of exposure will most often indicate which of these properties will be relevant to evaluating whether an alternative is likely to lead to substantially more, substantially less, or equivalent exposures by each route and scenario.

If there is a mix of higher and lower exposure potential predictions from evaluation of physical-chemical properties, various other tools could be used in conjunction with the hazard conclusions to identify a safer alternative, such as: direct and indirect exposure measurements; experimental values for transfer rates, dermal uptake, and bioavailability; questionnaires; and observational data. When necessary, modelling programs can take much of this information as inputs to help estimate exposures. Some models can be used to compare relative exposures based on physical-chemical properties alone while others require additional input parameters. Exposure modelling is beyond the scope of this OECD guidance document. Assessors who wish to conduct exposure modelling could consult established exposure modelling resources such as ECTOC TRA, EUSE or ConsExpo. It is important that an assessor consider exposure potential after considering the hazard conclusions, and not in isolation. Comparing exposure potential can also include consideration and comparison of functional equivalent concentrations. Considering the mass, volume, or concentration of an alternative chemical needed to achieve the same functional performance in a specific application as the substance of concern can impact exposure and is another factor to consider when determining if an alternative is safer, to avoid potential negative trade-offs, and is particularly important for chemicals with different hazard concerns. For example, a specific solvent in a cleaning formulation may be of concern for carcinogenicity but a potential alternative that must be used in higher quantities to achieve the same level of performance may be ecotoxic. Understanding this trade-off may lead to deprioritizing an alternative or to consideration of how to optimize its performance to reduce the amount required.

Exhibit 12 summarizes the minimum criteria and assessment practices to qualitatively estimate exposure potential to assist with making a safer alternative determination.

Exhibit 12. Using Physical-Chemical Properties and/or Exposure Models to Compare Exposure Data for Alternatives

MINIMUM CRITERIA AND RECOMMENDED ASSESSMENT PRACTICE	MOVING BEYOND THE MINIMUM
Step 1: Exclude routes of exposure that are unlikely based on measured exposure data or physical-chemical properties such as: • physical state • vapour pressure • molecular weight • water solubility • log kow • boiling point • melting point • Henry Law's Coefficient • particle size **Step 2**: Qualitatively compare the above exposure data or physical-chemical properties for the relevant exposure routes to identify if the alternative is likely to result in greater, equivocal, or less exposure.	If uncertainty or conflicting information prevents the identification of a safer alternative, collect and use exposure information to better understand use patterns and exposure pathways to assess trade-offs. Commonly used tools and references include: • The ConsExpo[5] modelling tool enables the estimation and assessment of exposure to substances from consumer products such as paint, cleaning agents, and personal care products. • "Descriptions of Existing Models and Tools Used for Exposure Assessment, Results of OECD Survey" includes a table of available exposure models with descriptions and links for each tool. • ECHA's Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.15: Occupational exposure assessment[6] provides a description of occupational exposure models. • ECHA's Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.15: Consumer exposure assessment[7] provides a description of consumer exposure models. • ECHA's Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment[8] provides a description of several environmental exposure tools. • ECHA's Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.18: Exposure scenario building and environmental release estimation for the waste life stage[9] provides a description of tools to estimate exposure from disposal. • EPA's ExpoBox is a compendium of assessment tools that contains links to guidance documents, databases, models, reference materials, and other resources. • The European System for the Evaluation of Chemicals (EUSES)[10] is a tool to help carry out rapid and efficient assessments of the general risks posed by chemical substances. • The European Centre for Ecotoxicology and Toxicology of Chemical's (ECETOC)[11] Targeted Risk Assessment (TRA) tool helps to calculate the risk of exposure from chemicals to workers, consumers, and the environment.

3.4. Integrating Comparative Hazard and Exposure Assessment Results and Assessing Trade-offs to Select a Safer Alternative

Making a safer alternative determination requires integrating the results from the hazard and qualitative exposure assessments to evaluate trade-offs and consider any lingering uncertainties. A broadly agreed-upon approach for integrating this type of information to support decision-making regarding alternatives does not exist, but there is agreement on the need to be transparent in the assessment process and to engage stakeholders. Stakeholder engagement is a key component in several stages of the alternatives assessment process. Bringing stakeholders together to consider the trade-offs when integrating hazard and comparative exposure assessment findings is a value-added process for decision-making regarding a preferred alternative(s) given that successful implementation of an alternative depends upon acceptance of the outcome of a safer alternative designation.

Two main components are considered in this step:

A. Integrate hazard and exposure assessment results; and

B. Consider trade-offs and make a decision regarding a safer alternative.

A. Integrate Hazard and Exposure Assessment Results

The U.S. NRC framework offers several strategies to consider for integrating the hazard and exposure assessment results based on existing alternatives assessment practices as outlined in **Exhibit 13** (National Research Council 2014). Given the lack of an agreed-upon best approach, a minimum step for selecting a safer alternative requires transparently documenting the strategy used for the integration. Narrative summaries or comparison matrices are the simplest of the approaches listed. The pros and cons of various strategies to consider are described in **Exhibit 13**. The hypothetical company in the solvent case example (See Case Example at the end of Section 3) opted to use a form of exposure weighting and used the exposure potential results to examine in greater detail those hazard endpoints with at least a moderate level of concern or a data gap. To go beyond the minimum, further detailed assessment of the relative potency of substances can be considered in cases where they may have the same hazard classification or route-specific toxicity information could be applied in the comparison of alternatives.

B. Consider Trade-offs and Make a Decision Regarding a Safer Alternative

As outlined in **Exhibit 14**, the U.S. NRC framework reviewed a number of strategies that have been used to integrate hazard and exposure data and to navigate the trade-offs across the range of endpoints being considered (National Research Council 2014). Some of these strategies are relatively simple to implement, such as eliminating "high ratings," while others require more sophisticated assessments, such as "weighted scoring of endpoints." The best approach will depend on factors such as the resources available to the assessor. At a minimum, the assessor should engage stakeholders and apply and document one of the strategies listed in **Exhibit 14.** Decision-rules established during the scoping stage of the alternatives assessment can be very helpful here, such as "avoid chemicals with high hazard for any endpoint" or "avoid creating new hazards for workers." It is important to underscore that if uncertainty is high across multiple hazard endpoints of primary interest and significant trade-offs exist, an appropriate strategy may be a decision that no safer alternative is currently available. The strategy should be one of filling in gaps in knowledge, where that can be done in a relatively short period, and focusing on research and development to create a safer/suitable replacement using observations about the shortcomings of specific alternatives to guide innovation needs. In the solvent example (See Case Example at the end of Section 3), the company used a weighted scoring of endpoints strategy in their considerations of trade-offs and weighted those endpoints considered “minimum hazard criteria” (Exhibit 6) more heavily in the trade-off assessment.

Exhibit 13. Integrating Hazard and Exposure Assessment Results Minimum Assessment Practices

RECOMMENDED ASSESSMENT PRACTICES: Transparently document strategies used to integrate hazard and exposure results. Use one or more of the strategies listed below:	
Comparison Matrices: For hazard endpoints that are not classified as "low," integrate exposure potential for each alternative being considered as less than (-), equivalent (0) or greater than (+) the chemical being replaced. The resulting heat map can be visually used to integrate the hazard and exposure information.	**Pros:** Useful to have an integrated visual display of all of the hazard and exposure assessment findings. These heatmaps/matrices are useful especially when the assessor is not making a decision (e.g., assessment is generated by government agencies or NGOs) and supports decision-making by other entities. **Cons:** When exposure potential is not equivalent, it will be difficult to use these comparison matrices alone to adjust the hazard assessment findings in light of the exposure assessment results.
Adjusting for Exposure Potential: Focuses on the integration of exposure potential with individual hazard endpoints. This weighting can upgrade or downgrade the severity of a particular hazard (category) based on the potential for exposure information.	**Pros:** Supports further weighting of specific endpoints when considering trade-offs (Exhibit 14). **Cons:** There may be toxicological knowledge and nuances to consider regarding how exposure potential modifies the hazard assessment results.
Narrative Exposure Summary: Focuses on a narrative summary of potential exposure concerns for an alternative to allow the assessor to understand trade-offs.	**Pros:** Simple narrative phases are easy to develop and understand. **Cons:** May not help adequately discern between alternatives.
Descriptive Exposure Phrases: Similar to hazard phrases (such as high, medium, and low), such phrases would help with hazard assessment results provide an indication of how an alternative might increase or decrease exposure compared to alternatives.	**Pros:** A simple characterization that can be used by multiple assessors. **Cons**: May not help adequately discern between alternatives.

Exhibit 14. Navigating Trade-offs and Making a Decision

RECOMMENDED ASSESSMENT PRACTICES Engage stakeholders and document strategies and tools used to address trade-offs and to assist the decision-making process. At a minimum, use one or more of the strategies listed below to address trade-offs in the integration of hazard and exposure data to make a safer alternative determination. In some cases, this step may determine that a safer alternative is not currently available, and research and de novo design are needed to create one.	
Comparative evaluation matrices. Uses notations such as colouring the results of the hazard assessment for a given endpoint as Red, Yellow, Green OR +, 0, - or some other ranking scheme.	**Pros:** Useful when the assessor is not making a decision (e.g., assessment is generated by government agencies or NGOs) and supports decision-making by other entities. **Cons:** It may be difficult to see a clear preferred and safer alternative if a large number of alternatives were included in the assessment, numerous endpoints/assessment criteria addressed, and if uncertainties and trade-offs abound.
Eliminate the "high" rating: In this strategy, the alternative is eliminated if it scores "high" on any toxicity endpoint.	**Pros:** Any chemical with high inherent hazards should not be considered a safer alternative. **Cons:** Depending upon exposure potential and the hazard endpoint involved, this may eliminate a viable alternative. Requires exposure mitigation to protect against a regrettable substitute.
Strict ordering of endpoints: Hazard endpoint are strictly ranked such that the highest-ranked endpoint governs the overall preference ordering of alternatives.	**Pros:** Useful if specific hazard endpoints are of greater concern than others to stakeholders. **Cons:** This approach requires a strict ordering of the importance of endpoints, which may not be justifiable on public health grounds and is not likely to be supported by all stakeholders.
Equal weighting of endpoints: Each endpoint is considered to have equivalent importance, and the trade-off is resolved by assigning a relative weight to the high, medium, and low categories and then adding up the score. The total would indicate the preference ordering of alternatives.	**Pros:** Easily executed. **Cons:** This approach may unnecessarily exclude alternatives that would be safer.
Rule-based ranking: Preferences can be ordered by a series of logical statements. The basis for implicit or explicit weighting should be carefully considered before applying a rule-based system to ensure that the organization's values with respect to the different health outcomes are appropriately represented.	**Pros:** An organization's value system, once codified in the form of these rules, can be consistently applied, which makes the process less prone to an individual's personal judgments or manipulation of the weighting schemes toward otherwise preferred outcomes. **Cons:** Difficult to operationalize if stakeholders cannot weight one health endpoint over another.
Weighted scoring of endpoints: Endpoints are given an unequal weight, and the relative score is determined by summing up the weighted scores across the endpoints. This approach also requires weighting high, medium, and low hazard levels or on the raw toxicity values. This approach will often require the use of analytic decision tools such as multi-criteria decision analysis (MDCA).	**Pros:** Analytic decision tools enable the processing of many endpoints/attributes and varying weights. **Cons:** Requires expertise in the use of analytic decision tools. Use of these tools should be used to support discussion about preferable alternatives, not replace critical and strategic thinking.

3.5. CASE EXAMPLE: Solvent for High-Performing Cleaning Products

To illustrate application of the minimum criteria for a safer alternative determination, this section uses the example of a hypothetical solvent manufacturer who currently uses a solvent that has no experimental data for carcinogenicity, though carcinogenicity models predict with good reliability that this solvent has the potential to cause cancer. Experimental data for this solvent also suggest that specific organ toxicity from repeated inhalation exposures and skin irritation are likely. The manufacturer offers this solvent to formulators of high-performing cleaning products who wish to market to retailers with a preference for safer products. The manufacturer would like to replace the solvent with one that meets its clients' needs. Performance requirements for this market are rigorous, so when used in targeted formulations, the solvent must perform as well as solvents now being used in market-leading products.

Determining the Assessment Scope

- **Engage stakeholders –** The manufacturer's principal goal is to find a safer solvent with functionality and cost-effectiveness that will make the product competitive in the marketplace. In this example, because of the rigorous performance needs, the company directly engaged downstream product manufacturing customers and cleaning product brands to help define both the functional performance needs (not addressed in this guidance, but a key part of any alternatives assessment) and the health and safety criteria of primary concern. Consultation with scientists at academic institutions and environmental and health advocacy organizations provided insights on critical environmental and human health endpoints and added credibility with institutional purchasers and retailers.
- **Clarify goal, associated principles, assessment criteria, and decision rules –** In this example, the goal is two-fold: (1) limiting liability by staying ahead of regulation; and (2) taking advantage of a growing marketplace. Considering input from downstream customers and other stakeholders, the company decided that the scope of the assessment should consider hazards and potential exposures during several use stages: (a) manufacturing, (b) customer/consumer use, and (c) down-the-drain end of life. Specific hazard criteria to be addressed included those endpoints that meet the minimum requirements for a safer alternative determination (see Section 3.2, Exhibit 6) and skin irritation. Skin irritation was added because of potential impacts to workers during manufacturing processes and during consumer use. Given the company's sustainability goals, the company chose to review greenhouse gas emission potential of the various alternatives.

Comparative Hazard Assessment

- **Use authoritative lists to screen out alternatives –** The solvent manufacturer identified and benchmarked eight potential alternatives based on its own Research and Development (R&D). Given the intended consumer use of the product, it was necessary to go beyond the minimum set of authoritative lists provided in Exhibit 5. The solvent manufacturer included skin irritation and skin sensitization as additional endpoints to consider beyond the minimum criteria listed in Exhibit 6.[12] Use of authoritative lists screened out four of the eight potential alternatives.
- **Use GHS hazard endpoints** – For the remaining four alternatives, the manufacturer evaluated hazard endpoints using GHS classifications to form a basis for ranking. For the hazard criteria included in the assessment, the company followed the "human toxicity" and

"dangerous for the environment" hazard ranking methods outlined in the Guide on Sustainable Chemicals, developed by the German Environment Agency. Given that harmonized GHS classifications were not available for all endpoints for all alternatives, the company conducted a literature review and used GHS criteria to help structure and categorize the hazard levels.

- **Use transparent decision rules and consider data gaps and uncertainties –** The firm adopted the data hierarchy outlined in Exhibit 8 to address data gaps and uncertainty levels in the summary heat map matrix (shown below) and adopted the minimum decision rule requirements for considering an alternative as safer. As a consequence, alternatives A and D were excluded from consideration because of concern for carcinogenicity, reproductive toxicity, and developmental toxicity.

Exhibit 15. Recommended Assessment Practice to Identify Safer Alternatives for the Chemical Targeted for Substitution Using the recommended assessment practices described in Exhibit 7, Alternatives A and D were removed from consideration due to high hazards associated with reproductive and developmental toxicity, respectively (listed as "R" on authoritative CMR lists), and moderate concern for carcinogenicity for Alternative A**.**

	Human Health Hazards								Environmental Hazards				Physical Hazards
	Carcinogenicity*	Germ Cell Mutagenicity*	Reproductive Toxicity*	Developmental Toxicity *	Acute Toxicity*	Specific Organ Toxicity, Repeated Exposure*	Skin Sensitization#	Skin Irritation#	Acute Aquatic Toxicity*	Chronic Aquatic Toxicity*	Bioaccumulation Potential*	Rapid Biodegradation*	Flammability*
Chemical targeted for substitution	M	L	L	L	L	H	L	H	L	L	L	M	M
Alternative A	~~M~~	~~L~~	~~H~~	~~L~~	~~L~~	~~DG~~	~~L~~	~~L~~	~~M~~	~~H~~	~~L~~	~~L~~	~~L~~
Alternative B	L	L	M	*M*	L	DG	L	L	M	M	L	L	L
Alternative C	L	L	L	L	L	L	L	L	*M*	M	L	VL	L
Alternative D	~~L~~	~~L~~	~~M~~	~~H~~	~~L~~	~~M~~	~~L~~	~~L~~	~~M~~	~~M~~	~~L~~	~~L~~	~~L~~

*Minimum criteria for a safer alternative determination; #Beyond the minimum criteria; L=low hazard level; M=moderate hazard level; H= High hazard level; DG=data gap; *Italicized* hazard rankings reflect lower levels of confidence in the data.

Comparative Exposure Assessment

- **Identify exposure pathways and reasonable use scenarios –** During the scoping step, the company's stakeholders expressed concern for specific exposure pathways given the chemical's physical chemical characteristics, use, and auxiliary chemicals used in the production process. Within a manufacturing environment, there is particular concern for inhalation exposure among workers given the vapour pressure of the potential alternatives and how they are expected to be used in manufacturing settings. During the consumer use phase, inhalation and dermal exposures are the most likely during use of the cleaning product.
- **Compare exposure potential –** Given the exposure pathways for the various use scenarios, the manufacturer developed a qualitative comparative exposure matrix to show

whether the exposure potential of a given alternative was greater than (+), equivalent to (0) or less than (-) that of the chemical targeted for substitution. The vapour pressure for Alternative B was greater than the chemical targeted for substitution, suggesting higher potential for inhalation exposure to workers during manufacturing. Alternative C had a slightly lower water solubility than the chemical targeted for substitution, and experimental data indicated the chemical readily biodegraded within 10 days, indicating lower exposure potential in the aquatic environment.

Exhibit 16. Comparison of Exposure Potential for the Relevant Human Health and Ecological Exposure Routes

Using the identified exposure potential for the chemical targeted for substitution as a baseline, the company relied on physical-chemical properties and available data to determine Alternative B has greater potential for inhalation exposure to workers during manufacturing and consumers during product use. Alternative C has lower potential for exposure to aquatic organisms and leaching through soil.

Chemical	Relevant Human Health Exposure Routes			Relevant Ecological Exposure Routes		
	Oral	Dermal	Inhalation	Water	Air	Soil
Chemical targeted for substitution	Baseline for comparison					
Alternative B	0	0	+	0	0	0
Alternative C	0	0	0	-	0	0

0=equivalent exposure to the chemical targeted for substitution; + = greater exposure than the chemical targeted for substitution; - = less exposure than the chemical targeted for substitution.

Integrating Comparative Hazard and Exposure Assessment Results and Assessing Trade-offs to Select a Safer Alternative

- **Integrate hazard and exposure assessment results –** The company engaged its R&D leadership to discuss the assessment results. The decision makers gave special weight to endpoints with at least a moderate level of concern or data gap and examined the exposure potential results (greater than (>), equivalent (≈), or less than (<)) against those hazard endpoints. This integration served as a starting point to consider trade-offs and select a safer alternative. The company also determined Alternatives B and C have similar greenhouse gas potential, so this sustainability consideration does not change or influence the selection of a safer alternative in this case study.
- **Consider trade-offs and select a safer alternative –** The company used both a narrative exposure summary and a weighted scoring of endpoints strategy to consider trade-offs and select a safer alternative. The company weighed endpoints identified as the minimum human health and ecological hazard endpoints in Exhibit 6 as more important in selecting an alternative. As shown in **Exhibit 16** and **17**, inhalation exposure potential for Alternative B was expected to be greater than the chemical targeted for substitution. This could be problematic given the concern for worker and consumer exposure and "moderate" concern for reproductive toxicity and developmental toxicity (although there is uncertainty in the data). In addition, there was no data available to understand specific organ toxicity associated with repeated exposure – an endpoint *necessary* to make a safer alternative determination – and thus Alternative B was removed from consideration. For Alternative C, exposure was considered equivalent to the chemical targeted for substitution for all human health endpoints. While acute and chronic aquatic toxicity were considered a "moderate" concern, the potential for exposure to aquatic systems was determined to be lower as compared to the chemical targeted for substitution based on data demonstrating the chemical readily biodegraded within 10 days. As a result, Alternative C met most of the criteria to be a safer alternative.

For comparison and to check their results, the company also used a weighted scoring of endpoints approach using the same information, as depicted in **Exhibit 18** below. To consider trade-offs under this approach, the manufacturer assigned human health and environmental hazard endpoints a numerical score of 1 for low hazard, 2 for moderate hazard, 3 for high hazard, and assigned a score of 4 for endpoints with data gaps. Hazard endpoints considered minimum criteria contributed more to the overall score of each alternative; the hazard score for these endpoints were multiplied by two. For each chemical evaluated, the hazard and exposure scores were added together to make a hazard and exposure total score. The total scores were then compared to one another to make a selection. Using this approach, Alternative C has the lowest score and was recommended as the safer alternative.

Given the results of both the narrative exposure summary (described above based on the information in **Exhibit 17**) and the weighted scoring of endpoints (**Exhibit 18**, the solvent manufacturer made a safer alternative determination for Alternative C based on the reduced likelihood for exposure to aquatic systems despite there being moderate concern for aquatic toxicity.

Exhibit 17. Comparison Matrix to Integrate Hazard and Exposure Assessment Results For endpoints with moderate hazard (yellow), high hazard (red), or a data gap (grey), the company considered and compared the exposure potential for the alternative with the chemical targeted for substitution.

Chemical	Human Health Hazards								Environmental Hazards				Physical Hazards
	Carcinogenicity*	Germ Cell Mutagenicity*	Reproductive Toxicity*	Developmental Toxicity *	Acute Toxicity*	Specific Organ Toxicity, Repeated Exposure*	Skin Sensitization#	Skin Irritation#	Acute Aquatic Toxicity*	Chronic Aquatic Toxicity*	Bioaccumulation Potential*	Rapid Biodegradation*	Flammability*
Chemical targeted for substitution	M	L	L	L	L	H	L	H	L	L	L	M	M
Alternative B hazard considerations	L	L	M	*M*	L	DG	L	L	M	M	L	L	L
Alternative B exposure considerations			≈oral ≈dermal >inhalation	≈oral ≈dermal >inhalation		≈oral ≈dermal >inhalation			≈water	≈water			
Alternative C hazard considerations	L	L	L	L	L	L	L	L	*M*	M	L	VL	L
Alternative C exposure considerations									<water	<water			

*Minimum criteria for a safer alternative determination; #Beyond the minimum criteria; L=low hazard level; M=moderate hazard level; H= High hazard level; DG=data gap; ≈ =equivalent exposure potential to the chemical targeted for substitution; > =greater exposure potential than the chemical targeted for substitution; < =lower exposure potential to the chemical targeted for substitution; *Italicized* hazard rankings reflect lower levels of confidence in the data.

Exhibit 18. Weighted Scoring of Endpoints Approach to Select a Safer Alternative The minimum criteria for hazard endpoints were weighed twice as much (multiplied by 2) towards the overall numerical score. Each endpoint's score for hazard and exposure is included in the table. This approach suggests Alternative C is the safer alternative based on it having the lowest score.

	Human Health Hazards								Environmental Hazards				Physical Hazards	Sum	Hazard & Exposure Total
	Carcinogenicity*	Germ Cell Mutagenicity*	Reproductive Toxicity*	Developmental Toxicity*	Acute Toxicity*	Specific Organ Toxicity, Repeated Exposure*	Skin Sensitization#	Skin Irritation#	Acute Aquatic Toxicity*	Chronic Aquatic Toxicity*	Bioaccumulation Potential*	Rapid Biodegradation*	Flammability*		
Chemical targeted for substitution Hazard considerations	**M (2)**	**L (1)**	**L (1)**	**L (1)**	**L (1)**	**H (3)**	L (1)	H (3)	**L (1)**	**L (1)**	**L (1)**	**M (2)**	**M (2)**	36	36
Chemical targeted for substitution Exposure considerations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Alternative B Hazard considerations	**L (1)**	**L (1)**	**M (2)**	**M (2)**	**L (1)**	**DG (4)**	L (1)	L (1)	**M (2)**	**M (2)**	**L (1)**	**L (1)**	**L (1)**	38	40
Alternative B Exposure considerations	0	0	+1	+1	0	0	0	0	0	0	0	0	0	+2	
Alternative C Hazard considerations	**L (1)**	**L (1)**	**L (1)**	**L (1)**	**L (1)**	**L (1)**	L (1)	L (1)	**M (2)**	**M (2)**	**L (1)**	**VL (1)**	**L (1)**	28	26
Alternative C Exposure considerations	0	0	0	0	0	0	0	0	-1	-1	0	0	0	-2	

**Minimum criteria for a safer alternative determination; #Beyond the minimum criteria; L=low hazard level received 1 point per endpoint; M=moderate hazard level received 2 points per endpoint; H= High hazard level received 3 points per endpoint; DG=data gap received 4 points per endpoint; If exposure for an alternative was less than the chemical targeted for substitution, the alternative chemical received a -1 score for the relevant endpoints. If exposure for an alternative was greater than the chemical targeted for substitution, the alternative chemical received a +1 score for the relevant endpoints. If exposure for an alternative was equivalent to the chemical targeted for substitution, the alternative chemical received a 0 score for the relevant endpoints.*

Notes

[1] See for example: Natural Resources Defense Council (2017), Protection of the most Vulnerable: A Discussion Draft, https:/www.nrdc.org/sites/default/files/toxic-chemicals-vulnerable-populations-report.pdf

[2] The Commons Principles are a set of principles to guide alternatives assessment practice, developed by a group of academic, NGO, business, and government professionals. https://www.bizngo.org/resources/entry/commons-principles-for-alternatives-assessment

[3] http://www.oecdsaatoolbox.org/Home/Tools

[4] https://p2oasys.turi.org/

[5] https://www.rivm.nl/en/consexpo

[6] ECHA’s Guidance on Information Requirements and Chemical Safety Assessment ChapterR.14: Occupational exposure assessment

[7] ECHA’s Guidance on Information Requirements and Chemical Safety Assessment Chapter R.15: Consumer exposure assessment

[8] ECHA’s Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment

[9] ECHA’s Guidance on information requirements and chemical safety assessment Chapter R.18: Exposure scenario building and environmental release estimation for the waste life stage

[10] https://ec.europa.eu/jrc/en/scientific-tool/european-union-system-evaluation-substances

[11] http://www.ecetoc.org/tools/targeted-risk-assessment-tra/

[12] Given the potential for inhalation and dermal exposure, a practitioner is encouraged to consider additional endpoints beyond those identified in this case study, such as specific target organ toxicity- single exposure, neurotoxicity, eye irritation, respiratory sensitization, aspiration hazard, and endocrine disruption, as applicable to the scope of the assessment.

4. Self-Assessment Checklist

Exhibit 19, a self-assessment checklist, summarizes the minimum criteria and recommended assessment practices discussed in Section 3. This check list does not include recommendations that go beyond the minimum criteria as outlined in Section 3. However, the assessor is strongly encouraged to consider these additional recommendations on hazard and exposure, as well as the broader sustainability endpoints in Section 5, to avoid a regrettable substitution

Exhibit 19. Minimum Assessment Practices and Criteria Checklist

Assessment Step	Minimum Criteria and Recommended Assessment Practices
Determining the Assessment Scope	
Include appropriate stakeholder input in determining the scope of the assessment	• At a minimum, include stakeholder input and concerns. Establish an understanding of stakeholder concerns through informal discussions, conducting research (literature and document reviews), attending conferences, and listening to stakeholder presentations. • Use stakeholder input to help bound the assessment by including assessment criteria that are most relevant.
Clearly document the goals, principles, and decision rules used	Clarify goals, associated principles, assessment criteria, and decision rules to focus the scope of the assessment using stakeholder input to the extent possible.
Comparative Hazard Assessment	
Use Authoritative Lists to quickly screen out non-suitable alternatives from consideration before a full hazard evaluation is performed	• Montreal Protocol – List of Controlled Ozone-depleting Substances • Stockholm Convention – List of Persistent Organic Pollutants (POPs) • World Health Organization's International Agency for Research on Cancer – List of Classified Carcinogens • Canada – Toxic Substances List and the Virtual Elimination List • European Chemicals Agency (ECHA) – Candidate List of Substances of Very High Concern for Authorization; Substances classified as CMR 1a or 1b under Annex VI of CLP • U.S. Environmental Protection Agency – Toxic Release Inventory's Persistent, Bioaccumulative and Toxic (PBT) Chemicals List and PBT Chemicals under the Toxic Substances Control Act (TSCA) Section 6(h) • U.S. National Toxicology Program – Report on Carcinogens • State of California – Proposition 65 List
Select endpoints and apply criteria/thresholds	Evaluate the "Minimum Criteria" endpoints shown in Exhibit 6, using GHS criteria to ascribe level of concern/classification for a given hazard.
Establish transparent decision rules to organize and prioritize information	Exclude alternatives that are classified as "High" concern based on GHS criteria for: • Carcinogenicity • Germ Cell Mutagenicity • Reproductive/Developmental Toxicity • PBT • vPvB

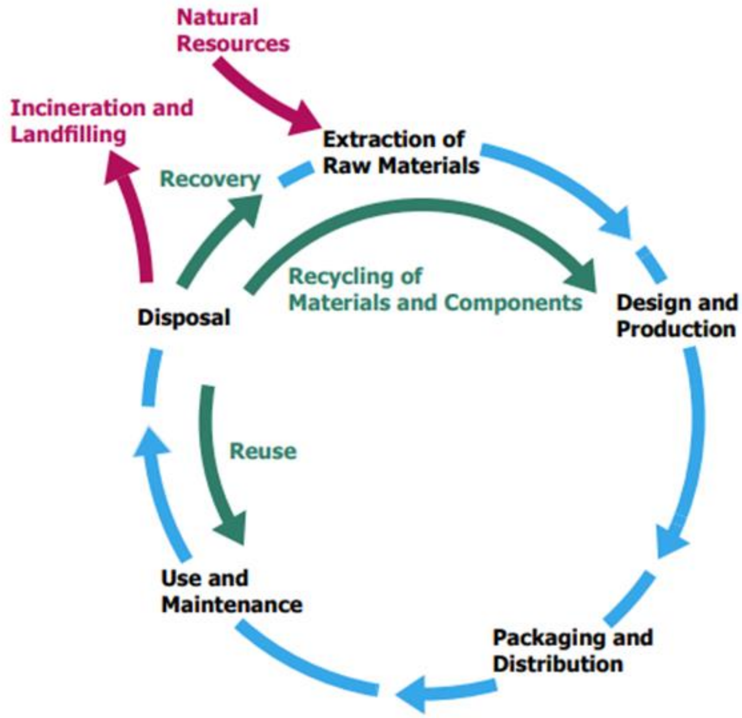
<table>
<tr><th>Assessment Step</th><th>Minimum Criteria and Recommended Assessment Practices</th></tr>
<tr><td>Consider data gaps and uncertainty</td><td>Use one or more of the practices listed below, and described in Exhibit 9, to address data gaps and provide explicit documentation on the practice/method used.
• Tier 1 Practices: Lower Level of Expertise and Resources Required
– Provide descriptions of the confidence level in the data associated with a specific hazard classification
– Use external expert knowledge
– Exclude alternatives with missing data
– Penalize data gaps
– Remain neutral about uncertainty and missing data
• Tier 2 Practices: Higher Level of Expertise and Resources Required
– Use additional tools
– Use quantitative uncertainty analysis</td></tr>
<tr><td colspan="2">Comparative Exposure Assessment</td></tr>
<tr><td>Identify exposure pathways and reasonably foreseeable exposure scenarios throughout the lifecycle</td><td>Identify potential routes of exposure (such as dermal, inhalation, and ingestion pathways for human health and air, water, and soil pathways for the environment) for the substance that needs to be substituted and each alternative given conditions of use, using the following steps:
• Based on the scope of the assessment, identify the life cycle stage(s) where concerns for exposure trade-offs may occur.
• Within each life cycle stage, identify potential routes of exposure and receptors given conditions of use and conditions of potential misuse of the substance.</td></tr>
<tr><td>Compare exposure potential of alternatives</td><td>• Exclude routes of exposure that are unlikely based on measured exposure data or physical-chemical properties such as those listed in Exhibit 12.
• Qualitatively compare the above exposure data or physical-chemical properties for the relevant exposure routes to identify if the alternative is likely to result in greater, equivocal, or less exposure.</td></tr>
<tr><td colspan="2">Integrating Comparative Hazard and Exposure Assessment Results and Assessing Trade-offs to Select a Safer Alternative</td></tr>
<tr><td>Integrate hazard and exposure assessment results</td><td>Transparently document strategies used to integrate hazard and exposure results. Use one or more of the strategies listed below, and described in Exhibit 13.
• Comparison matrices
• Adjusting for exposure potential
• Narrative exposure summary
• Descriptive exposure phrases</td></tr>
<tr><td>Consider trade-offs and make a decision regarding a safer alternative</td><td>Engage stakeholders and document the rationale for a decision including the strategies and tools used to address trade-offs and to assist the decision-making process. At a minimum, use of one or more of the strategies listed below, and described in Exhibit 14, to address trade-offs in the integration of hazard and exposure data to make a safer alternative determination. In some cases, this step may determine that a safer alternative is not currently available, and research and de novo design are needed to create one.
• Comparative evaluation matrices
• Eliminate the “high” rating
• Strict ordering of endpoints
• Equal weighting of endpoints
• Rule-based ranking
• Weighted scoring of endpoints
•</td></tr>
</table>

5. Beyond Safer to More Sustainable Substitution

In addition to the considerations for designating “safer” alternatives, there is a growing emphasis on sustainable chemistry and product stewardship across OECD delegations. The concept of sustainable chemistry includes a broader set of environmental, social, and economic factors beyond the molecular design focus of green chemistry. These include “upstream” and “downstream” chemical or product impacts, resource depletion, circularity, energy use, climate change potential, environmental justice considerations, and worker and community health and well-being. These considerations can form a critical part of the decision about a preferred alternative and are first identified at the scoping stage of an assessment.

Sustainability attributes or trade-offs associated with a chemical choice are often considered in the context of a product’s lifecycle (or footprint). In addition to hazard and exposure, life-cycle approaches take into account energy use and resource consumption at all points of the lifecycle: raw material extraction, manufacturing, use, and end-of-life management (see **Exhibit 20**). For example, there is increasing corporate and policy attention to the circularity of materials, with the goal of transitioning from a linear economy to one that uses renewable resources and recycled materials. As defined by the Ellen MacArthur Foundation,[1] the circular economy is based on three principles: designing out waste and pollution, keeping products and materials in use, and regenerating natural systems. Considerations in chemical selection for circularity include whether that substance will increase contamination of secondary materials or impede reuse and recyclability.

Exhibit 20. Product Lifecycle



Source: UNEP/SETAC. Life Cycle Management: A Business Guide to Sustainability. Paris, 2007

For example, an alternative may be identified as safer based on the steps identified in Section 3 of this report, but may significantly increase energy use across a process or product lifecycle or decrease recyclability. These attributes may make the alternative a non-preferable option. It is important to identify potential sustainability trade-offs associated with alternatives during the scoping phase of the assessment and then evaluate and seek to resolve them. Identifying process improvements to reduce embedded energy of an alternative, exploring design modifications to enhance circularity, or making a decision to develop new alternatives while ensuring adequate management of the existing option are possible solutions. To build upon the case example presented in Section 3, evaluating potential impacts of concern along the life cycle and end-of life (recycling) (identified in the scoping phase of the assessment and noted in Exhibit 20) for each alternative could lead to improved decision-making that minimizes potential trade-offs between toxicity and other sustainability attributes. For example, Alternative B is bio-based, but its feedstock chemical is sourced from a non-sustainably-grown source and uses an energy intensive process to convert to the final solvent. Alternative C is petrochemical-based and requires high processing energy to remove problematic residuals. Since both alternatives require energy intensive processes, but Alternative B’s source material is determined to be less sustainable, the assessor decides Alternative C remains the preferred alternative from both a hazard and sustainability perspective. The assessor may prioritize green chemistry solutions to improve separation and refinement processes to reduce the processing energy for Alternative C. In another example, Chemical D is hazardous and could be replaced by chemical E in mixture formulations eliminating hazard and risk. Both chemicals are critical raw materials and Chemical E cannot be recycled and when mined or manufactured induces the production of chemicals with the same properties and as chemical D, which then need to be disposed. In such a case, a more in-depth assessment of the trade-offs related to hazard, risk, possible risk management measures that can be put in place and broader sustainability aspects would need to be performed for the assessor to make an informed choice on the preferred alternative. In parallel, efforts should be pursued to find or develop alternatives which are inherently safer and more sustainable along their life-cycle and end-of-life.

Considering the implication of a chemical substitution throughout the lifecycle can involve approaches ranging from quantitative life-cycle assessments (LCAs), such as those that follow well-defined ISO 14040 methodology, to less resource-intensive “life-cycle thinking,” which can qualitatively evaluate impacts across life-cycle stages. While chemical alternatives assessments are not instruments for conducting full LCAs, many frameworks incorporate life-cycle thinking. For example, Jacobs et al. (2016) found that 18 of 20 reviewed frameworks included life-cycle thinking. The authors found that while most frameworks consider life-cycle attributes in the context of hazard, exposure, economic, or technical feasibility assessments, some frameworks (e.g., the German Guide on Sustainable Chemicals and the U.S. NRC framework) include it as a discrete process component to provide information for identifying potential unintended consequences or discerning between alternatives (Jacobs et al. 2016). Additionally, some regulatory alternatives assessment requirements, such as alternative analyses conducted under California’s Safer Consumer Products regulation, require the inclusion of relevant life cycle segments and impacts. Moreover, life-cycle practices continue to evolve; for example, Fantke et al. (2020) describe new research on how to combine LCAs and chemical safety considerations.

The sustainability of a potential substitute is also dependent on the economic viability of alternatives. Jacobs’ et al. (2016) review of 20 alternatives assessment frameworks found that all included some form of economic assessment. Across the reviewed frameworks, economic measures ranged from commercial availability, direct costs (such as manufacturing and transition costs), and internal costs (such as insurance and regulatory compliance costs), to external costs and benefits (such as environmental impact costs and worker morale) and long-term costs (such as economies of scale). While the breadth and depth of economic considerations may vary according to what is possible or desirable for a given alternatives assessment, making an informed substitution relies on understanding the substitution’s economic impacts across the chemical’s lifecycle.

Exhibit 21 below includes additional resources that may be useful in identifying, considering, and evaluating broader sustainability impacts in chemical substitution decision-making. While these impacts are not the focus of this guidance, they are important to consider in minimizing potential trade-offs of substitution decisions and should be considered in the context of transitioning to safer alternatives.

Exhibit 21. Resources on Sustainable Chemical Substitution.

Examples of Sustainability Policies
European Green Deal (European Commission 2019) – *A strategy for transforming the European Union into a carbon-neutral society and decoupling its economic growth from resource use. The EU Green Deal calls for decarbonisation of the chemical industry and directs the European Commission to create a "chemicals strategy for sustainability."*
United Nations Sustainable Development Goals[2] – *Sustainable Development Goal 12 – Ensure sustainable consumption and production patterns – includes "Chemicals and Waste" as a focus area.*
Examples of Technical Tools and Resources
BREFs[3] – *A set of Best Available Techniques (BAT) reference documents developed by the European Integrated Pollution Prevention and Control (IPPC) Bureau (EIPPCB). The BREFs give information on specific industrial and agricultural sectors, and are referenced by EU Member States when issuing operating permits for installations with significant pollution potential.*
Framework for Portfolio Sustainability Assessments (PSA)[4] – *A guide developed by the World Business Council for Sustainable Development (WBCSD) that helps companies develop and apply PSA approaches that will result in more sustainable product portfolios.*
Guide on Sustainable Chemicals (Umweltbundesamt (German Environment Agency) 2016) – *The German Environment Agency's guide to help manufacturers, formulators, and end users of substances to put greater emphasis on sustainability criteria in the selection of substances and use of chemicals.*
Material Input per Service Unit (MIPS) Calculator[5] – *A spreadsheet-based tool that helps the user estimate the resource consumption of a product or service across its entire life cycle.*
Non-Hazard Assessment Tools in the OECD Substitution and Alternatives Assessment Tool Selector[6] – *A tool inventory that provides information on tools that address life cycle and materials management considerations in alternatives assessment.*
ProBas[7] – *A database maintained by the German Environment Agency that includes life cycle information, such as air emissions and water consumption, for various product and substance types.*
PROSA – Product Sustainability Assessment (Griesshammer et al. 2007) – *A tool developed by Öko-Institut that identifies system innovations and options for action toward sustainable development. PROSA helps structure decision-making processes and reduce their complexity.*
Sustainability Method Selection Tool[8] – *A tool developed by the Dutch National Institute for Public Health and the Environment (RIVM) that helps the user find the best method for answering their sustainability questions.*
Technical Tools and Approaches in the Design of Sustainable Plastics[9]-- *A guide prepared as a background document for the "Global Forum on Environment focusing on Plastics in the Circular Economy – Sustainable Design of Plastics from a Chemicals Perspective" workshop that summarizes technical tools and approaches that support sustainable plastics design and identify key gaps that need to be addressed.*

Exhibit 22 includes an overview of life-cycle aspects relevant to chemical substitution decisions from the German Environment Agency.

Exhibit 22. Life-Cycle Analysis (LCA) Aspects of Alternatives Assessments – An Overview from the German Environment Agency

To foster and mainstream sustainable development, holistic assessments of hazardous chemicals and their alternatives from chemical-intensive sectors are becoming increasingly important. Whereas alternative assessment addresses aspects like chemical hazards and exposure, physical/chemical properties, and information on human toxicology and ecotoxicology, life-cycle assessment (LCA) instruments take into account additional aspects that allow a more holistic sustainability assessment.

For LCA in production and services with chemicals, the following considerations are particularly important:

- physical/chemical properties
- hazardous properties for human health and for the environment
- mobility (long-range transport potential) of a substance
- greenhouse gas emissions
- resource consumption
- recycling potential of a substance

Mobility of a substance should be understood in conjunction with human and environmental hazard. High mobility can exacerbate concern for hazard, and low mobility may reduce it. Mobility also affects resource efficiency because it could lead to substance loss. Mobility can be assessed through partitioning and distribution in air and water. For health aspects, the potential to penetrate the skin should be explored as a mode of mobility.

Assessment of greenhouse potential and resource consumption should be performed in a comparative manner, using different substances or products for comparison. The **greenhouse potential** of a substance can be described as CO_2 equivalents emitted along the lifecycle of a substance (e.g., “20 kg CO_2-equivalents / kg substance”). The assessment of **resource consumption** should include the demand of energy, raw materials, and water for the production of a substance, chemical product, or service.

Evaluation of the **recycling potential of a substance** has to consider three main aspects: Assessment of the extent to which a substance and possible other substances and/or associated materials can be recovered without risk to human health and for the environment; assessment of the purity levels of recycling fractions in order to allow the highest possible level of re-use; and assessment of the quantity of recyclable substances and materials in a recycling process in order to avoid losses. Substances and chemical products and services that are not designed for recycling should either fully degrade or mineralize during disposal.

An LCA can be complemented by use-specific aspects like the quantity of the used substance, the emission potential during use, and consideration of related user groups (professional or consumer). Additionally, substitutability of a substance by a more sustainable one should be evaluated before its use and during design of chemical products and services. This also encompasses the comparative evaluation of substances’ innovation potential, leading to potential benefits for society.

Another aspect that is important for sustainable development relates to responsibility in supply chains. The supplier of a substance should fulfill high environmental and social standards. Raw materials should be selected according to their sustainability, the conditions of environmental protection and safety and health at the workplace, and social standards like fair pay.

Notes

[1] https://www.ellenmacarthurfoundation.org/circular-economy/concept

[2] https://sustainabledevelopment.un.org/topics/chemicalsandwaste

[3] https://eippcb.jrc.ec.europa.eu/reference/

[4] https://www.wbcsd.org/Projects/Chemicals/Resources/Framework-for-portfolio-sustainability-assessments

[5] https://wupperinst.org/en/topics/resources/calculating-resources/

[6] http://www.oecdsaatoolbox.org/Home/NonHazTools

[7] https://www.probas.umweltbundesamt.de/php/index.php

[8] http://www.sustainabilitymethod.com/

[9] https://www.oecd.org/chemicalsafety/risk-management/technical-tools-and-approaches-in-the-design-of-sustainable-plastics.pdf

References

California Code of Regulations. (2013). Title 22, Division 4.5, §69501–§69599. Chapter 55: Safer Consumer Products Regulation. Retrieved from https://dtsc.ca.gov/wp-content/uploads/sites/31/2018/07/SCP-Final-Regs-Text-10-01-2013.pdf

Council of the European Union. (1998). Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work. Retrieved from https://eur-lex.europa.eu/eli/dir/1998/24/2014-03-25

European Commission. (2019). Communication from the Commission to the European Parliament, the European Council, the Council, the European Economic and Social Committee and the Committee of the Regions: The European Green Deal. Brussels. Retrieved from https://ec.europa.eu/info/sites/info/files/european-green-deal-communication_en.pdf

Fantke, P., Huang, L., Overcash, M., Griffing, E., & Jolliet, O. (2020). Life cycle based alternatives assessment (LCAA) for chemical substitution. Green Chemistry. Retrieved from https://doi.org/10.1039/D0GC01544J

Greggs, W., Burns, T., Egeghy, P., Embry, M., Fantke, P., Gaborek, B., Heine, L., Jolliet, O., Lee, C., Muir, D., Plotzke, K., Rinkevich, J., Sunger, N., Tanir, J., & Whittaker, M. (2019). Qualitative Approach to Comparative Exposure in Alternatives Assessment. Integrated Environmental Assessment and Management, 15(6), 880-894. Retrieved from https://doi.org/10.1002/ieam.4070

Griesshammer, R., Buchert, M., Gensch, C-O., Hochfeld, C., Manhart, A., Reisch, L., & Rüdenauer, I. (2007). PROSA – Product Sustainability Assessment: Guideline. Freiburg: Öko-Institut e.V. Retrieved from https://research.cbs.dk/en/publications/prosa-product-sustainability-assessment-guideline

Jacobs, M., Malloy, T., Tickner, J., & Edwards, S. (2016). Alternatives Assessment Frameworks: Research Needs for the Informed Substitution of Hazardous Chemicals. Environmental Health Perspectives, 124(3), 265-280. Retrieved from https://doi.org/10.1289/ehp.1409581

National Research Council. (2014). A Framework to Guide Selection of Chemical Alternatives. Washington, DC: The National Academies Press. Retrieved from https://doi.org/10.17226/18872

Ökopol and Kooperationsstelle Hamburg. (2003). Report compiled for the Directorate General Environment, Nuclear Safety and Civil Protection of the Commission of the European Communities: Substitution of Hazardous Chemicals in Products and Processes. Hamburg. Retrieved from http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.306.5104&rep=rep1&type=pdf

Tickner JA, Schifano JN, Rudisill C, Mulvihill MJ. (2015). Advancing safer alternatives through functional substitution. Environmental Science & Technology, 49(2), 742–749. Retrieved from https://doi.org/10.1021/es503328m

Umweltbundesamt (German Environment Agency). (2016). Guide on Sustainable Chemicals: A decision tool for substance manufacturers, formulators and end users of chemicals. Dessau-Roßlau: Umweltbundesamt. Retrieved from https://www.umweltbundesamt.de/en/publikationen/guide-on-sustainable-chemicals

United Nations Economic Commission for Europe (UNECE). (2019). Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Retrieved from https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev08/ST-SG-AC10-30-Rev8e.pdf

U.S. Environmental Protection Agency (EPA). (2015). EPA's Safer Choice Standard. Retrieved from https://www.epa.gov/sites/production/files/2013-12/documents/standard-for-safer-products.pdf

U.S. Occupational Safety and Health Administration (OSHA). Basics of Informed Substitution & Alternatives Assessment. Retrieved from https://www.osha.gov/dsg/safer_chemicals/basics.html

Wood Environment & Infrastructure Solutions UK Limited and Lowell Center for Sustainable Production, under commission to the European Commission. (2019). Chemicals Innovation Action Agenda: Transition to Safer Chemicals and Technologies: Final Report. Luxembourg: Publications Office of the European Union. Retrieved from https://op.europa.eu/en/publication-detail/-/publication/2d7fc4d1-96f6-11e9-9369-01aa75ed71a1

Wood Environment & Infrastructure Solutions UK Limited, prepared for Ministerie van Infrastructuur en Waterstaat. (2018). Safe Chemicals Innovation Agenda: Towards a Research Agenda for Safe Chemicals, Materials and Products. Retrieved from https://www.chemischestoffengoedgeregeld.nl/sites/default/files/39982%20-%20Safe%20Chemicals%20Innovation%20Agenda%20-%2020180613i6%20final%20copy.pdf

As the demand for safer chemicals and technologies grows, the field of alternatives assessment is becoming increasingly important in guiding the transition towards safer, less toxic alternatives.

While the use and practice of alternatives assessment approaches have advanced considerably in the last decade, important gaps in alternatives assessment approaches remain. A major limitation that can hinder efforts to evaluate and adopt alternatives for priority chemicals is the lack of consistent criteria for defining "safer." Practitioners face challenges on what constitutes "safer" when evaluating alternatives from both a hazard and exposure perspective.

This guidance aims to identify and outline key considerations for the identification and selection of safer alternatives. It is intended to advance a consistent understanding of the minimum requirements needed to determine whether a chemical alternative is safer than the priority chemical, product, or technology for substitution, independent of the entity performing the assessment or the alternatives assessment framework being used.

oe.cd/chemicals-risk-management