

Evolving Directions in Alternatives Assessment Methods and Practice: Driving Growth of Safer, More Sustainable Chemicals and Products

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ZeroPM Workshop

February 8, 2023

Different lenses to approach safe and sustainable chemistry solutions



Research and
Strategic
Engagement



Supply chain needs
and applications
and innovation
policy

Adoption in industry,
particularly SMEs



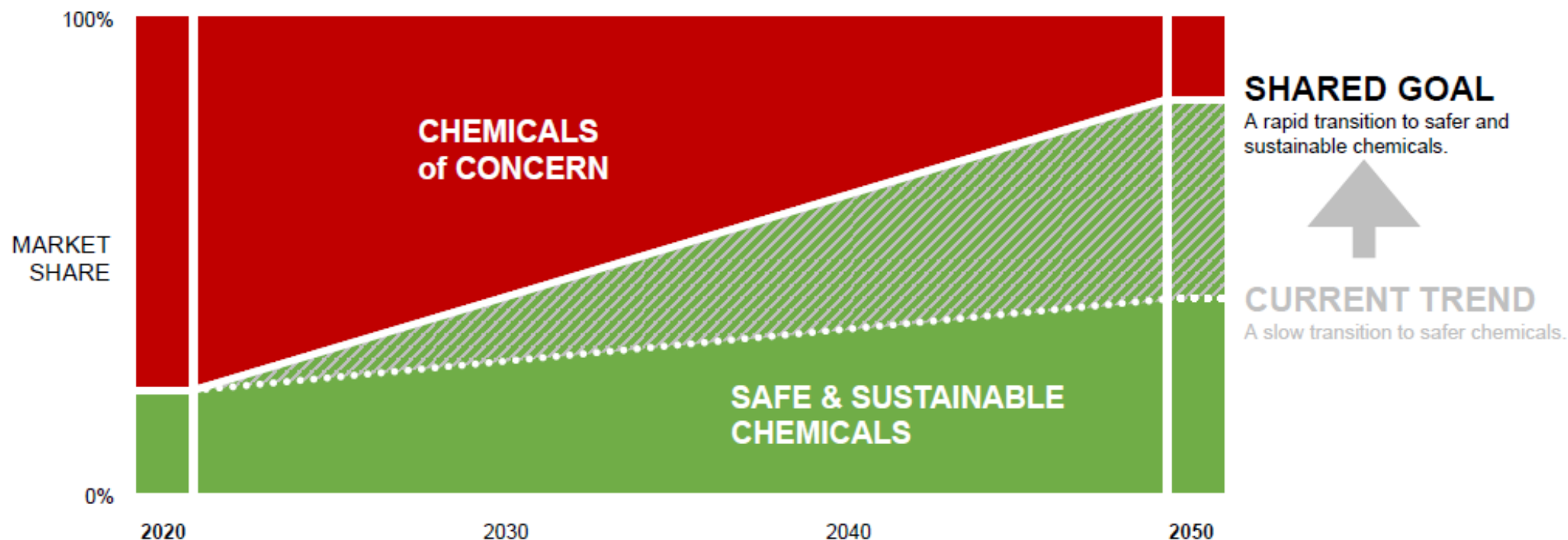
Building multi-
disciplinary science
and practice



Topline messages

- It will be difficult to reduce or eliminate PMTs without a supply of safer, more sustainable solutions at scale
- The use of alternatives assessment is essential to help guide the transition process, to avoid regrettable substitutions and identify areas where additional R&I are needed
- Identifying alternatives is not enough. They have to be adoptable in the marketplace. Substitution is hard!
- Need to create an interdisciplinary community of practice to design, identify, develop, evaluate, scale safer, more sustainable solutions.

A shared goal: Accelerate the growth of green and sustainable chemistry and its adoption and scale in the market



The Goal: Substitution

- “Substitution means the replacement or reduction of hazardous substances in products and processes by less hazardous or non-hazardous substances, or by achieving an equivalent functionality via technological or organizational measures.”
- A “hazard reduction” approach

Report compiled for the
Directorate General Environment, Nuclear Safety and Civil Protection
of the Commission of the European Communities

Contract No B3-4305/2000/293861/MAR/E1

SUBSTITUTION OF HAZARDOUS CHEMICALS IN PRODUCTS AND PROCESSES

FINAL REPORT

Hamburg, March 2003

Revision 1

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US EPA 2010 - Informed Substitution

A considered transition from a chemical of particular concern to safer chemicals or non-chemical alternatives.

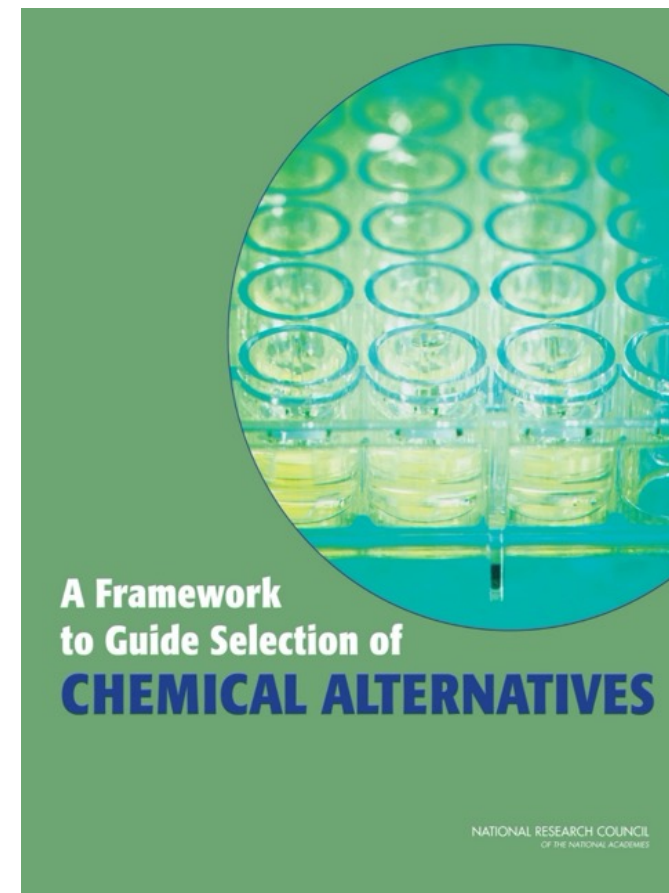
The goals of informed substitution are to:

- Minimize the likelihood of unintended consequences, which can result from a precautionary switch away from a chemical of concern without fully understanding the profile of potential alternatives, and
- Enable a course of action based on the best information - on the environment and human health - that is available or can be estimated.

Alternatives Assessment as a step-wise process to support substitution

“A process for identifying, comparing, and selecting safer alternatives to chemicals of concern on the basis of their hazards, comparative exposure, performance, and economic viability.”

- NAS 2014



NAS 2014: Alternatives Assessment

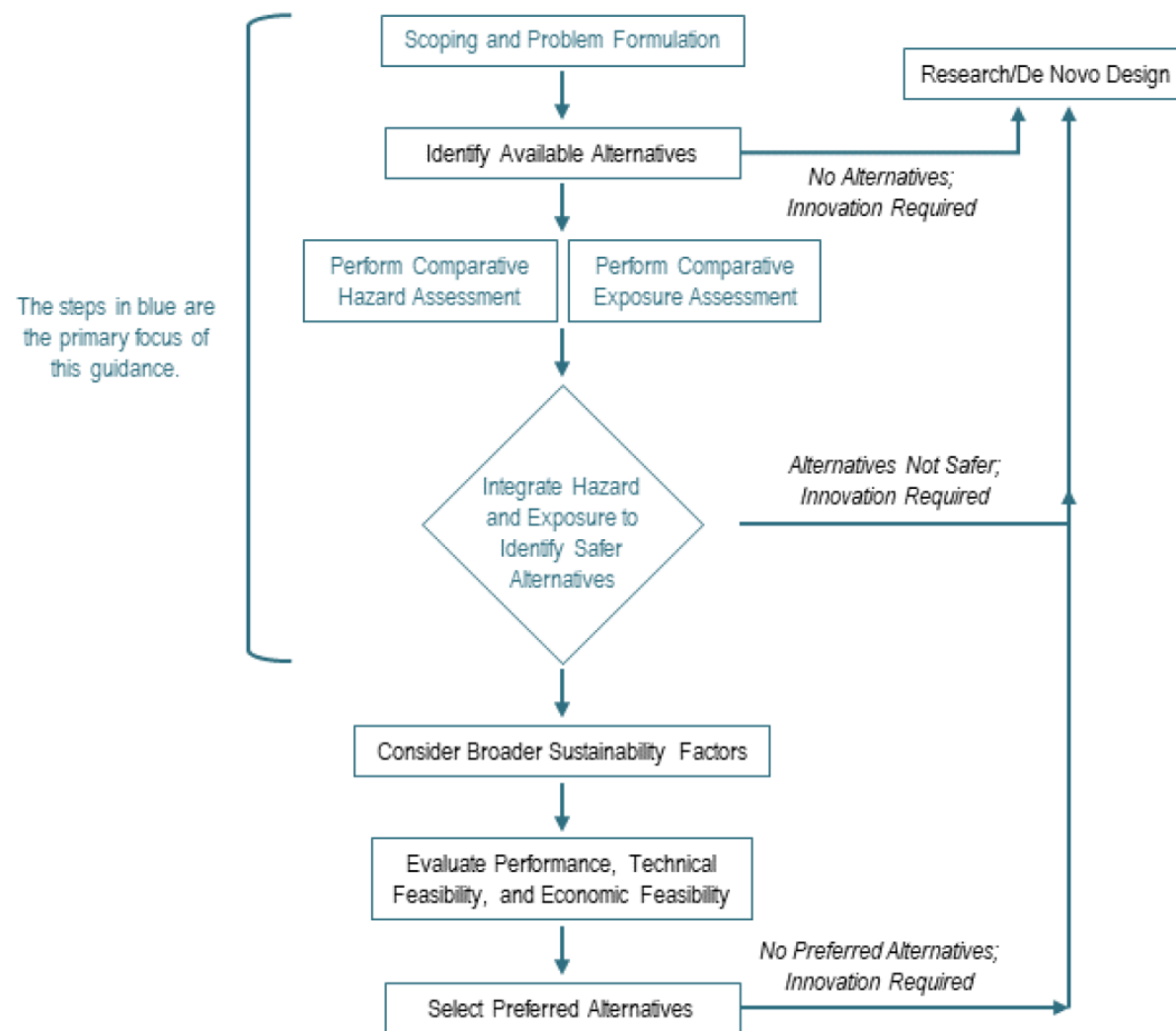
IS:

- a process for identifying, comparing and selecting safer alternatives to chemicals of concern.
- has a goal of facilitating an informed consideration of the advantages and disadvantages of alternatives to a chemical of concern.

IS NOT:

- a *safety assessment*, where the primary goal is to ensure that exposure is below a prescribed standard.
- a *risk assessment* where risk associated with a given level of exposure is calculated.
- a *sustainability assessment* that considers all aspects of a chemicals' life cycle, including energy and material use.

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



Commons Principles for Alternatives Assessment

- Reduce Hazard
- Minimize Exposure
- Use Best Available Information
- Require Disclosure and Transparency
- Resolve Trade-Offs
- Take Action

www.bizngo.org/alternatives-assessment/commons-principles-alt-assessment

THE COMMONS PRINCIPLES FOR ALTERNATIVES ASSESSMENT

Addressing Chemicals of Concern to Human Health or the Environment

In October 2012, a group of 26 environmental health scientists, advocates, funders and policy makers met in Boston, Massachusetts for two days of meetings entitled **Building a Chemical Commons: Data Sharing, Alternatives Assessment and Communities of Practice**. One of the key outcomes of this meeting was an agreement regarding the need for a common definition and set of principles for chemicals alternatives assessment. Following this meeting, a subcommittee met over four months in 2013 to refine a consensus set of principles. These principles were based on earlier foundational work by the Lowell Center for Sustainable Production, the Massachusetts Toxics Use Reduction Institute, the Environmental Defense Fund, and the BizNGO Working Group. These principles are now available to be shared and used in framing discussions about alternatives assessment and to guide decision making about safer chemical use.

Alternatives Assessment is a process for identifying, comparing and selecting safer alternatives* to chemicals of concern (including those in materials, processes or technologies) on the basis of their hazards, performance, and economic viability. A primary goal of Alternatives Assessment is to reduce risk to humans and the environment by identifying safer choices.

These Principles for Alternatives Assessment are designed to guide a process for well informed decision making that supports successful phase out of hazardous products, phase in of safer substitutes and elimination of hazardous chemicals where possible.

REDUCE HAZARD Reduce hazard by replacing a chemical of concern with a less hazardous alternative. This approach provides an effective means to reduce risk associated with a product or process if the potential for exposure remains the same or lower. Consider reformulation to avoid use of the chemical of concern altogether.

MINIMIZE EXPOSURE Assess use patterns and exposure pathways to limit exposure to alternatives that may also present risks.

USE BEST AVAILABLE INFORMATION Obtain access to and use information that assists in distinguishing between possible choices. Before selecting preferred options, characterize the product and process sufficiently to avoid choosing alternatives that may result in unintended adverse consequences.

REQUIRE DISCLOSURE AND TRANSPARENCY Require disclosure across the supply chain regarding key chemical and technical information. Engage stakeholders throughout the assessment process to promote transparency in regard to alternatives assessment methodologies employed, data used to characterize alternatives, assumptions made and decision making rules applied.

RESOLVE TRADE-OFFS Use information about the product's life cycle to better understand potential benefits, impacts, and mitigation options associated with different alternatives. When substitution options do not provide a clearly preferable solution, consider organizational goals and values to determine appropriate weighting of decision criteria and identify acceptable trade-offs.

TAKE ACTION Take action to eliminate or substitute potentially hazardous chemicals. Choose safer alternatives that are commercially available, technically and economically feasible, and satisfy the performance requirements of the process/product. Collaborate with supply chain partners to drive innovation in the development and adoption of safer substitutes. Review new information to ensure that the option selected remains a safer choice.

* "Safer Alternative: An option, including the option of not continuing an activity that is healthier for humans and the environment than the existing means of meeting that need. For example, safer alternatives to a particular chemical may include a chemical substitute or a re-design that eliminates the need for any chemical addition." From Tickner, J. and Eliason, P. *Alternatives Assessment for Chemicals: From Problem-Evaluation to Solutions-Assessment and Implementation: A background paper created expressly for use in the March 31-April 1, 2011 Interagency Discussion on Alternatives Assessment*, EPA Potomac: Verba Conference Facility, Crystal City, VA, March 24, 2011

The solutions-lens is critical

“One of the most essential, and powerful steps to change is understanding that there are alternatives.”

- Mary O'Brien, Making Better Environmental Decisions, 2001

“The focus on problem identification sometimes occurs at the expense of efforts to use scientific tools to develop safer technologies and solutions. Defining problems without a comparable effort to find solutions can diminish the value of applied research efforts.”

- National Academy of Sciences – Science for Environmental Protection: The Road Ahead, 2012

Critical to the action orientation...

- A decision to substitute. The desired outcome, informed substitution.
- Considering the function, including if that function is needed or its performance in an application overprescribed
- Clear and consistent, yet flexible, approaches adaptable to different decision contexts are needed
 - Minimum components that should be considered
 - Consistent definitions of “safer”
- Avoid paralysis by analysis – don’t let perfect be the enemy of good enough

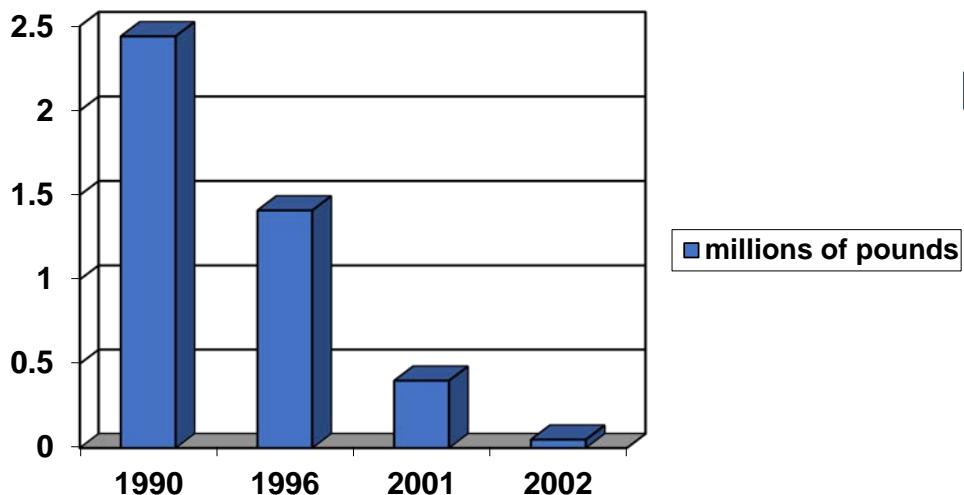
Starting with Functional Substitution – A Different Way to Look at Substitution

Table 1. Functional Substitution for Chemicals in Products, Chemicals in Processes

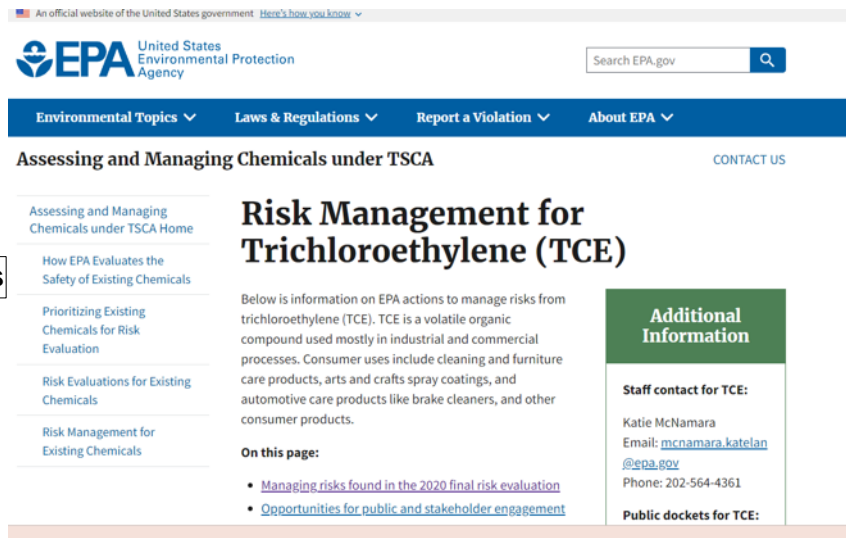
Functional Substitution Level	Chemical in Product Bisphenol-a in Thermal Paper	Chemical in Process Methylene Chloride in Degreasing Metal Parts
Chemical Function (Chemical Change)	Is there a functionally equivalent chemical substitute (i.e., chemical developer)? Result: Drop-in chemical replacement	Is there a functionally equivalent chemical substitute (i.e., chlorinated solvent degreaser)? Result: Drop-in chemical replacement
End Use Function (Material, Product, Process Change)	Is there another means to achieve the function of the chemical in the product (i.e., creation of printed image)? Result: Redesign of thermal paper, material changes	Is there another means to achieve the function of the process (i.e., degreasing)? Result: Redesign of the process (e.g., ultrasonic, aqueous)
Function As Service (System Change)	Are cash register receipts necessary? Are there alternatives that could achieve the same purpose (i.e. providing a record of sale to a consumer)? Result: Alternative printing systems (e.g., electronic receipts)	Is degreasing metal parts necessary? Are there other alternatives that could achieve the same purpose (i.e., providing metal parts free of contaminants for other end uses)? Result: Alternative metal cutting methods

Tickner, et al, Environmental Science and Technology, 2014

Example – Trichloroethylene substitution



Massachusetts Toxics Use Reduction Data – TCE in Metal Finishing



**FRAM – CENTRE FOR FUTURE
CHEMICAL RISK ASSESSMENT AND
MANAGEMENT STRATEGIES**



Substitution of trichloroethylene in metal parts cleaning in the European Union

A survey-based study on the effects of the authorisation requirements in REACH

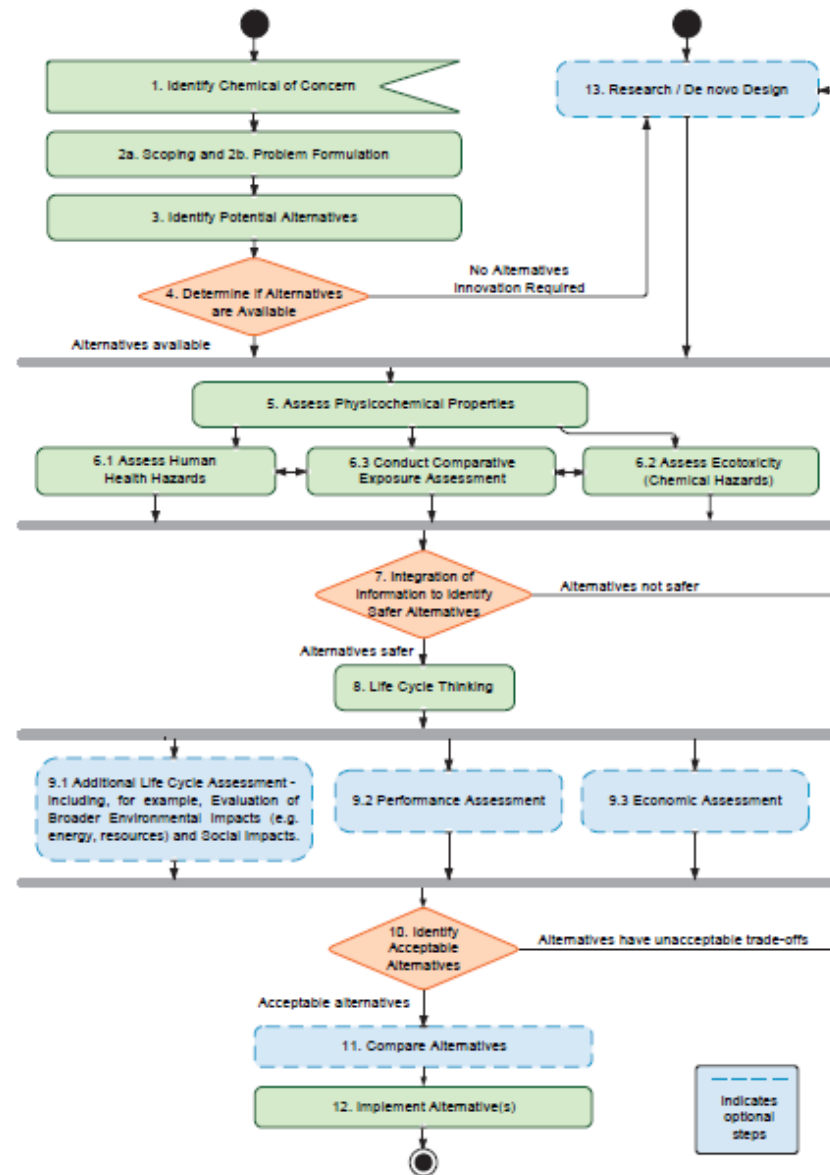
Ida Andersson and Daniel Slunge

WORKING PAPER, July 2021

The need for science to support alternatives assessment

“Given the paucity of data, which can slow down CAAs, it is important that future CAA frameworks incorporate the use of *in vitro* and other high-throughput assays, toxicity pathway-centric assays, into the assessment process to address gaps in traditional knowledge... It is important that emerging developments in toxicity testing be able to support the evaluation, comparison (including hazard categorization) and design of safer chemicals and materials, not simply to obtain more refined risk estimates.”

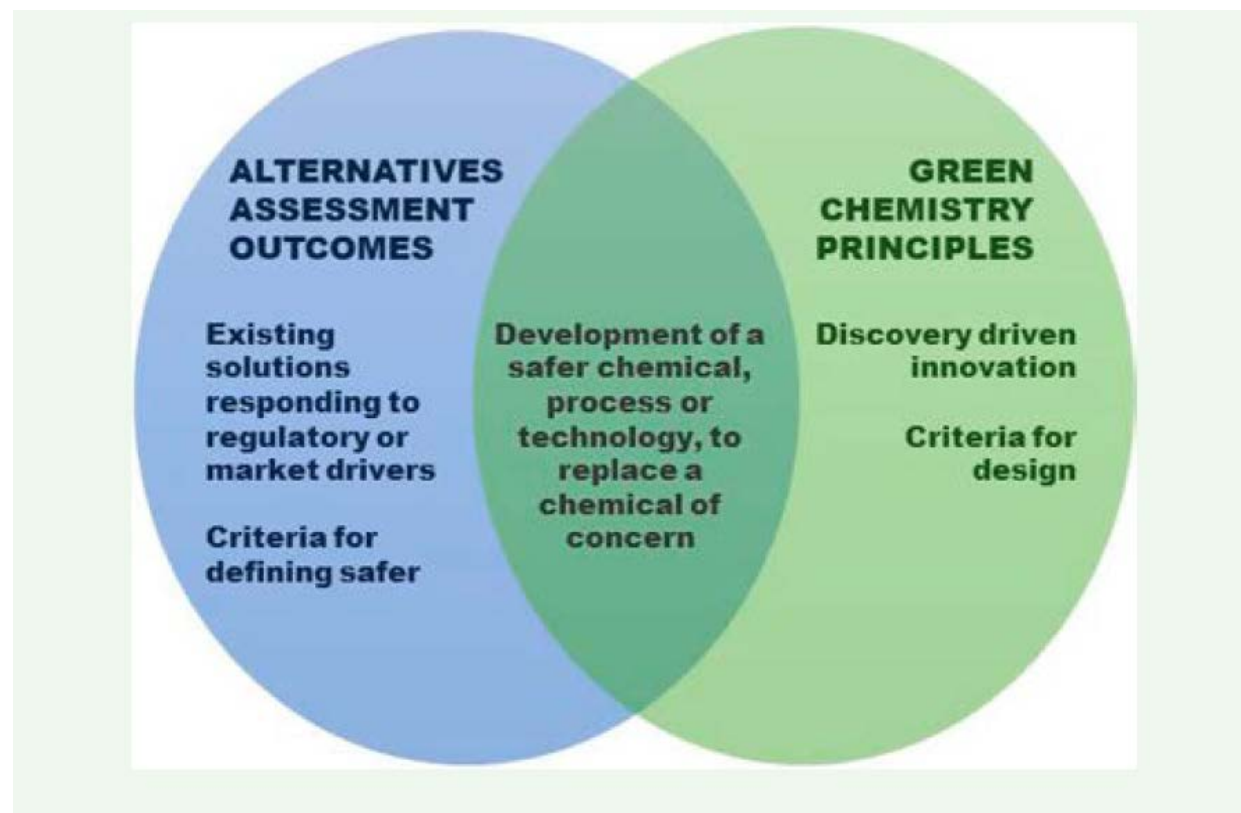
Environ. Sci. Technol. 2015, 49, 4, 1995–1996



Research Needs Moving Forward

- Hazard Assessment
 - Improve approaches for ecotox, integrating multiple data types, and addressing uncertainty
 - Establish approaches for mixtures and chemical to material comparisons
- Comparative exposure assessment
 - Identify how results from a comparative exposure assessment should be integrated with hazard assessment results to identify trade-offs in the AA process
- Decision-Analysis
 - Engage in method and tool development for different aspects of decision making (analysis and deliberation) for private and regulatory contexts
- Life cycle evaluation
 - Streamline life cycle assessment needs during the initial scoping and problem formulation stage of an AA by targeting life cycle stages and impact categories that are most significant

Connecting tools of alternatives assessment, substitution and safer chemical design



Green Chemistry Letters and Reviews, 14:1,23-44, DOI:10.1080/17518253.2020.1856427

Linking Chemical/Material Design and Safety – Rational Design



Article

pubs.acs.org/est

Evidence of Absence: Estrogenicity Assessment of a New Food-Contact Coating and the Bisphenol Used in Its Synthesis

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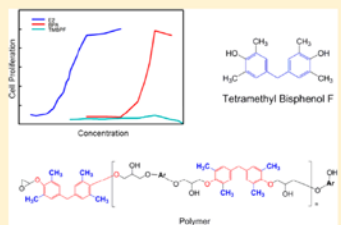
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Supporting Information

ABSTRACT: Consumer concerns about exposure to substances found in food contact materials with estrogenic activity (EA) have created substantial demand for alternatives. We assessed the potential EA of both a new bisphenol monomer used to synthesize polymeric coatings for metal food-contact applications and the nonintentionally added substances (NIAS) that may migrate into food. We evaluated tetramethyl bisphenol F (TMBPF) using *in vitro* and *in vivo* assays. We extracted the polymeric coating using food simulants ethanol (50% v/v) and acetic acid (3% w/v) and measured migration using tandem liquid chromatography (LC)/mass spectrometry (MS) and LC time-of-flight MS for TMBPF and NIAS, respectively. We also tested migrants for EA using the E-SCREEN assay. TMBPF did not show estrogenic activity in the uterotrophic assay and did not alter puberty in male and female rats or mammary gland development in female rats. Neither TMBPF nor the migrants from the final polymeric coating increased proliferation of estrogen-sensitive MCF7 cells. TMBPF did not show estrogen-agonist or antagonist activity in the estrogen receptor-transactivation assay. TMBPF migration was below the 0.2 parts per billion detection limit. Our findings provide compelling evidence for the absence of EA by TMBPF and the polymeric coating derived from it and that human exposure to TMBPF would be negligible.



Identifying and designing chemicals with minimal acute aquatic toxicity

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Edited by Helga West, Potsdam Institute for Climate Impact Research, Potsdam, Germany, and accepted by the Editorial Board January 28, 2014 (received for review August 7, 2013)

Industrial ecology has revolutionized our understanding of material stocks and flows in our economy and society. For this important discipline to have even deeper impact, we must understand the inherent nature of these materials in terms of human health and the environment. This paper focuses on methods to design synthetic chemicals to reduce their intrinsic ability to cause adverse consequence to the biosphere. Advances in the fields of computational chemistry and molecular toxicology in recent decades allow the development of predictive models that inform the design of molecules with reduced potential to be toxic to humans or the environment. The approach presented herein builds on the important work in quantitative structure-activity relationships by linking toxicological and chemical mechanistic insights to the identification of critical physical-chemical properties needed to be modified. This *in silico* approach yields design guidelines using boundary values for physicochemical properties. Acute aquatic toxicity serves as a model endpoint in this study. Defining value ranges for properties related to bioavailability and reactivity eliminates 99% of the chemicals in the highest concern for acute aquatic toxicity category. This approach and its future implementations are expected to yield very powerful tools for life cycle assessment practitioners and molecular designers that allow rapid assessment of multiple environmental and human health endpoints and inform modifications to minimize hazard.

green chemistry | safer chemicals | rational design | toxicity prediction

Industrial ecology and green chemistry are two rigorous scientific disciplines with global scientific communities that empower sustainability science. Sustainability science is the science, technology, and innovation in support of sustainable development—meeting human needs and reducing hunger and poverty while maintaining the life support systems of the planet (1, 2). With a systems view, industrial ecology investigates material and energy flows of coupled human-natural systems and has made significant strides in assessing the impacts of these flows on the environment and human health (3–8). The need for more sustainable products and processes has triggered (further) development of a large number of environmental assessment tools (9), including substance flow analysis (10), chemical product risk assessment (11), life cycle assessment (LCA) (12–14), and a variety of screening tools (15–19). The knowledge generated by these investigations and assessments provides key information about the chemicals, materials and processes with the most significant adverse impacts throughout the life cycle. We need to understand the inherent nature of these materials to not only quantify their impact on human health and the environment but also to facilitate the design of a more sustainable materials basis of our society. Analogous to the industrial ecology assessment tools, several National Academies of Science reports have identified the need for new green chemistry design tools (20–22), and specifically, tools focused on molecular design for reduced toxicity (23).

Although the majority of commercial chemicals are not intended to be biologically active, many have reported unintended biological activity that leads to a wide range of human health

and ecotoxicological impacts (11, 24). It has become increasingly evident that there are significant concerns about the adverse human health and ecosystem impacts resulting from chemical exposure and the challenge associated with predicting and modeling such endpoints (25). Several tools have emerged in this space with a consensus-building effort around USEtox (26–28). Many of these tools rely on the inherent nature of the chemicals being assessed, such as the octanol-water partition coefficient, as well as circumstantial information related to fate, transport, and exposure.

Extensive human health and ecotoxicological testing of all new chemicals to determine inherent toxicity characteristics is not feasible due to the number of new substances introduced daily, the time it takes to conduct reviews, and the prohibitive economic and social costs of testing, particularly *in vivo* (29). These concerns could be mitigated by addressing the significant challenge of designing molecules from first principles to have minimal biological activity. Advances in computational chemistry and mechanistic toxicology provide the fundamental knowledge to advance the rational design of chemicals with minimal unintended biological activity. Although risk models are very useful in regulatory decision making, models that can characterize the intrinsic hazard of a chemical can be useful to practitioners of industrial ecology, toxicology, chemistry, and engineering.

Development of *in silico* methods for estimation of toxicity from chemical structures has advanced considerably in recent decades, with significant emphasis on quantitative structure-activity relationships (QSARs) (30, 31). However, predictive ability of QSARs is often hindered by model training issues, such as

Significance

Two of the rigorous disciplines that have emerged over the last 20 y to empower sustainability science are industrial ecology and green chemistry. Robust assessment tools of industrial ecology identify the greatest opportunities to mitigate human health and environmental impacts resulting from human activity. Green chemistry designs and develops chemicals, materials, and processes that, throughout the life cycle, minimize hazard and maximize efficiency. This process often entails synthesizing new molecules while maintaining function and minimizing adverse outcomes, particularly toxicity. There is an urgent need to develop accurate and economical screening tools that predict potential toxicity and inform the design of safer alternatives. A computational approach is presented for the rational design of molecules for reduced acute aquatic toxicity.

Author contributions: J.K., A.V.-K., P.T.A., and J.B.Z. designed research; J.K. and A.V.-K. performed research; J.K., A.V.-K., and J.B.Z. analyzed data; and J.K., A.V.-K., P.T.A., and J.B.Z. wrote the paper.

The authors declare no conflict of interest.

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¹To whom correspondence should be addressed. E-mail: julie.beth.zimmerman@yale.edu. This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1314891111/-/DCSupplemental.

www.pnas.org/cgi/doi/10.1073/pnas.1314891111

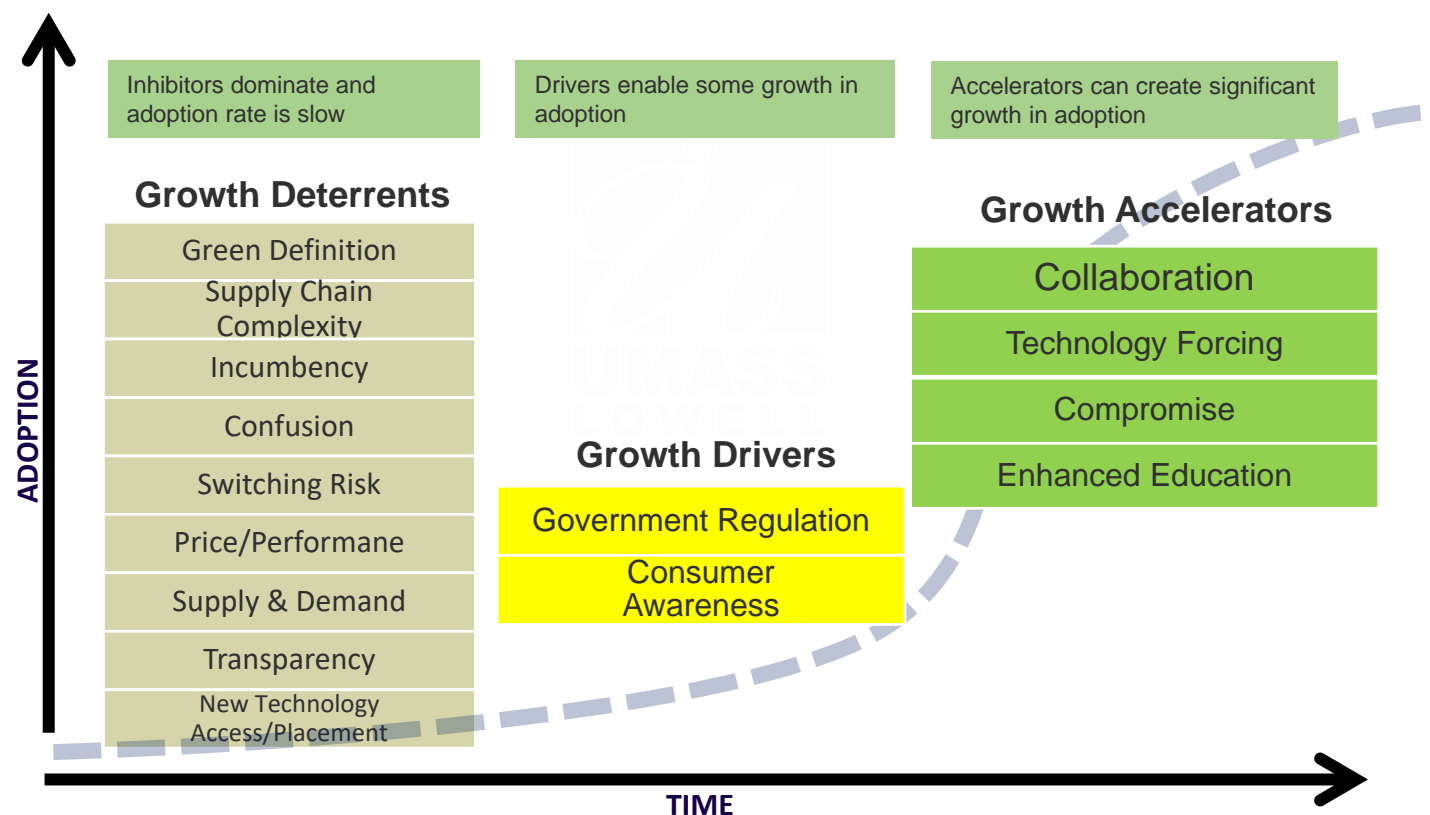
PNAS | May 19, 2015 | vol. 112 | no. 20 | 6289–6294

Identifying and evaluating alternatives is critical but not sufficient

- Substitution is hard and resource intensive.
- It is important to focus as well on the adoption phase to:
 - Address barriers to substitution
 - Identify unexpected trade-offs
 - Support companies that may not have knowledge or expertise
- Where alternatives don't exist or are sub-optimal, we'll need to develop new ones and expedite their time to market

Inhibitors and Accelerators of Green Chemistry Solutions

<https://greenchemistryandcommerce.org/resources/gc3-publications>



The barriers are real...

- Cost – r&d, capital, reformulation, retraining
- Performance – may not work the same or as good or multi-functionality needed; may need to reformulate multiple times
- Supply chain – single supplier/potential disruption, complexity
- Regulatory – barriers to new entrants, timeframes too short
- Lack of clarity of what's “safer” or “sustainable”

Landscape Analysis of Drivers, Enablers, and Barriers to Plasticizer Substitution

DECEMBER 2021

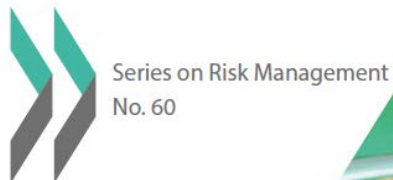


A REPORT FOR
GC3 GREEN CHEMISTRY &
COMMERCE COUNCIL

- Strong drivers are needed to motivate action creating a “pressurized” system that can overcome the incumbency of existing technologies
- Barriers must be clearly identified and addressed – enabling effective strategies and interventions to facilitate substitution.
- Sectoral and supply chain collaboration can overcome barriers to change, promoting understanding of challenges

<https://greenchemistryandcommerce.org/documents/GC3-Plasticizer-Report-Dec-2021.pdf>

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



Series on Risk Management
No. 60



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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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: <ul style="list-style-type: none"> Carcinogenicity Germ Cell Mutagenicity Reproductive/Developmental Toxicity PBT vPvB

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 <ul style="list-style-type: none"> Carcinogenicity Germ cell mutagenicity Reproductive toxicity² Acute toxicity Specific target organ toxicity – repeated exposure³ 	Environmental Hazards <ul style="list-style-type: none"> Acute aquatic toxicity Chronic aquatic toxicity Bioaccumulation potential Biodegradability⁴ 	Physical Hazards <ul style="list-style-type: none"> 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 <ul style="list-style-type: none"> Neurotoxicity Specific target organ toxicity – single exposure Skin corrosion/irritation Serious eye damage/eye irritation Respiratory or skin sensitization Aspiration hazard Endocrine disruption[*] 	Environmental Hazards <ul style="list-style-type: none"> Mobility Wildlife toxicity[*] Eutrophication[*] Greenhouse gas emissions, ozone depletion potential, waste generation, and other sustainability endpoints^{**} 	Physical Hazards <ul style="list-style-type: none"> 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.		

<https://www.oecd.org/chemicalsafety/risk-management/guidance-on-key-considerations-for-the-identification-and-selection-of-safer-chemical-alternatives.pdf>

Criteria for Safer AFFF replacements

TABLE 1. Minimum Requirements for a Safer AFFF Alternative

Part A	Part B
<p>A <i>safer</i> AFFF alternative <u>cannot</u> include the following classes of substances and/or substances:</p> <ol style="list-style-type: none"> 1. Fluorinated substances (No PFAS) 2. Alkylphenols and alkylphenol ethoxylates unless test data for endpoints in Part B demonstrate safety 3. Cyclic volatile methyl siloxanes: <ul style="list-style-type: none"> – octamethylcyclotetrasiloxane (D4) – decamethylcyclopentasiloxane (D5) – dodecamethylcyclohexasiloxane (D6) 	<p>A <i>safer</i> AFFF alternative <u>cannot</u> contain any chemical ingredient* classified as “high” concern associated with the following hazard endpoints:</p> <ol style="list-style-type: none"> 1. Carcinogenicity* 2. Germ cell mutagenicity* 3. Reproductive/developmental toxicity* 4. Acute mammalian toxicity 5. Systemic toxicity, repeated dose 6. Endocrine disruption 7. Acute aquatic toxicity 8. Chronic aquatic toxicity <p>Or either of the following classifications:</p> <ol style="list-style-type: none"> 9. Persistent, Bioaccumulative and Toxic (PBT)* 10. very Persistent, very Bioaccumulative (vPvB)* <p>A <i>safer</i> AFFF alternative tested at the product-level <u>cannot</u> be classified as “high” concern associated with the following hazard endpoint:</p> <ul style="list-style-type: none"> • Acute aquatic toxicity

TABLE 14. Beyond the Minimum: Additional Hazard Criteria to Consider in Comprehensive Hazard Assessments

Human Health Hazards	Environmental Hazards	Physical Hazards
<ul style="list-style-type: none"> • Aspiration hazard • Endocrine Disruption • Neurotoxicity • Respiratory and skin sensitization • Serious eye damage/eye irritation • Skin corrosion/irritation 	<ul style="list-style-type: none"> • Mobility • Wildlife toxicity • Eutrophication • Greenhouse gas emissions, ozone depletion, waste generation, and other sustainability endpoints 	<ul style="list-style-type: none"> • Corrosivity • Explosivity • Oxidizing properties • Pyrophoric properties • Self-reactivity • Other physical hazards: aerosols, gases under pressure, organic peroxides, ergonomics, vibration, noise, etc.

[OECD 2021: Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternatives](#)

Products of the formulated product ingredients cannot be of “high” concern as well.

https://research-and-innovation.ec.europa.eu/news/all-research-and-innovation-news/recommendation-safe-and-sustainable-chemicals-published-2022-12-08_en



Figure 7. Hierarchical principles underpinning the SSbD framework suggested

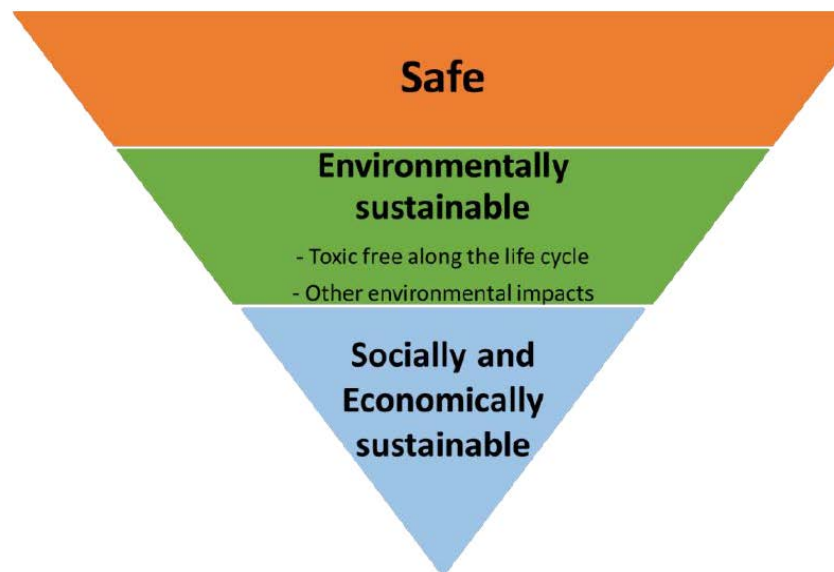
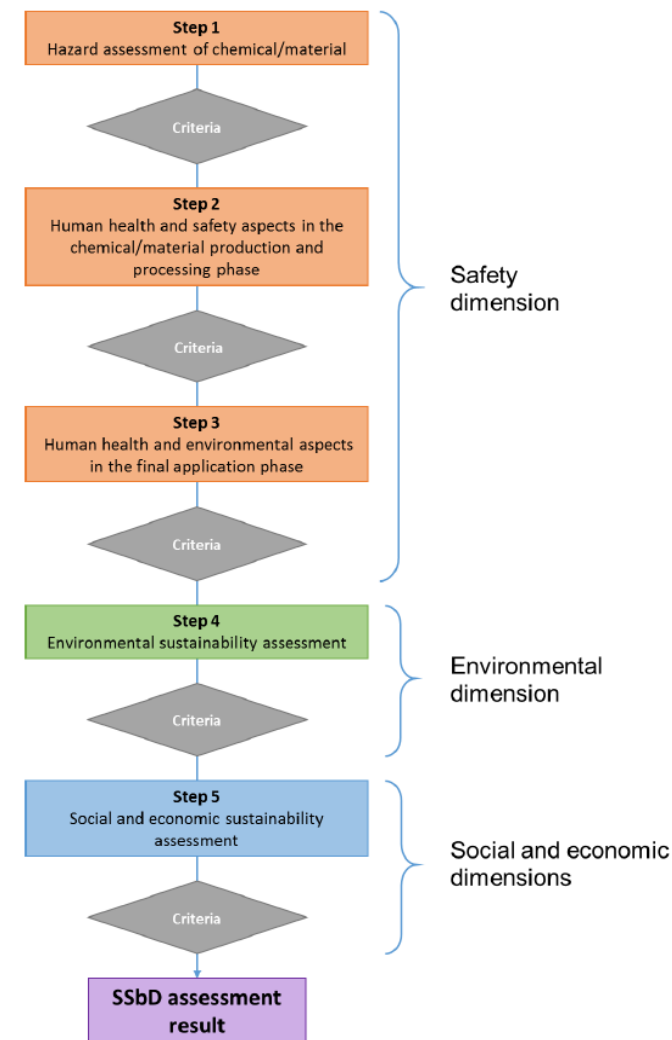


Figure 11. Stepwise approach for the SSbD framework safety and sustainability assessment. Note that steps in the framework to be explored as methods still need to be further developed



Need to rethink performance - fit for purpose/sufficient performance

1. Understand the function and the application specific functional needs
2. Establish or use performance standards independent of the standards dependent on using chemicals/ materials of concern and adjust based on what's on the horizon
4. Use a range of performance standard benchmarks,
 - E.g.,: “inadequate” to “sufficient” to “best in class”
5. Consider technical performance separately from technical feasibility
6. Consult stakeholders for determining acceptable tradeoffs between performance results and other elements such as environmental health and safety

Designing Smart Policies to Support Safer Chemistry

- Core Elements
 - Willingness
 - Restrictions, information requirements, planning requirements, purchasing policies, recognition
 - Capacity
 - Technical assistance, information requirements, R&D support, Education
 - Opportunity
 - R&D, education, tax incentives, grants

Ashford, Nicholas. 1999. An innovation-based strategy for a sustainable environment. In Innovation-Oriented Environmental Regulation: Theoretical Approach and Empirical Analysis. Potsdam, Germany: European Commission Joint Research Centre.

Lesson Learned: Regulation is Necessary

Regulations are needed to send **a firm signal** to the market to substitute

- Early regulatory signals critical for initiating innovation and informed substitution ahead of regulation

Regulatory actions that restrict the use of priority toxic chemicals of concern should be linked to **provisions for an evaluation of alternatives** to avoid regrettable substitution

- Need to include explicit criteria for what is considered “safer” and “sustainable” in policy

Lesson Learned: It's not just regulation – program support, capacity, collaboration are needed

Regulatory risk management actions should be supplemented with **dedicated government support** for the transition to safer chemicals

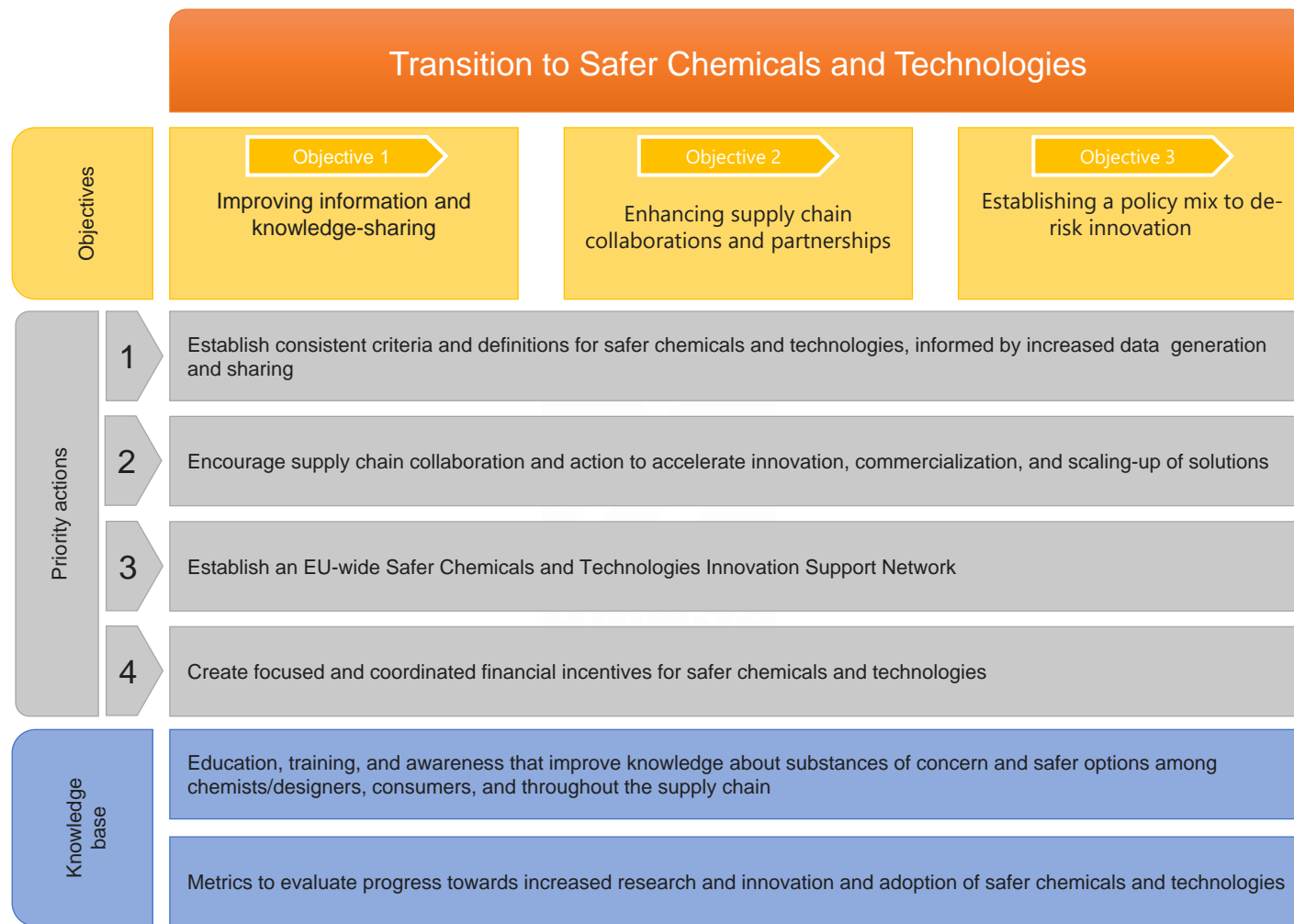
- e.g., tech assistance, demonstration projects, training, and supply chain engagement

Enhanced **capacity on the use of alternatives assessment** is needed to guide informed substitution long before agencies initiate restrictive risk management actions

- Elevate alternatives assessment as part-and- parcel to substitution thinking and practice

Enhanced **collaboration** across government authorities, enterprises and the scientific community is needed

- Networking and collaboration opportunities focused on solutions for specific functions/ chemistries



Wood and LCSP: Chemicals Innovation Action Agenda, 2019

<https://publications.europa.eu/en/publication-detail/-/publication/2d7fc4d1-96f6-11e9-9369-01aa75ed71a1>

A ubiquitous tire rubber-derived chemical induces acute mortality in coho salmon

Zhenyu Tian^{1,2}, Haoqi Zhao³, Katherine T. Peter^{1,2}, Melissa Gonzalez^{1,2}, Jill Wetzel⁴, Christopher Wu^{1,2}, Ximin Hu³, Jasmine Prat⁴, Emma Mudrock⁴, Rachel Hettinger^{1,2}, Allan E. Cortina^{1,2}, Rajshree Ghosh Biswas⁵, Flávio Vinicius Crizóstomo Kock⁵, Ronald Soong⁵, Amy Jenne⁵, Bowen Du⁶, Fan Hou³, Huan He³, Rachel Lundeen^{1,2}, Alicia Gilbreath⁷, Rebecca Sutton⁷, Nathaniel L. Scholz⁸, Jay W. Davis⁹, Michael C. Dodd³, Andre Simpson⁵, Jenifer K. McIntyre⁴, Edward P. Kolodziej^{1,2,3*}

6PPD-Quinone: Revised Toxicity Assessment and Quantification with a Commercial Standard

Zhenyu Tian,* Melissa Gonzalez, Craig A. Rideout, Haoqi Nina Zhao, Ximin Hu, Jill Wetzel, Emma Mudrock, C. Andrew James, Jenifer K. McIntyre, and Edward P. Kolodziej*

Juvenile coho salmon LC₅₀: 95 ng/L (ongoing: 70-130 ng/L)
USGS LC₅₀: 85 ng/L (J. Hansen, personal comm.)

Table 1. Comparison of the Toxicity of 6PPD-Q to Coho Salmon with Those of the Most Toxic Chemicals for Which the U.S. Environmental Protection Agency Has Established Aquatic Life Criteria^a

chemical class	name	most sensitive species	LC ₅₀ (ppb)	95% CI	ref	CMC (ppb)	EPA document
OP	parathion	<i>Orconectes nais</i>	0.04	0.01–0.2	25	0.065	EPA 440/5-86-007
quinone	6PPD-Q	<i>O. kisutch</i>	0.10	0.08–0.11	this study	not available	not available
OC	mirex	<i>Procambaris blandingi</i>	0.10	not reported	26	0.001	EPA 440/5-86-001
OP	guthion	<i>Gammarus fasciatus</i>	0.10	0.073–0.014	25	0.01	EPA 440/5-86-001
OP	chlorpyrifos	<i>Gammarus lacustris</i>	0.11	not reported	27	0.083	EPA 440/5-86-005
OC	endrin	<i>Perca flavescens</i>	0.15	0.12–0.18	28	0.086	EPA 820-B-96-001

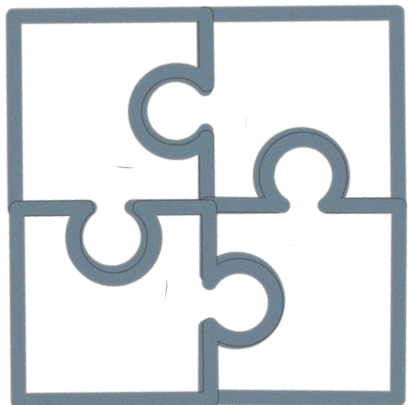
Options to address 6PPD

Change Bioavailability/Exposure

Change 6PPD Molecule

Change Rubber Material

Change Tire Design



Antidegradant Alternatives have many functions

Focus area:

Known alternatives to 6PPD that have the potential to be implemented in **the short term**



- Antiozonant



- Antioxidant



- Effective under stress

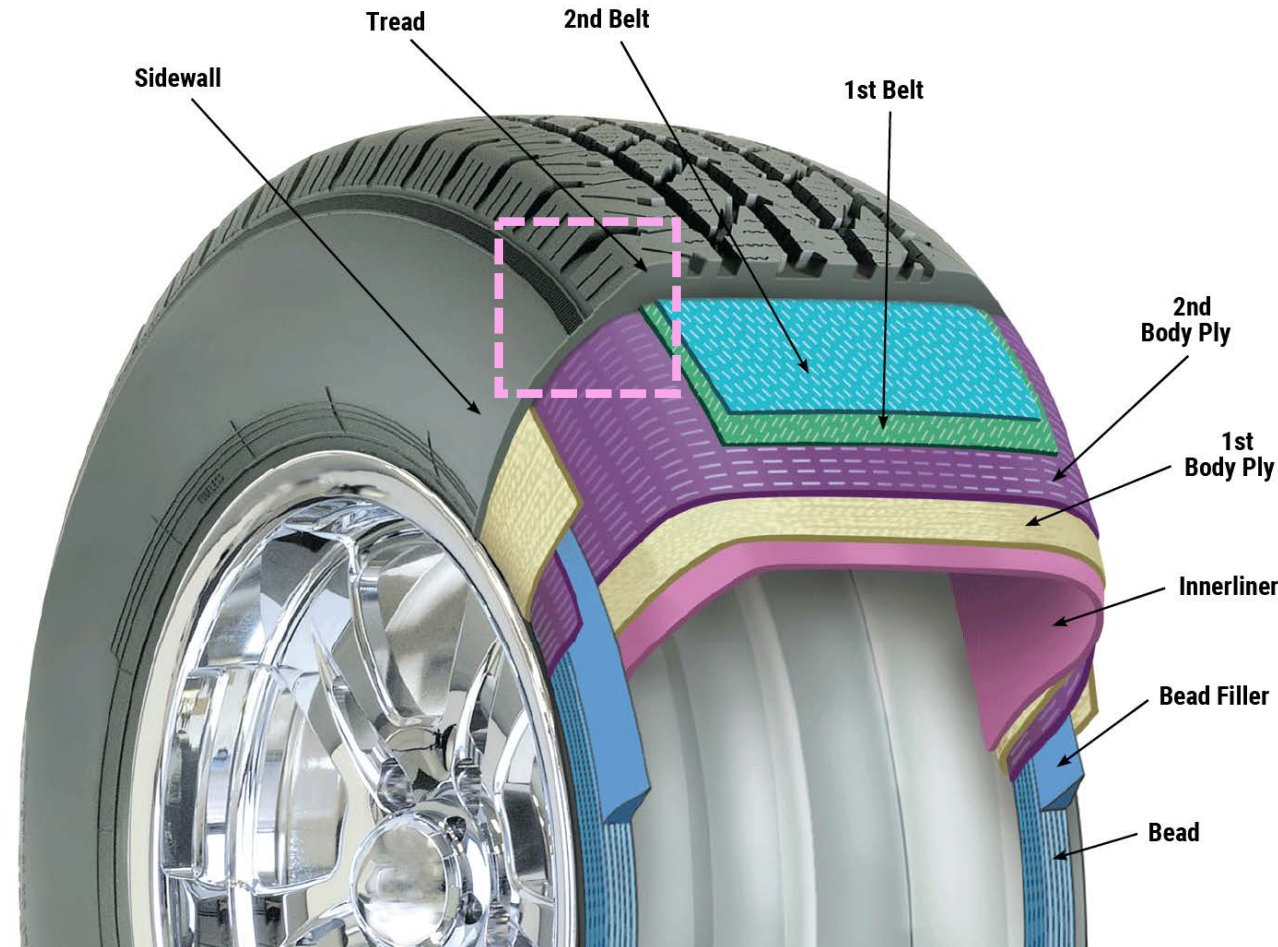


- Health and environmental safety

Disclaimer: Information presented here was gathered from a literature and web search (public sources)

Tires are complex composite structures that rely on chemistry, physics, and engineering for durability, road safety, fuel economy, etc.

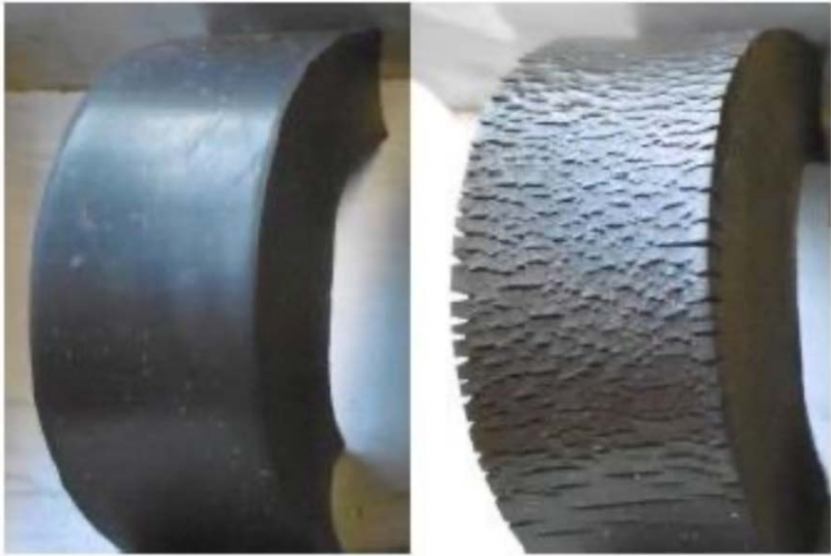
- Rubber compounds for tires have 10 to 15 ingredients
 - » Raw material substitution can lead to unintended interactions
- With exception of inner liner, all rubber compounds in tires have 0.5 to 1.5 wt.% 6PPD



6PPD in tires

with 6PPD

without 6PPD



<https://www.rubbernews.com/news/ustma-california-epa-seek-alternative-6ppd-tire-additive>

To act like 6PPD, a drop-in substitute must:

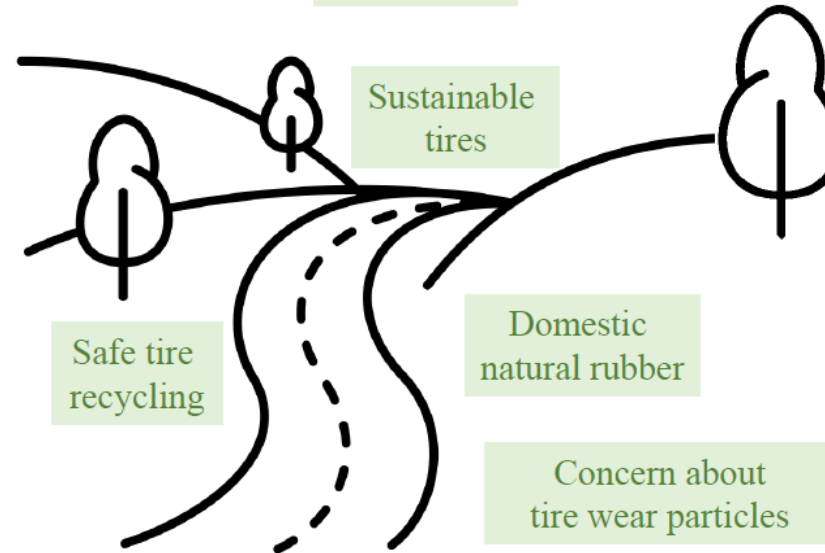
- Function as antiozonant and antioxidant to help prevent the degradation and cracking of rubber compounds (unsaturated elastomers) by protecting against ozone attack, oxidation, and heat aging
 - » Including internal rubber compounds which experience diffusion-limited oxidation (from tire air pressure) and thermal-mechanical degradation
- Protect the tire in static and dynamic loading conditions
- Undergo controlled blooming/diffusion to surfaces of sidewall and tread

- Not interfere with crosslinking chemistry (accelerated sulfur vulcanization)
- Not interfere with important bonding between rubber and tire reinforcement cords

Challenges

- Performance of alternatives (standards)
- Timeframes of designs and evolving materials
- What is “safer”
- Multiple suppliers
- ...
- This will require supply chain collaboration, government support, research, etc.

Long-term 6PPD Substitutes will have to align with other tire industry **macro-trends**



Necessary transformations to achieve safe and sustainable chemistry

Change policy

- Incentives
- Regulatory
- Push/Pull

Expand Science

- Green Chemistry
- Alternatives Assessment
- NAMs and other approaches

Transform Markets

- Demand-Side
- Supply-Side

Building a Community of Practice for Alternatives Assessment

ASSOCIATION FOR THE ADVANCEMENT OF ALTERNATIVES ASSESSMENT

A new professional association solely
dedicated to advancing the science,
practice, and policy of alternatives
assessment and informed substitution

*Working collaboratively to accelerate the the use of
safer chemicals, materials, processes, and products.*

JOIN THE A4!

Find out more at www.saferalternatives.org



Thank you!

Joel Tickner, ScD

Email: Joel_tickner@uml.edu

For more information, visit:

Association for the Advancement of Alternatives Assessment (A4) | www.saferalternatives.org

Green Chemistry & Commerce Council (GC3) | www.greenchemistryandcommerce.org