Comments on the Design for the Environment (DfE) Program Alternatives Assessment Criteria for Hazard Evaluation

Table of Contents

Alaska Community Action on Toxics; The Autism Society; Capital Region Action Against Breast Cancer; Center for Health, Environment and Justice - Citizens' Environmental Coalition; and other contributing organizations 3

Albemarle Corporation; Center for Environmental and Occupational Risk Analysis and Management, College of Public Health, University of South Florida; and, Institute of Public Health and Environmental Protection (Instytut Zdrowia Publicznego i Ochrony Środwiska)..... 11

Alkylphenols & Ethoxylates Research Council (APERC) 17

American Chemistry Council (ACC)..... 36

American Cleaning Institute® (ACI)..... 44

Boeing..... 51

Chemical Producers & Distributors Association (CPDA)..... 52

Clean Production Action..... 54

The Dow Chemical Company..... 55

Environmental Health Research Foundation 61

Environmental Working Group 68

Global Automakers, Inc. 72

IBM Corporation..... 77

ICL-IP America Inc. 79

Institute of Scrap Recycling Industries, Inc. 81

Intelligent Global Pooling Systems (iGPS) 82

National Institute of Environmental Health Sciences (NIEHS) 86

National Resources Defense Council (NRDC)..... 87

North American Metal Packaging Alliance, Inc. (nampa) 92

The Proctor & Gamble Company (P&G) 94

Washington State Department of Ecology..... 98

Alaska Community Action on Toxics; The Autism Society; Capital Region Action Against Breast Cancer; Center for Health, Environment and Justice - Citizens' Environmental Coalition; and other contributing organizations

January 31, 2011

Alaska Community Action on Toxics - The Autism Society - Capital Region Action Against Breast Cancer - Center for Health, Environment and Justice - Citizens' Environmental Coalition – Citizens for A Clean Environment - Clean New York – Clean Production Action - Clean Water Action - Commonweal – Ecology Center of Michigan - The Endocrine Disruption Exchange - Environmental Health Fund - Environmental Health Strategy Center - Environmental Justice Action Group of Western NY - Great Lakes Green Chemistry Network - Great Lakes United - Greenpeace - Green Science Policy Institute - Health Care Without Harm - Healthy Building Network - Huntington Breast Cancer Action Coalition, Inc. - Institute for Health and the Environment, University at Albany - Kentucky Environmental Foundation - Mira's Movement - NY Public Interest Research Group - New York State Nurses Association - NY Lawyers for the Public Interest - Pesticide Action Network North America - Physicians for Social Responsibility - US Public Interest Research Group - Washington Toxics Coalition - WE ACT for Environmental Justice

Comments on:
Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation
Draft - November 2010
U.S. Environmental Protection Agency, Office of Pollution Prevention & Toxics

We applaud the US EPA Design for Environment Program (DfE) program for developing draft criteria for performing chemical hazard evaluations and releasing them for public review. Increasingly, companies and state government agencies are developing criteria for identifying which chemicals are safer for humans and the environment. The draft DfE AA (Alternatives Assessment) criteria for hazard evaluations, if designed appropriately, would provide important guidance to these organizations.

We wish to particularly emphasize our strong support for the inclusion of endocrine activity in the assessment. Endocrine effects are now recognized as the critical link to serious damage to human health and development from certain chemicals, and no assessment is complete without a serious assessment of the data on endocrine activity. EPA must not only keep the endocrine assessment element but strengthen it by addressing it in the table to inform the matrix decision making process.

General comments:
We have the following concerns about important elements of DfE's AA criteria:

- **Harmonization**: We agree with DfE's decision to harmonize with other existing hazard evaluation protocols and regulations including the Globally Harmonized System for the Classification and Labeling of Chemicals (GHS) and Clean Production Action's (CPA's) Green Screen for Safer Chemicals (Green Screen). In general, DfE has done a good job of harmonizing. There are some notable exceptions, however, with room for greater harmonization.
    - We suggest lists (see below) that should be added and some specific thresholds – most notably for bioaccumulation, which should be adjusted.
    - We suggest that DfE explicitly acknowledge relevant and similar chemical hazard assessment protocols, including most notably the Green Screen, which is now being used by state governments, including Maine and Washington, and the electronics sector, including HP and Apple, to evaluate chemicals and identify safer alternatives.
- **Authoritative lists**: There are some important authoritative lists which should be added to the criteria:
    - We suggest addition of California Proposition 65 LIST, NIOSH's Carcinogen list, the EU CMR list, certain EU Risk Phrases, and the NTP reports on Reproductive and Development Toxicity.
- **Endocrine activity**: Endocrine activity is too important to leave buried in the narrative and must be part of the matrix decision making process.
    - We suggest integration of endocrine activity into the summary assessment table.
- **Degradation products of concern**: It is critical to identify when a compound leads to degradation products -- be it through metabolism, environmental degradation or combustion -- that are of greater concern than the parent compound. For example, we know this can be an issue with halogenated flame retardants. An alternatives assessment that does not include an explicit degradation assessment may well result in regrettable, rather than informed, substitutions.
    - We suggest explicit integration of degradation products of concern into the AA criteria -- both the summary table and narrative – for persistence and for other health endpoints.
- **Respiratory Sensitization**: We are concerned that this assessment provides no guidance on characterization of respiratory sensitization. DfE has already established criteria for respiratory sensitization for fragrances and there are several useful authoritative lists to draw from at least as flagging lists as well.
- **Physical hazards**: GHS has developed criteria for classifying chemicals according to their physical hazards. DfE should integrate physical hazards into the assessments and include them in the hazard assessment table. They are legitimate criteria for evaluating chemical hazards, being used by others to evaluate alternatives and should be part of DfE assessments.
    - We suggest integration of physical hazards (Flammability, Reactivity and Corrosivity) s into the AA assessment criteria -- both the summary table and narrative.

Section-specific comments:

1. **Section 4.1.2, Carcinogenicity**: Add to Table 3:
   a. State of California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA) California Proposition 65 (Safe Drinking Water and Toxic Enforcement Act Of 1986) Chemicals Known to the State to Cause Cancer or Reproductive Toxicity (http://www.oehha.ca.gov/prop65/prop65_list/Newlist.html)
   b. National Institute for Occupational Safety and Health (NIOSH) Carcinogen List (http://www.cdc.gov/niosh/topics/cancer/npotocca.html)

2. **Section 4.1.4 Reproductive and Developmental Toxicity**: add Table on Authoritative Lists Used to Designate **High** Hazard for Reproductive/ Development Hazard and include:
   a. State of California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA) California Proposition 65 (Safe Drinking Water and Toxic Enforcement Act Of 1986) Chemicals Known to the State to Cause Cancer or Reproductive Toxicity (http://www.oehha.ca.gov/prop65/prop65_list/Newlist.html)
   a. EU CMR List (ECB, *Annex I of Directive 67-548-EEC*. 2007)
      - Reproduction Category 1: "known" to impair fertility in humans or cause developmental toxicity in humans"
      - Reproduction Category 2: "should be regarded as if" they impair fertility to humans or cause developmental toxicity to humans"
   a. EU Risk Phrases (ECB, *Annex I of Directive 67-548-EEC*. 2007)
      - R60 "May impair fertility"
      - R61 "May cause harm to the unborn child"
   b. US National Institutes of Health, National Institute of Environmental Health Sciences, National Toxicology Program (NTP), Center for the Evaluation of Risks to Human Reproduction. Expert Panel Reports & Monographs on Reproductive and Developmental Toxicity.
      - Clear Evidence of Adverse Effects
      - Some Evidence of Adverse Effects
      - Limited Evidence of Adverse Effects

Add Table on Authoritative Lists Used to Designate **Moderate** Hazard for Reproductive/ Development Hazard and include:

   c. US National Institutes of Health, National Institute of Environmental Health Sciences, National Toxicology Program (NTP), Center for the Evaluation of Risks to Human Reproduction. Expert Panel Reports & Monographs on Reproductive and Developmental Toxicity.
      - Limited Evidence of no Adverse Effects

Add Table on Authoritative Lists Used to Designate **Low** Hazard for Reproductive/ Development Hazard and include:

d. US National Institutes of Health, National Institute of Environmental Health Sciences, National Toxicology Program (NTP), Center for the Evaluation of Risks to Human Reproduction. Expert Panel Reports & Monographs on Reproductive and Developmental Toxicity.
   - Some Evidence of no Adverse Effects
   - Clear Evidence of no Adverse Effects

2. **Section 4.1.5 Neurotoxicity:** We agree with DfE's decision to include neurotoxicity in the summary table.

3. **Section 4.17 Respiratory and Skin Sensitization:** Add Table on Authoritative Lists Used to Designate **High** Hazard for Respiratory and Skin Sensitization
   a. EU Risk Phrases (ECB, Annex I of Directive 67-548-EEC. 2007)
      - R42 "May cause sensitization by inhalation"
      - R43 "May cause sensitization by skin contact"
   b. MAK Commission of Germany; Occupational Toxicants and MAK Values: Annual Thresholds and Classifications for the Workplace
      - Sensitizing Substances Sh (Skin)
      - Sensitizing Substances Sa (Respiratory)
      - Sensitizing Substances Sah
      - Sensitizing Substances SP

   Add Table on Authoritative Lists Used to Designate **Medium** Hazard for Respiratory and Skin Sensitization
   c. Association of Occupational and Environmental Clinics (AOEC) Exposure Code List
      - Asthmagen Rs
      - Asthmagen Rr

   Table 14 - Create guidelines for how qualitative assessment for Respiratory Sensitization will be done for chemicals not on the authoritative lists

4. **Section 4.1.9 Endocrine Activity**
   a. Endocrine activity must be part of the hazard assessment table and should be assigned a level of concern. The present decision to assign endocrine activity to the narrative and to exclude it from the hazard assessment table downplays the potential significant adverse effects of endocrine active chemicals.
   b. At a minimum, the current proposed criteria should be included in the hazard assessment table as:
      - "P" (potential for adverse endocrine activity) - If data show evidence of endocrine activity then the chemical will be designated as potentially endocrine active (while providing details in the narrative).
      - "ND" - no data available to evaluate this endpoint, endocrine activity is unknown, untested

- "Low" or "NE" (no evidence) - If data conclude no evidence of activity (no binding, perturbation, or evidence of endocrine-related adverse effects) then the chemical will be designated as having no evidence of endocrine activity.

5. **Section 4.2.2 Degradation Products of Concern**
   a. Create a protocol for evaluation of degradation products. This protocol should include criteria for defining when a degradation product is a chemical of concern, how that affects the Persistence Designation and how to handle that in other endpoint criteria.
      - We propose that a degradation chemical is a chemical of concern if it has been met the moderate, high or very high criteria in any one endpoint
      - Establish a Breakdown Persistence Designation and include it I the table and narrative. Add the half life of any designated chemical in any other category within the AA be added to the half life of the parent product to determine a Breakdown Persistence Designation.
      - Indicate in both the summary table and the narrative the Designation level for breakdown products under the Designation for each endpoint, such as carcinogenicity, to which the breakdown product applies and for which the Breakdown Designation is higher than the parent products Designation.
   b. Table 14 - Create guidelines for how qualitative assessment for Persistence in air will be done

6. **Section 4.2.3 - Bioaccumulation**
   a. Adjust "Very High" down from BCF/BAF >100,000 to BCF/BAF >5,000
      - This is consistent with very high bioaccumulation definitions of the EU and Stockholm Convention on Persistent Organic Pollutants
        1. EU defines very bioaccumulative as BCF > 5,000
        2. Stockholm Convention defines very bioaccumulative as BCF/BAF > 5,000
      - DfE's new definition of very high as BCF/BAF > 100,000 is wildly out of alignment with existing criteria for very high.
   b. Adjust "High" accordingly to be BCF/BAF 5,000-1,000

Mark S. Rossi, PhD
Research Director
Clean Production Action

Tom Lent
Policy Director
Healthy Building Network

Kathleen A. Curtis, LPN
Policy Director
Clean New York

Lynn Thorp
National Campaigns Coordinator
Clean Water Action

Lois Gibbs, Executive Director
Mike Schade, Campaign Coordinator
Center for Health, Environment and Justice

Judith Robinson
Associate Director
Environmental Health Fund

Judith Anderson
Executive Director
Environmental Justice Action Group of WNY

Christine Brouwer
Co-Founder & Executive Director
Mira's Movement

Karl A. Tupper
Staff Scientist
Pesticide Action Network North America

Rick Hind
Legislative Director
Greenpeace

David O. Carpenter, M.D.
Director, Institute for Health and the Environment
University at Albany

Arlene Blum PhD
Executive Director
Green Science Policy Institute

Mike Belliveau
Executive Director
Environmental Health Strategy Center

Margaret Byrne, MS
Northampton, MA

Thomas J. Lowe, RN, MPH, COHN-S
Health and Safety Representative
New York State Nurses Association

Derek Stack
Executive Director
Great Lakes United

Barbara J. Warren
Executive Director
Citizens' Environmental Coalition

Cecil Corbin-Mark
Deputy Director and Director of Policy Initiatives
WE ACT for Environmental Justice

Sharyle Patton
Director, Health and Environment Program
Commonweal

Lin Kaatz Chary, PhD, MPH
Executive Director
Great Lakes Green Chemistry Network

Kristen Welker-Hood, ScD MSN
Director, Environment and Health
Physicians for Social Responsibility

Karen Joy Miller
President
Huntington Breast Cancer Action Coalition, Inc.

Miranda Massie
Litigation Director
NY Lawyers for the Public Interest

Elizabeth Hitchcock
Public Health Advocate
US Public Interest Research Group

Jeff Sell
Vice President Public Policy
Autism Society

Tracey Easthope, MPH
Director, Environmental Health Project
The Ecology Center of Michigan

Russ Haven
Legislative Counsel
New York Public Interest Research Group (NYPIRG)

Joan Sheehan, President
Margaret Roberts, Program Coordinator
Capital Region Action Against Breast Cancer (CRAAB!)

Elizabeth Crowe
Executive Director
Kentucky Environmental Foundation

Cynthia Wilson
Projects Coordinator
Citizens for a Clean Environment, Inc.

Theo Colborn, PhD
President
The Endocrine Disruption Exchange

Gary Cohen
President
Health Care Without Harm

Laurie Valeriano
Policy Director
Washington Community Action on Toxics

Pamela Miller
Executive Director
Alaska Community Action on Toxics

Albemarle Corporation; Center for Environmental and Occupational Risk Analysis and Management, College of Public Health, University of South Florida; and, Institute of Public Health and Environmental Protection (Instytut Zdrowia Publicznego i Ochrony Środwiska)

January 31, 2011

Date: 31 January 2011

Subject: Comments on the U.S. EPA's "Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation, Draft, November 2010"

Dear Ms. Sommer,

We appreciate the opportunity to comment on the Design for the Environment (DfE) program's draft document titled "Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation."[1]

We support the comments submitted by the American Chemistry Council. Therefore, as discussed in Appendix 1, our comments are limited to sections "4.2.2. Environmental Persistence"[2] and "4.2.3. Bioaccumulation."[3]

In closing, we appreciate the opportunity to provide comments and additional information on this important draft document.

Respectfully yours,

[1] EPA (2010). *Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation [Draft, November 2010]*, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 35 pp.
[2] *Id.* at p. 18.
[3] *Id.* at pp. 18-19.

Marek Banasik, M.D., Ph.D.
Director & Medical Scientist
Institute of Public Health and
Environmental Protection
(Instytut Zdrowia Publicznego i
Ochrony Środowiska)
Warsaw, Poland

Todd Stedeford, Ph.D., J.D., DABT
Toxicology Advisor & In-house Counsel
Health, Safety & Environment
Albemarle Corporation
Baton Rouge, Louisiana, U.S.A.

Raymond D. Harbison, Ph.D., ATS
Professor & Director
Center for Environmental and
Occupational Risk Analysis and
Management
College of Public Health
University of South Florida
Tampa, Florida, U.S.A.

Appendix 1

Comments on 4.2.2. Environmental Persistence

The DfE document states that "[i]n the absence of measured data on the substance of interest, DfE will evaluate data for suitable analogs and estimated values from models such as EPI Suite or SPARC [reference omitted]."[4] Specific criteria are listed,[5] which are suitable for estimates generated by EPI Suite (*e.g.*, Biowin v4.10 and Level III Fugacity Model). However, no criteria are provided for using and interpreting other data or estimates, which may be used to inform persistence (*e.g.*, logarithmic values for *n*-octanol:water partition coefficients [$\log K_{OW}$] or organic-carbon:water partition coefficients [$\log K_{OC}$]).

Under the European Commission's chemical control law known as REACH (*i.e.*, Registration, Evaluation, Authorisation and Restriction of Chemicals), the European Chemicals Agency (ECHA) issued guidance that applies specific values for interpreting $\log K_{OW}$ and $\log K_{OC}$. For example, a substance with $\log K_{OW}$ greater than 5 or $\log K_{OC}$ greater than 4 is expected to exhibit strong binding behavior to soil.[6] Since highly sorptive substances are less bioavailable to microorganisms and are 'shielded' to some extent from abiotic degradation processes (*e.g.*, hydrolysis or photodegradation), these types of substances are expected to have longer residence times in the environment.[7] Therefore, because $\log K_{OW}$ and $\log K_{OC}$ may be used in a weight-of-evidence approach to inform persistence, we recommend including criteria for these measures.

In addition to the foregoing comments, we also note that the persistence criteria seem to designate as undesirable, substances that are of 'moderate' to 'very high' persistence. Though this may be an appropriate default for small molecules, it is inappropriate for specific types of polymers. For example, the U.S. Environmental Protection Agency (EPA) stated the following in its polymer exemption guidance:

> "A polymer is not eligible to be manufactured under the new exemption rule if the polymer is designed or reasonably anticipated to substantially degrade, decompose, or depolymerize, including those polymers that could substantially decompose after manufacture and use, even though they are not actually intended to do so."[8]

Under the above requirement, the U.S. EPA defined 'degradation,' 'decomposition,' or 'depolymerization' as:

> "[A] type of chemical change in which a polymeric substance breaks down into simpler, smaller weight substances as the result of (for example) oxidation, hydrolysis, heat, sunlight, attack by solvents or microbial action."[9]

---

[4] *Id.* at p. 18.
[5] *Id.* (*See* Table 14. Criteria for Persistence Designations).
[6] ECHA (2008a). *Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint Specific Guidance*, GUIDANCE FOR THE IMPLEMENTATION OF REACH, 431 pp., at p. 155.
[7] *Id.*
[8] EPA (1997). *Polymer Exemption Guidance Manual*, EPA 744-B-97-001, Office of Pollution, Prevention and Toxics, U.S. Environmental Protection Agency, 54 pp., at p. 9.
[9] *Id.*

The U.S. EPA's polymer exemption guidance identifies those properties for polymers, including persistence, which are "...unlikely to present unreasonable risks [of injury to human health or the environment]."[10] Therefore, the DfE criteria should recognize persistence in a favorable light for those substances meeting the U.S. EPA's criteria for polymers of low concern.

Comments on 4.2.3. Bioaccumulation

The DfE document lists criteria for bioaccumulation and includes specific thresholds for use with data or estimates on bioconcentration factors (BCFs) or bioaccumulation factors (BAFs).[11] It states that the criteria were: "...derived from OPPT's New Chemicals Program [citation omitted], and Arnot & Gobas 2006 [citation omitted]."[12] The Arnot-Gobas BAF-QSAR was incorporated into EPI Suite v4.00 (*see* BCFBAF v3.00).[13]

The Arnot-Gobus BAF-QSAR is based on the following assumptions:

> "The BAF-QSAR therefore identifies sorption in the water phase as the main reason why the BAF decreases with increasing K_{OW} for these high K_{OW} chemicals. The decline is not due to a lack of biomagnification or steric factors affecting membrane permeation. The overriding influence of sorption in the water can therefore cause the BAF to fall to low numbers (e.g. less than 5 000) while the substance may still have a significant potential to biomagnify in the food web."[14]

These assumptions are, however, in stark contradiction to well-established molecular size and shape measures that affect membrane permeation. For example, the ECHA use the following information on molecular size and weight data for determining a molecule's potential to bioaccumulate:

> "If [the maximum molecular length of a substance] exceeds 4.3 nm, it is assumed that the substance disturbs the entire interior structure of the lipid bilayer of cell membranes and therefore does not accumulate to a significant amount, i.e., has a BCF value lower than 2000 L/kg."[15]

> "From a diverse set of chemicals it appeared that for compounds with a Dmaxaver [average maximum diameter] larger than 1.7 nm the BCF value was less than 5000 L/kg."[16]

---

[10] *Id.*at p. 2.
[11] EPA (2010), *supra* note 1, at p. 18.
[12] *Id.*
[13] *Id.* at p. 19. (*Note*: the DfE document recommends using the EPI Suite BCFBAF model, which is based on Arnot and Gobas (2003), *infra* note 14).
[14] Arnot and Gobas (2003). *A Generic QSAR for Assessing the Bioaccumulation Potential of Organic Chemicals in Aquatic Food Webs*, QSAR COMB SCI, Vol. 22, pp. 337-345, at p. 342.
[15] ECHA (2008b). *Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11: PBT Assessment*, GUIDANCE FOR THE IMPLEMENTATION OF REACH, pp. 1-97, at p. 27.
[16] *Id.*

> "A molecular weight higher than 1100 g/mol is an indicator that the aquatic BCF of the respective substance is lower than 2000 L/kg. If the substance has a molecular weight higher than 700 g/Mol this is an indicator that the BCF is below 5000 L/kg."[17]

Further, Burreau *et al*. (2004) reported experimental biomagnification data on polybrominated diphenyl ethers (PBDEs). In contrast to the assumptions employed in the Arnot-Gobas BAF-QSAR, Burrea *et al*. (2004) found that the biomagnification potential was decreased for PBDEs with six or more bromines and concluded that it was not hydrophobicity, but rather the molecular size and/or weight that restricted biomagnification.[18]

We also note that the Arnot-Gobas BAF-QSAR:

> "...[I]dentifies chemicals with a log K_{OW} greater than approximately 4.0 and less than approximately 12.2 that are not being metabolized at a significant rate to exhibit BAFs larger than 5 000 in upper trophic level fish species and to have a bioaccumulation potential in aquatic food webs."[19]

Though not specific to BAFs, the REACH guidance on logK_{OW} states the following about its relationship to BCFs: "[f]or the PBT and vPvB assessment a screening criterion has been established, which is log K_{OW} greater than 4.5...At log K_{OW} values between 4 and 5, log BCF increases linearly with log K_{ow}. This linear relationship is the basis for the B screening criterion of log K_{OW} > 4.5."[20] The guidance further clarifies, "[h]owever, at very high log K_{OW} (>6), a decreasing relationship between the two parameters is observed...The aquatic BCF of a substance is probably lower than 2000 L/kg [i.e., the Annex XIII cutoff[21]] if the calculated log K_{OW} is higher than 10."[22,23]

---

[17] *Id.*

[18] Burreau et al. (2004). *Biomagnification of Polychlorinated Biphenyls (PCBs) and Polybrominated Diphenyl Ethers (PBDEs) Studied in Pike (Esox lucius), Perch (Perca fluviatilis) and Roach (Rutilus rutilus) from the Baltic Sea*, CHEMOSPHERE, Vol. 55, pp. 1043-1052, at p. 1049.

[19] Arnot and Gobas (2003), *supra* note 14, at p. 343.

[20] ECHA (2008b), *supra* note 15, at p. 28.

[21] EC (2006). REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, at p. 124.

[22] ECHA (2008b), *supra* note 15, at p. 28.

[23] *See also*: the former European Chemicals Bureau considered substances with a log KOW < 4.5 or > 9 to have a BCF < 2,000 L/kg. A biomagnification factor of 1 was applied to these substances. In contrast, substances with a log KOW between 5 to 8 were considered to have a BCF > 5,000 L/kg. For these very bioaccumulative substances, a BMF of 10 was applied. ECB (2003). *Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances, Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market*, Technical Guidance Document (TGD), Part II, EUR 20418 EN/2, 328 pp., at p. 128 (Table 21 Default BMF values for organic substances).

Finally, the ECHA guidance on assessing the bioaccumulative potential of chemicals states: "[i]f the substance is not taken up by mammals, or if only trace amounts of the substance were incorporated, then it is also likely that the substance will not easily pass across fish gill membranes and therefore may not have a high bioconcentration factor (BCF) in fish."[24]

In conclusion, we recommend that DfE reconsider the use of Arnot and Gobas (2006)[25] as part of its criteria for evaluating bioaccumulation. The assumptions employed in Arnot and Gobas (2006) are based on those specified in their 2003 study. As noted above, these assumptions contradict more recent evaluations of the influence of molecular size, shape, and logKOW on the potential of substances to bioaccumulate. We also recommend that the DfE utilize data from mammalian studies, which may be used to inform the potential for a substance to bioaccumulate.

[24] ECHA (2008b), *supra* note 15, at p. 26.

[25] Arnot and Gobas (2006). *A Review of Bioconcentration Factor (BCF) and Bioaccumulation Factor (BAF) Assessments for Organic Chemicals in Aquatic Organisms*, ENVIRON REV, Vol. 14, pp. 257-297.

ALKYLPHENOLS & ETHOXYLATES RESEARCH COUNCIL COMMENTS ON US EPA DESIGN FOR ENVIRONMENT PROGRAM DRAFT ALTERNATIVES ASSESSMENT CRITERIA FOR HAZARD EVALUATION (NOVEMBER 30, 2010)

JANUARY 31, 2011

1.0 INTRODUCTION

The Alkylphenols & Ethoxylates Research Council (APERC) respectfully provides the following comments on the US EPA Office of Pollution Prevention and Toxics (OPPT), Design for the Environment (DfE) Program Draft Alternatives Assessment Criteria for Hazard Evaluation (November 2010). [1] The DfE website indicates that chemicals for which EPA has developed Chemical Action Plans (CAPs) currently "are the primary source for identifying chemical candidates for risk management and specifying actions EPA proposes to further evaluate the chemicals and address risks" and further notes "alternatives assessments are one of the risk management approaches that may be specified". The draft Alternatives Assessment (AA) Criteria document indicates that the criteria will be applied during upcoming DfE Alternative Assessments and that "lessons learned" during those assessments will be incorporated into a finalized version of the criteria. [2] Also, EPA announced in a press release on November 30, 2010 that an Alternative Assessment process will begin for nonylphenol ethoxylates (NPEs) in 2011. APERC membership is comprised of suppliers and manufacturers of alkylphenols (APs) and their ethoxylates (APEs), including NPEs; as such APERC has great interest in both the basis for the DfE Alternative Assessment program and the Alternative Criteria.[3]

For more than twenty years APERC and its member companies have been actively engaged in the conduct and review of toxicological and environmental fate and effects research on NPEs and their environmental degradation intermediates; consequently, APERC can contribute considerable information and expertise relevant to the environmental and toxicological assessment of these substances. Based on APERC's review of the data for NPEs and their degradation intermediates, including nonylphenol (NP), the scientific weight-of-evidence continues to support their safety to the workers and consumers that use them in formulated products as well as to the environment in their current uses and exposure levels. As such, APERC has great concerns about the fact that DfE plans to embark on an Alternatives Assessment for NPEs that is intended to have a regulatory impact when these compounds have

[1] US EPA Office of Pollution Prevention and Toxics, Design for the Environment Program (US EPA, DfE). (2010, November). Alternatives Assessment Criteria for Hazard Evaluation," Available at http://www.epa.gov/dfe/alternatives_assessment_criteria_hazard_eval_nov2010_final_draft2.pdf. .
[2] US EPA Press Office (2010, November 30). News Release (HQ): EPA Announces New Tool to Promote Safer Chemicals and Products.
[3] Current members of the Alkylphenols & Ethoxylates Research Council include: Dover Chemical Corporation; SI Group; TPC Group; and The Dow Chemical Company.

not been demonstrated to pose a risk to human health or the environment or to be "chemicals of concern".

APERC questions the need to launch yet another Design for the Environment (DfE) initiative aimed at assessing alternatives without proving a quantitative and clear basis for the human health and/or environmental benefit expected from such a program. With regard to NPEs, the Agency should assess whether there is a need for a new Alternatives Assessment program on these compounds in light of the fact that other DfE-sponsored programs such as the Formulators Initiative, the Safer Detergent Stewardship Initiative and the CleanGredients Database already exist to accomplish the purpose of comparing and promoting the use of "safer" surfactants.

The following comments address APERC's concerns and suggestions with the DfE Alternatives Assessment program, process and draft criteria.

2.0 COMMENTS ON THE PROCESS AND APPROACH TAKEN TO DEVELOP THE CRITERIA

APERC offers the following comments regarding the process and general approach being used to develop the AA criteria.

2.1 The current draft Alternatives Assessment (AA) criteria should not be used to assess alternatives to any chemicals until EPA applies the standards of the Administrative Procedure Act (APA) to solicit and consider public comment on the criteria.

The DfE website indicates that chemicals for which EPA has developed CAPs currently "are the primary source for identifying chemical candidates for risk management and specifying actions EPA proposes to further evaluate the chemicals and address risks" and further notes "alternative assessments are one of the risk management approaches that may be specified". The draft AA Criteria document indicates that the criteria will be applied during upcoming DfE Alternative Assessments and that "lessons learned" during those assessments will be incorporated into a finalized version of the criteria. [4] Specifically, EPA announced in a press release on November 30, 2010 that an AA process will begin for nonylphenol ethoxylates (NPEs) and several other CAP chemicals in 2011.

Considering this, it is reasonable to conclude that the results of DfE Alternative Assessments will ultimately be used or referenced by other EPA programs, federal agency programs and by state and local legislation and regulations related to chemicals and/or environmentally preferable purchasing standards. Thus the impact of both the AA Criteria and the recommendations arising from specific chemical AAs will be very broad in scope with wide regulatory and market implications. Therefore, EPA should meet the standards for providing public notice and opportunity to comment on all aspects of both the development of the AA Criteria and the application of the Criteria within the DfE's Alternatives Assessments Program as well as within EPA's broader risk-management decision making process. There should, at a minimum, be an

[4] US EPA. (2010, November 30). News Release (HQ): EPA Announces New Tool to Promote Safer Chemicals and Products.

official notice in the Federal Register of the availability of the draft AA Criteria documents and related assessment programs with appropriate comment periods, as well as EPA's consideration of and a response to comments that are received.

2.2 DfE should establish criteria - based on risk - for what constitutes a "chemical of concern" before embarking on an assessment of alternatives for any specific chemical.

APERC supports the stated purpose of the AA Criteria, which is to reduce the likelihood of unintended consequences that might result if poorly understood alternatives are chosen to replace "chemicals of concern". However, EPA should establish risk-based criteria for "chemicals of concern" and determine that a specific compound actually meets those criteria before embarking on initiatives to establish alternatives. This is particularly of concern since, as noted above, the identification of "chemicals of concern" and any alternatives under a DfE Alternatives Assessment will likely form the basis for decision-making by other governmental organizations, non-governmental organizations and in the marketplace generally.

EPA Administrator Lisa Jackson announced that one of the Administration's core principles to strengthen chemical management is that "chemicals should be reviewed against safety standards that are based on sound science and reflect risk-based criteria protective of human health and the environment". [5] [6] APERC supports this principal as risk, which considers chemical hazards and exposure, provides the best mechanism to identify and prioritize chemicals of concern. EPA has not established any need based on risk for either a CAP or an AA for NPEs. APERC recommends that before launching a new Design for the Environment (DfE) initiative aimed at assessing alternatives, EPA should clearly articulate the human health and/or environmental benefit expected from such a program. With regard to NPEs, the Agency should assess whether there is a need for a new AA on these compounds in light of the fact that other DfE sponsored programs such as the Formulators Initiative, the Safer Detergent Stewardship Initiative and the CleanGredients Database already exist to accomplish the purpose of encouraging the use of safer surfactants.

2.3 The AA Criteria document should clarify that hazard assessment is only one step in the AA process; hazard-based criteria do not provide an adequate basis to ensure that decision making about alternatives will result in the selection of alternatives that are actually safer in use.

2.3.1 The AA criteria do not explain adequately that hazard evaluation is only one step in the alternatives assessment process

The AA criteria do not explain that hazard evaluation is only one step in the alternatives assessment process. Risk assessment, economic and social impact evaluations, and cost and

[5] US EPA Press Office (2009, September 29). Press Release: EPA Administrator Jackson Unveils New Administration Framework for Chemical Management Reform in the United States
[6] US EPA. (2009) Essential Principles for Reform of Chemicals Management Legislation. Accessed at http://www.epa.gov/oppt/existingchemicals/pubs/principles.html

efficacy are other steps in the AA process that should also be referenced in the AA Criteria document. DfE has acknowledged that the criteria may well be used by governments, industry and non-governmental organizations. Without further clarification in the document itself, the AA Criteria may suggest EPA supports hazard-based decision-making. A hazard-based approach is inconsistent with EPA's statutory responsibility under the Toxic Substances Control Act (TSCA), as well as EPA's priority to include risk assessment its principles for chemical management.[7]

2.3.2 Hazard-based criteria do not provide an adequate basis to ensure that decision making about alternatives will result in the selection of alternatives that are actually safer in use.

The Criteria do not take into account important physical chemistry properties such as molecular weight, vapor pressure, exposure in use, dermal absorption or the actual use concentrations of the alternative needed in a product to attain a similar efficacy. Based on the draft AA Criteria, it is possible that "safer" alternative chemicals could be identified by the described process based entirely on the hazard of the pure alternative compound, while in fact posing a greater risk due to higher concentration in formulated products, increase use of product to achieve similar efficacy, and increased exposure potential and risk profile. The AA Criteria also do not consider whether there might be changes in characteristics (e.g., pH, irritation, acute toxicity) of either the alternative or the reformulated product due to interactions with other ingredients. This would be of particular concern for alternatives that are based on different chemistries than the original chemical of concern.

EPA may plan to rely on the AA stakeholder process to develop chemical-specific determinations about how to rank the collective hazard of alternatives or alternately how to identify the endpoints of greatest concern. However, the AA Criteria document will stand as an authoritative reference separate from any chemical specific assessments. Without guidance for how to determine the end points of primary concern, or the overall risk of a compound of concern, it would seem that the primary goal of the AA Criteria – to inform substitution to safer alternatives – will not be addressed. The use of risk-based criteria would resolve this issue.

2.4 The AA Criteria should provide guidance on how to determine the most important characteristics and/or the collective hazard of alternatives versus the compound of concern.

In its discussion about the conduct of a hazard assessment, the DfE AA website states "*the most instructive endpoints are those that reveal differences in toxicity among alternatives; these endpoints make it possible to distinguish the inherently safer chemicals from the less safe.*"[8]

[7] US EPA, (September, 2009).
[8] U.S. EPA, Design for Environment Program (US EPA, DfE) (2010). Alternatives Assessment website http://www.epa.gov/dfe/alternative_assessments.html Accessed January 30, 2011.

However, the draft AA Criteria do not provide sufficient explanation as to determine "real differences" between the chemical of concern, or among alternatives. DfE should provide additional guidance about how to determine relative hazard (or safety) of one compound versus another.

The draft AA Criteria notes that the intent of the DfE AA process is to utilize hazard-based criteria to place chemicals on a "continuum of relative hazard" to inform alternative selection with alternatives being categorized as either "High", "Moderate", or "Low" concern. While this concept may be useful in comparing the relative hazard of a particular effect or endpoint, the Agency needs to clarify how one would utilize these criteria to rank the collective hazards of one alternative versus another or, more importantly, the improved safety (or risk reduction) associated with a particular alternative. For instance, in comparing two compounds, is a ranking of "Very High" Acute Toxicity more important than "High" Carcinogenicity? Does a ranking of "Low" for reproductive and developmental effects based on multi-generational rat studies carry more weight than a ranking of "potentially endocrine active" on the basis of an *in vitro* estrogenic screening test since the former study type is higher on the data hierarchy?

2.5 EPA should clarify how the AA process and criteria will be applied to specific substances still under consideration by the Agency for further risk assessment and/or regulatory notice and comment (i.e. CAP chemicals) as well as how "lessons learned" will be incorporated.

APERC is particularly concerned that, without further clarification, DfE's announced intention to utilize the Criteria to conduct alternatives assessments for CAP chemicals could result in the perception that potential alternatives to CAP substances could be identified solely based on hazard. It is APERC's view that this approach would undermine the risk basis for decision-making under the Toxic Substances Control Act (TSCA); EPA's plan to conduct AAs on CAP chemicals before they have been subject to risk assessment under TSCA could be viewed as circumventing the regulatory constraints imposed by TSCA and the Administrative Procedures Act (including notice and comment rulemaking). This could result in the DfE utilizing Agency and stakeholder resources to conduct alternative assessments on compounds that do not in fact represent a risk in the United States. It could allow the DfE to make a representation that the use of one substance is preferred over another based solely on hazard profile; such a representation by EPA will convey a regulatory overtone to the market.

Therefore, EPA should clarify how the AA process and criteria will be applied to specific substances still under consideration by the Agency for further risk assessment and/or regulatory notice and comment (i.e. CAP chemicals) as well as how "lessons learned" from these assessments will be applied.

APERC also seeks clarification about the meaning and impact of the statement in the AA Criteria document that "*(l)essons learned from the application of the criteria during those assessments will be incorporated into a finalized version*".

2.6 The AA criteria process places too much weight on the hazard-based assessment and does not reflect the realities of chemical substitution; DfE should provide guidance on conducting an Economic and Lifecycle Assessment – and all other steps in the AA process – to ensure that the goal of informed substitution is accomplished and that the alternatives that the Agency will be promoting de facto in the market place will have no unintended consequences.

The DfE website on Alternative Assessments [9] includes a brief description of the key steps to conducting an AA, including Step 6, "Apply Economic and Life Cycle Context". However, the description of Step 6 is quite broad in its coverage. The agency should prepare guidance on this step – and all other steps in the alternatives assessment process – for public notice and comment to ensure that no step is given disproportionate or undue weight and so that all characteristics of the goal of *informed substitution* may be satisfied.

2.6.1 The AA criteria process places too much weight on the hazard-based comparison of alternatives relative to a chemical of concern and other alternatives and does not reflect the realities of chemical substitution.

The AA Criteria document clearly indicates that EPA intends to rely disproportionately on hazard-based criteria when evaluating safety potential alternatives. This approach presumes that most alternative chemicals are "drop-in" substitutes; however, the realities of substitution are much more complex and "drop-in" substitution is very rare. In some cases, substitution involves reformulation with a greater amount of a replacement ingredient. More often, more than one ingredient – a replacement package – is required to achieve similar technical performance.

2.6.2 The draft AA Criteria does not consider broader sustainability issues when evaluating chemicals of concern and their potential alternatives for the same uses.

The hazard-focus proposed for the DfE AA Criteria also fails to consider other significant factors which influence the health and environmental impacts associated with a product. For many products, such as detergents and cleaning products, changes in certain components often can have significant impacts on the energy and water consumption characteristics associated with the use of the products. Therefore, for an AA to effectively consider the potential human and environmental impacts of an alternative, consideration must be given to all phases of the product's lifecycle to significantly improve the sustainability profile of a particular product. Minor changes in the formulation of a high volume product can result in significant and unintended impacts on health and the environment. If the AA process fails to adequately take into account non-hazard based factors, such as the compatibility of alternative ingredients with the current and next-generation equipment that is designed to be less energy- and water-consumptive, then energy and water efficiency improvements might not be achieved and other unintended consequences are likely to result.

[9] US EPA. DfE (2010)/

There is also no consideration given to the life-cycle impact of the alternative versus the chemical of concern in the AA Criteria. What impact do the intermediates, manufacturing process, and/or waste stream of the replacement have relative to the than the chemical being replaced? It could be that the process involved in the manufacture of the replacement makes the replacement less a friend to the environment than the chemical being replaced.

EPA's AA criteria should require information about an ingredient's concentration in products and/or exposure in use to inform a hazard in use assessment. The hazard assessment should also be applied to all ingredients in a substitution package. The assessment process should also more fully assess a product's entire lifecycle and consider the health and environmental impacts of substituting alternative chemistries across the entirety of the product's lifecycle.

2.7 The AA Criteria Lack Harmonization with Other National and International Hazard Classification Systems

2.7.1 DfE should harmonize with the GHS System.

It appears that some of the draft DfE criteria for some endpoints are consistent with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS)[10] while – for no apparent reason – others are not. As the Agency is aware, the GHS is a system for standardizing and harmonizing the classification and labeling of chemicals. Among other things it contains a comprehensive approach to:

- Defining health, physical and environmental hazards of chemicals; and,
- Creating classification processes that use available data on chemicals for comparison with the defined hazard criteria.

The GHS classifications are the result of significant effort at the international level with input from the International Labor Organization (ILO), Organization for Economic Cooperation and Development (OECD), and other governmental and non-governmental stakeholders. In fact, EPA played a significant part in the GHS development process.

The European Union is already implementing the GHS. In the US, the Occupational Safety and Health Administration (OSHA) is responsible for implementing the GHS system for workplace use in the United States and has issued proposed regulations to modify its existing Hazard Communication Standard (HCS) to conform with the GHS.[11] The proposed modifications to the standard include revised criteria for classification of chemical hazards.

Considering the tremendous effort that went into developing the GHS as well as the efforts of OSHA to implement GHS, the justification for DfE to set out to develop yet another classification scheme seems questionable. However, assuming that DfE proceeds, consistency

[10] United Nations Economic Commission for Europe.(2008). Globally Harmonized System of Classification and Labelling of Chemicals (GHS) http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html. Accessed January 30, 2011.

[11] U.S. Department of Labor, Occupational Safety and Health Administration (OSHA). (2009). Fact Sheet on aligning the hazard communication program with GHS requirements. Accessed at http://www.osha.gov/as/opa/facts-hcs-ghs.html.

with GHS will make the assessment of chemical hazards much more efficient than having to apply hazard assessment criteria that are unique to DfE. It should be noted that the GHS hazard criteria for mixtures for a number of chronic or target-organ toxicity criteria include both a dose-response value and a product concentration value in deriving the particular classification. The AA criteria should also include a product concentration trigger in order to be consistent with the GHS criteria.

Consistent criteria will also reduce the potential for misapplication and confusion on the part of those applying the criteria in alternatives assessments.

2.7.2 DfE Should Remove the Endocrine Criterion from the AA criteria as it is untested.

The Endocrine Activity criterion described in the draft AA criteria (Section 4.1.9) has not been used previously in government assessment programs in the United States. EPA's Endocrine Disruptor Screening and Testing Program (EDSTP), which is developing and validating methods for testing and defining potential endocrine effects, is still underway. By making use of the established screening level endocrine criterion now, as part of the DfE AA Program, EPA will be establishing a precedent that suggests screening-level information is considered to be definitive and generally acceptable and reliable in the scientific community. More definitive testing for adverse effects of potential endocrine active substances are currently under development, therefore in the absence of finalized testing for endocrine disruption it is premature to use this criteria in an alternatives assessment.

Until such time as there is general agreement in the scientific community and sufficient opportunity for public comment on the appropriateness of this criterion it should be eliminated from the DfE Alternatives Assessment Criteria.

Additional comment regarding this criterion is provided in the comments about the AA Criteria provided below.

2.8 The DfE AA Criteria document does not address whether and how the DfE AA Criteria will be finalized; nor does it address whether and how the Criteria can be modified.

DfE has stated that "lessons learned" from the application of these draft Criteria to certain chemicals will be applied to revise the draft AA Criteria. DfE should clarify how and when this will occur. DfE should also clarify how changes to the AA Criteria and its sources (e.g. the GHS criteria) will be considered and/or incorporated on an ongoing basis. Since the AA Criteria were developed based on other criteria, some of which are undergoing revisions, will EPA's alternative recommendations change based on changes to the AA criteria over time?

3.0 COMMENTS ON THE GENERAL REQUIREMENTS AND TERMS IN THE AA CRITERIA

The AA Criteria are described in the draft document as "transparent," a term that is undefined in both the Criteria document and the AA program. APERC considers "transparent criteria" to mean that the criteria are clear and provide sufficient guidance so that, to the greatest extent possible, little is left to subjective judgment. A "transparent process" should be open and accessible to stakeholders. The comments below address the need for additional guidance in the Criteria to ensure that they are clear and objective as well as suggestions to improve the overall transparency and clarity of the criteria and process.

3.1 Data quality, hierarchy and weight-of-evidence

APERC supports DfE's requirement to use the "best available data" as well as the use of use of a data-quality hierarchy that prefers measured data to analogs, and analogs to modeled data. DfE should also require the replacement of lower tier data with higher tier data as it becomes available, to ensure that assessments are updated to reflect the best data available.

While APERC generally supports a weight-of-evidence approach to assessing hazard, it is not clear what is meant in the AA Criteria by the use of a "weight-of-evidence evaluation... with a conservative approach". There is no explanation of what a conservative approach means in either the AA Criteria or in the cited ECHA reference. DfE should clarify and solicit public comment on what constitutes a "conservative approach" to assessing weight-of-evidence.

3.2 DfE should add a "not applicable" designation for situations when an endpoint is not relevant to a compound.

DfE proposes that AAs include the "no data" designation for situations where there is no suitable measured, analog, or modeled data. There are also situations where an endpoint may not be relevant to a particular compound. For example, the octanol-water partition coefficient (LogKow) is not relevant for metals and surfactants, and boiling point is not relevant for solids. APERC recommends that DfE's criteria include the additional designation of "not applicable" in such cases, to better classify these substances.

3.3 Hazard Ranking of Chemicals

The use of "Low" as a criterion indicates there is a potential for toxicity. While in theory everything may be toxic at a sufficiently high dose, practically speaking, some chemicals produce no toxicity in some of assays in which they are tested. For example, for a chemical acutely non-toxic at dose levels ≥2000 mg/kg, "Low" would not be appropriate hazard ranking, especially if exposure paradigms indicate the potential for exposure to exceed 2000 mg/kg to be implausible. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Detection of Toxicity to Reproduction for Medicinal Products & Toxicity to Male Fertility S5(R2) guideline states: (1) "*Under most circumstances 1 g/kg/day should be an adequate limit dose*, and (2) *For compounds causing no lethality at 2 g/kg and no evidence of repeated dose toxicity at 1 g/kg..... might pose the*

question ..... whether the compound was an effective medicine. The interpretation under this pharmaceutical guideline, where humans will be intentionally exposed to a chemical, is that chemicals that do not produce toxicity in animal species at ≥1000 mg/kg will not be toxic to humans. This is deserving of a criteria score of "less than Low" as defined in the DFE Alternatives Assessment Criteria for Hazard Evaluation. Perhaps "essentially non-toxic" is a more appropriate alternative for the category with the least possible likely hazard.

In addition, special circumstances regarding absorption, distribution, metabolism and elimination (ADME) for a chemical can result in incorrect and misleading classifications. For example, if total absorption is the same for a chemical at either 50 or 500 mg/kg (i.e., the absorptive mechanisms saturate), and the developmental toxicity studies were conducted with 50 mg/kg (which is also the NOAEL), then the chemical would receive a "Moderate" classification. However, as blood levels are the same at all dose levels ≥50 mg/kg, the classification for this chemical should be "Low" (see previous paragraph as classification should be "nontoxic"). Another example would be a chemical that produces the same toxicity in rats and rabbits but at vastly differing dose levels due to differences in ADME. The classification should then be based on which animal is more "human" in their ADME response and not on the lowest NOEL value. Basing classification only on administered dose level will oversimplify the classification process and may result in environmentally-friendly alternatives being classified as "non-green".

3.4 DfE should include among the general requirements that any alternative must provide sufficient data of sufficient quality to prove that it does not have hazards that are more severe than the chemical of concern; data for all endpoints in the criteria should be required.

The general requirements section of the AA Criteria document state that "data for all relevant routes of exposure will be evaluated". This should be expanded to require that data be provided for all endpoints of concern for the reference compound being replaced.
For example, if there is concern about ecotoxicity, the alternative should provide all the test data for the endpoints in that category. If there is concern about estrogenicity, the alternative should provide test data in that endpoint category. All efforts should be made to ensure that the alternative will be less hazardous than the chemical of concern in every category. In no case should an alternative without sufficient data to address each endpoint be viewed as an acceptable replacement.

3.5 The draft AA criteria do not consider absorption, distribution, metabolism and excretion (ADME) characteristics.

No consideration is given for absorption, distribution, metabolism and excretion (ADME). For example, if absorption is the same for a chemical at either 50 or 500 mg/kg, and the developmental toxicity studies were conducted with 50 mg/kg (which is also the NOEL), then the chemical would receive a "Moderate" classification. However, as blood levels are the same at all dose levels ≥50 mg/kg, the classification for this chemical should be "Low" (see previous paragraph as classification should be "nontoxic"). Another example would be a chemical that produces the same toxicity in rats and rabbits but at vastly differing dose levels due to differences in ADME. The classification should then be based on which animal is more "human"

in their ADME response and not on the lowest NOEL value. Basing classification only on dose level will oversimplify the classification process and may result in environmentally-friendly alternatives being classified as "non-green".

3.6 DfE should clarify how "relevant routes of exposure" will be determined.

The AA criteria document states "data for all relevant routes of exposure will be evaluated." In order for "relevant route of exposure" to be determined and used in the process, the product use characteristics would need to be described. For example, if a substance is only used in a surface-applied spray cleaner, oral toxicity data would not be relevant. Would oral toxicity data not be used in the classification process for such a product? Also, how will DfE address the use of studies on compounds that are not anticipated to have oral exposure in use (e.g. cleaning products) that, because of practical considerations, are conducted by the oral route (developmental toxicity, reproductive toxicology, etc.)?

3.7 It is inappropriate to give equal weight to No Observable Adverse Effect Level (NOAEL) and Lowest Observable Adverse Effect Level (LOAEL) results in a hazard assessment.

Throughout the AA criteria, NOAELs and LOAELs appears to given equal weight when placing a test result based on dose into either High , Moderate or Low categories. This ignores the important distinction between a NOAEL and LOAEL, which often vary by a factor of 3-10. More important, these values are a function of dose selection for a study and would reward studies that are intentionally tested at only at higher doses with the intent of obtaining a relatively high LOAEL and not determining a NOAEL. For example, if one material tested at doses of 30, 100 and 300 mg/kg/day has a LOAEL of 100 and a NOAEL of 30, it would be classified as "High" Reproductive hazard (NOAEL < 50 mg/kg/day), whereas if the same compound was tested at 100, 300 and 1000, with a LOAEL of 100, it would be would be classified as "moderate" (LOAEL between 50- 250). Therefore, it is not appropriate to give the same weight to NOAELs and LOAELs in determining classification category.

3.8 DfE should provide clear guidance as to how assessments of potential impact to vulnerable populations and life stages will be done.

The AA criteria state "All reviews will include an assessment of potential impact to vulnerable populations and life stages." How will this be done in practice? Will the same evaluation schemes be used? Will additional quantitative safety factor be applied as is done with the "FQPA Safety Factor" for FIFRA-regulated products?[12]

[12] Fenner-Crisp, Penelope A.(2001, January 31).. "The FQPA 10X Safety Factor: How Much is Science? How Much is Sociology?" Human and Ecological Risk Assessment: An International Journal 7.1.

3.9 DfE should provide clear guidance about what constitutes a "suitable analog".

There needs to be a much more thorough discussion in the AA criteria about what constitutes a "suitable analog" and how such a determination is made. Various resources exist on this topic. [13] [14] [15] [16] How will DfE determining toxicity for chemicals without data based on analog data?

4.0 COMMENTS ON THE TOXICOLOGICAL CRITERIA

4.1 Carcinogenicity

In discussing rankings for carcinogenicity, the AA Criteria document states "*When equivocal data or only positive structural alerts are present, a designation of Moderate will be used*". Positive carcinogenicity findings based on structural modeling, in the absence of actual carcinogenicity screening tests or studies, may be suitable to justify a "Moderate" carcinogenicity ranking. However, equivocal data should not be used to support a moderate ranking since, by definition, equivocal data are of uncertain significance. DfE should require that additional testing be conducted or submitted to address equivocal results. Alternatively, an additional ranking, "unknown" should be included to more accurately reflect compounds that have either equivocal data or no data at all.

4.2 Mutagenicity/Genotoxicity

4.2.1 The mutagenicity/genotoxicity criteria are not consistent with other national and international criteria and can misrepresent this hazard endpoint.

The AA Criteria states:

> *"The Mutagenicity/Genotoxicity criteria classify compounds based upon capacity to cause gene mutations and/or chromosomal aberrations, whether current data are equivocal, or whether adequate studies have been conducted that show lack of mutagenic potential. Mutagenic/Genotoxic designations will be made according the criteria in Table 4. Those compounds showing positive results and/or categorized by one of the*

[13] OECD QSAR Toolkit – Developed by Danish Ministry of the Environment, Environment Canada, European Chemicals Bureau, Japanese MITI, US EPA. (http://www.oecd.org/document/54/0,3746,en_2649_34373_42923638_1_1_1_1,00.html)
[14] Pavan M, Worth A (2008) Publicly-accessible QSAR software tools developed by the Joint Research Centre. SAR QSAR Environ Res 19, 785-799
[15] Worth A, Patlewicz G eds. (2007) A Compendium of Case Studies that helped to shape the REACH Guidance on Chemical Categories and Read Across. European Commission report EUR 22481 EN. Office for Official Publications of the European Communities, Luxembourg. Available at: http://ecb.jrc.it/qsar/publications/
[16] Worth A, Bassan A, Fabjan, E et al (2007). The Use of Computational Methods in the Grouping and Assessment of Chemicals - Preliminary Investigations, European Commission report EUR 22941 EN, Office for Official Publications of the European Communities, Luxembourg, 2007. Available at: http://ecb.jrc.it/qsar/publications/

authoritative bodies in Table 5 will receive a High designation. When equivocal data or only positive structural data are present, a designation of Moderate will be used."[17]

The proposed approach would apply the same category (High) to chemicals considered under other classification schemes to be "known," "likely," or "probable" human carcinogens as to those that have descriptors such as "suggestive," "possible," or "limited." There is a profound difference in the weight-of-evidence needed to use the first set of descriptors versus the second set. Chemicals associated with descriptors such as "suggestive," "possible," or "limited" should be of moderate concern, not high.

The criteria document further states "*A Low hazard designation will be assigned for chemicals with negative test data and no structural alerts.*[18] Additional guidance should be developed to clarify what justifies a "low" hazard rating for mutagenicity/genotoxicity. As written, compounds with negative test data but a single positive structural alert would be assigned a "Low" ranking. This would contradict the requirement in the criteria to consider data according to a data hierarchy.

In addition, Category 2 carcinogen, mutagen and reproductive (CMA) toxins, according to GHS, should be considered as 'moderate' hazards as these are generally considered to be of low risk to humans and Category 2 carcinogens according to GHS are normally non-genotoxic, and thus are threshold-based. Such animal carcinogens are generally
regarded as less of a concern to humans and are often manifest in animals only at very high doses. Harmonization with GHC would resolve confusion related to this endpoint.

4.2.2 The list of authoritative bodies cited in Table 5 should be revised.

The list of different Authoritative bodies' classification systems should be revised to reflect the current status of each system. The Dangerous Substances Directive (DSD) in the EU is now replaced by the Classification Labelling and Packaging (CLP) directive; thus, the list should refer to CLP and not DSD. It is redundant to include the CMR categories and also a separate line for the Risk phrases as they are directly linked in EU directives. Also, the EU implementation of GHS is consistent with the global version so DfE should only cite the global version.
4.2.3 DfE should clarify how GHS classifications will be used under the DfE Alternatives Assessment Program.

It is not clear from the AA Criteria as written how GHS classifications will be used in the DfE Alternatives Assessment program. There is no harmonized list of GHS classifications for all countries. Rather, each country or region has their own lists of 'agreed' classifications and these are not always consistent. So, is the suggestion that if one country considers a substance to be a C or M category 1a,b or 2 then that compound will be assigned a High hazard under the AA criteria? Or is the suggestion that the GHS system be used by DfE to decide if something should be classified?

[17] US EPA (2010, Nov.)
[18] US EPA (2010, Nov.)

4.3 Reproductive and Developmental Toxicity

4.3.1 DfE should clarify the reasoning for the AA criteria for reproductive and developmental toxicity endpoints, or alternatively harmonize with the GHS rankings for these endpoints.

The AA hazard designation criteria for reproductive and developmental endpoints, which are listed in Table 6 of the document, are based upon US EPA's Office of Pollution Prevention and Toxics (OPPT) criteria for High Production Volume (HPV) chemical categorization.[19] As noted previously in these comments, criteria that are consistent with GHS hazard rankings would create less confusion.

4.3.2 DfE should provide more guidance regarding the interpretation and ranking of data from reproductive and developmental toxicity studies.

The relevance and severity of effects noted in animal studies need to be taken into account in the AA Criteria. For example, a rat- or rabbit-specific reproductive toxicant, i.e., developmental toxicity due to metabolite that is not produced by humans, should not be classified as "Moderate" or "High" if NOEL is <250 mg/kg. This point should be included in guidance for the interpretation of reproductive and developmental study results.

As noted above in Section 3.7 of these comments, NOAELs and LOAELs should not be given equal weight when placing a test result based on dose into either High, Moderate or Low categories. Moreover, it is essential that the AA Criteria make the distinction between maternal and development or reproductive NOAELs and LOAELs. Chemicals which cause reproductive and/or developmental effects only at doses that also cause maternal toxicity should not be of the same level of concern as chemicals for which the developmental and/or reproductive NOAEL/LOAEL are lower than the corresponding NOAEL/LOAEL for maternal toxicity.

4.4 Neurotoxicity

DfE should provide more guidance regarding the interpretation and ranking of data from neurotoxicity studies. What are the criteria for being considered neurotoxic? Transient clinical signs reflecting a neurologic response are common at high doses in toxicity studies, yet this is not evidence of neurotoxicity. Without a clear definition of what constitutes a neurotoxic effect it impossible to assess this criterion.

[19] U.S. EPA. Office of Pollution Prevention and Toxics (EPA OPPT). (2009). Methodology for Risk-Based Prioritization Under ChAMP.

4.5 Repeated Dose Toxicity

4.5.1 DfE should clarify the reasoning for the AA criteria for repeat dose toxicity endpoints or alternatively harmonize them with the GHS rankings for these endpoints.

According to the AA Criteria, hazard designations for repeated dose toxicity will be made based on the criteria in Table 8, which was derived from the US EPA OPPT criteria for HPV chemical categorization. As noted previously in these comments, criteria that are consistent with GHS hazard rankings would create less confusion.

4.5.2 DfE should provide more guidance regarding the interpretation and ranking of data from repeat dose toxicity studies.

How will the 'similarly modified' criteria be used for studies of duration longer than 90 days? NOELs in 90-day studies and 28-day studies are not always going to be as little as or as much as 3 times lower. The NOELs could even be the same for both studies. Will the severity of the toxicity be considered? In GHS, it is noted that when considering repeated dose toxicity it is important to assess the severity of effects observed when deciding if something really poses a significant repeated dose toxicity threat.

Also, as noted above in these comments, NOAELs and LOAELs should not be given equal weight when placing a test result based on dose into either High, Moderate or Low categories.

4.6 Endocrine Activity

The AA Criteria propose to evaluate "endocrine activity" in the form of a narrative rather than characterize a hazard in terms of "endocrine disruption". The narrative will be developed in consultation with EPA toxicologists and risk assessors and will include a summary statement of the available data, including the presence of equivocal or conflicting data and any limitations to the available data. The level of confidence in the assessment will be noted.

4.6.1 DfE should not address endocrine activity or endocrine disruption in the AA criteria until there is scientific consensus and resolution about the methods of test to identify endocrine activity and endocrine disruptors under the EPA Endocrine Disruptor Screening Program (EDSP).

The EPA Office of Chemical Safety and Pollution Prevention's (OCSPP's) EDSP is still in the process of developing requirements for the screening and testing of chemicals for their potential to disrupt the endocrine system. The EPA EDSP website acknowledges "*the science related to measuring and demonstrating endocrine disruption is relatively new and validated testing methods are still being developed.*" [20] When complete, EPA will use these validated methods or assays to identify and characterize the endocrine activity in relation to estrogen, androgen, and thyroid hormones.

[20] EPA EDSP (Accessed Jan. 2011). Endocrine Disruption Screening Program: Background. http://www.epa.gov/endo/pubs/edspoverview/background.htm

While the EDSP program is still underway, EPA has clearly determined that a two-tiered screening and testing process will be used. Through Tier 1 screening tests, EPA hopes to identify chemicals that have the potential to interact with the endocrine system through estrogen, androgen and thyroid receptors (i.e. have endocrine activity). Through Tier 2, EPA will develop and validate study protocols that will determine the endocrine-related effects and obtain information about effects at various doses (i.e. endocrine disruption). EDSP Tier 1 assays, which determine the potential of a chemical to interact with components of the endocrine system, are not intended to signal a concern for health or environmental risks – the kind of risks that would lead to substitution and alternative assessments as proposed in the DfE AA criteria.

Recently, EDSP requested public input on its draft "Weight-of-Evidence Guidance Document: Evaluating Results of EDSP Tier 1 Screening to Identify Candidate Chemicals for Tier 2 Testing" for public comment.[21] This represents an attempt by EPA to obtain stakeholder input on the guidance that will be used for the evaluation and classification of chemicals for Tier 2 testing based on Tier 1 results that evaluate interactions with endocrine system in sensitive screening level studies. The fact that EPA still has not completed the process of developing this guidance clearly indicates that it is premature for DfE to incorporate a review of endocrine activity into the AA Criteria. DfE has an obligation to ensure that its programs follow EPA science and regulatory policies being developed under EDSP. Currently proposed definitions for "endocrine activity" and "endocrine disruptor" in the DfE AA Criteria do not conform to the definitions established under EPA's Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC)[22] and/or the WHO International Programme on Chemical Safety (IPCS).[23] DfE's proposal to utilize endocrine activity as a basis for hazard categorization is not consistent with the EDSP two-tier approach to determine hazards associated with endocrine mediated effects. As such, DfE should not address endocrine activity as a hazard endpoint in the AA Criteria until there is scientific consensus and resolution about the methods of testing and identifying endocrine disruptors under the EPA EDSTP.

4.6.2 If "endocrine activity" is discussed in the AA Criteria document DfE must make a clearer distinction between "endocrine activity" and "endocrine disruption", clearly stating that endocrine activity does not imply that an adverse effect has occurred.

If the DfE AA Criteria do discuss endocrine activity they should clearly describe, in accordance with EDSP, the distinction between "endocrine activity" and "endocrine disruption." The

[21] .S. EPA Office of Pollution Prevention and Toxics, Endocrine Disruptor Screening Program. (EPA, OPPT, EDTP). (2010, November 4). Notice: Announcing the Availability of a Draft for Weight-of-Evidence Guidance Document: Evaluating Results of EDSP Tier 1 Screening To Identify Candidate Chemicals for Tier 2 Testing. Federal Register/ Volume 75, Number 213, pages 67963-67965.
[22] Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) (1998, August). Final Report. http://www.epa.gov/endo/pubs/edspoverview/finalrpt.htm
[23] World Health Organization, International Programme on Chemical Safety(WHO-IPCS) (2002). Global assessment of the State-of-the-science of endocrine disruptors, In WHO/PCS/EDC/02.2. Edited by T. Damstra, S. Barlow, A. Bergman, R. Kavlock, and G. Van Der Kraak, eds. Geneva, Switzerland: World Health Organization, International Programme on Chemical Safety.

definitions currently in the draft AA criteria document are too vague and fail to address the essential point that endocrine activity does not reflect an adverse effect or a hazard.

Acknowledging that consensus was not achieved on a definition developed under the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) definition,[24] EPA issued a memo to clarify the Agency "...does not consider endocrine disruption to be an adverse effect per se, but rather to be a mode or mechanism of action potentially leading to other outcomes, for example carcinogenic, reproductive, or developmental effects, routinely considered in reaching regulatory decisions."[25]

APERC recommends that if DfE discusses endocrine activity or endocrine disruptors in the AA Criteria it should incorporate the working definition developed by the WHO International Programme on Chemical Safety (IPCS):

> *"An endocrine disruptor is an exogenous substance or mixture that alters "An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and* ***consequently causes adverse health effects in an intact organism****, or its progeny, or (sub)populations. A potential endocrine disruptor is an exogenous substance or mixture that possesses properties that might be expected to lead to* ***endocrine disruption in an intact organism, or its progeny****, or (sub)populations."*[26] [emphasis added]

Most noteworthy, for a chemical to be considered an endocrine disruptor, the endocrine mediated effects must occur in a whole organism and they must be adverse. IPCS stresses that:

> *"Endocrine disruption is not considered a toxicological end point per se but a functional change that may lead to adverse effects."*

Thus, chemicals that show some endocrine activity (e.g., estrogenic, androgenic, thyroidogenic) are not necessarily endocrine disruptors and should not be considered to be such.

These IPCS definitions were endorsed at the workshop "OECD Countries Activities Regarding Testing, Assessment and Management of Endocrine Disruptors", which was held in Copenhagen on September 22-24, 2009. [27] One output from this workshop was a recommendation that a guidance document on the assessment of chemicals for endocrine disruption should be developed

---

[24] Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) (1998, August). Final Report. http://www.epa.gov/endo/pubs/edspoverview/finalrpt.htm

[25] U.S. EPA Endocrine Disruptor Screening Program (U.S. EPA EDSP) (1998). Memorandum to Endocrine Disruptor Screening and Testing Advisory Committee. Accessed at http://www.epa.gov/endo/pubs/edsparchive/2-3attac.htm

[26] World Health Organization, International Programme on Chemical Safety(WHO-IPCS) (2002). Global assessment of the State-of-the-science of endocrine disruptors, In WHO/PCS/EDC/02.2. Edited by T. Damstra, S. Barlow, A. Bergman, R. Kavlock, and G. Van Der Kraak, eds. Geneva, Switzerland: World Health Organization, International Programme on Chemical Safety.

[27] Organisation for Economic Co-operation and Development (OECD). (2010, January 18). Workshop Report on OECD Countries Activities Regarding Testing, Assessment and Management of Endocrine Disrupters Series on Testing and Assessment. Number 118. Part 2 Sept. 22-24, 2009. Document ENV/JM/MONO(2010)2. Avaiable at http://www.oecd.org/dataoecd/48/17/44439921.pdf

by the OECD. The draft Guidance Document on the Assessment of Chemicals for Endocrine Disruption was released in November 2010 and the above IPCS definitions were selected for use in this guidance.[28]

If the AA Criteria address "endocrine activity", the Criteria document should define this term and the term "endocrine disruptor" using these most recently vetted IPCS definitions.

4.6.3 If endocrine activity is discussed in the AA criteria document, further discussion is needed of how the various types of endocrine data will be assessed, which should be in a manner with that which is being developed by the EPA EDSP.

In addition to the addressing the definitional concerns expressed above, if the DfE AA Criteria discuss endocrine activity, additional discussion is needed about how the various types of endocrine data will be assessed. Guidance, consistent with that developed under EDSTP, should address the question of how many and what combination of positive responses in *in vitro and in vivo* screens will be required to classify a compound as having "endocrine activity". *In vitro* receptor binding is not evidence of *in vivo* receptor binding OR *in vivo* biological endocrine activity. If only *in vitro* receptor binding data is available, it should be considered as part of a weight-of-evidence determination that would include all available data including that from more apical tests.

4.6.4 The currently proposed hazard categories for endocrine activity in the DfE AA Criteria are incomplete, inconsistent with the policies of the EDSP and will result in the unwarranted stigmatization of many chemicals that may show limited evidence of endocrine activity but for which apical studies indicate no endocrine related toxicity.

There are currently three hazard categories proposed for endocrine activity in the DfE AA Criteria: "no data", "potentially endocrine active", and "no evidence of endocrine activity". These categories are incomplete and, by default render identical classifications for chemicals with *any* evidence of endocrine activity and chemicals that, on the balance of the weight-of-evidence are *clearly* endocrine disruptors according to the EDSTAC and IPCS definitions discussed previously. This is completely inappropriate and, caveats notwithstanding, will result in the unwarranted stigmatization of many chemicals that may show limited evidence of endocrine activity (from *in vivo* screens for example) but for which apical studies indicate no endocrine related toxicity. Under the proposed scheme, such a chemical would be in the same category as a known endocrine disruptor that shows true endocrine-mediated adverse effects in whole organisms.

Under the proposed categories, the only way to not be considered potentially endocrine active is to have no data or have *only* negative data. This completely ignores the need to use a weight-of-evidence approach to evaluating the entire body of evidence with respect to endocrine disruption

[28] Organisation for Economic Co-operation and Development (OECD). (2010, November) Guidance Document on the Assessment of Chemicals for Endocrine Disruption Version 9. Accessed at http://www.oecd.org/dataoecd/63/8/46436593.pdf

and glosses over the complexity and nuance associated with such efforts and ignores other significant efforts within the EDSP to address these topics.

5.0 COMMENTS ON THE ENVIRONMENTAL TOXICITY AND FATE CRITERIA

5.1 Aquatic Toxicity

The DfE criteria for aquatic toxicity should be revised to be consistent with the GHS system for aquatic toxicity category criteria.

5.2 Environmental Persistence

Additional guidance and clarification is needed in the AA criteria to describe the requirements for environmental persistence. For example, the relevant modes of degradation, in addition to biodegradation, should be noted (e.g. hydrolysis, photolysis, oxidation/reduction). Also, the criteria should clarify what attributes would be associated with a "degradation product of concern". Otherwise, almost any degradation product could be of concern for one reason or another, by virtue of its formation.

It is not clear how a "qualitative assessment of atmospheric persistence" will be conducted. EPA should provide additional guidance about how such a qualitative assessment will be conducted. Also, EPA should consider referencing the AOPWIN estimation tool as a reliable and semi-quantitative method for assessing atmospheric persistence.[29]

Finally, the 10-day window should not be incorporated into the criteria; alternatively, DfE should mention that this should be applied only for pure/discrete organic substances. Substances which are technical mixtures (e.g. , surfactants, polyols, fatty acids and derivatives, etc.) should not be classified on basis of the 10-day window, as specifically stated in the OECD Guidelines. [30]

5.3 Bioaccumulation

Additional guidance and clarification is needed in the AA criteria to describe the requirements for bioaccumulation. In cases where measured *in-vitro* fish metabolism data are available, it should be stated how these data (and associated Km value) could be used to categorize bioaccumulation potential or lack thereof.

[29] USEPA. 2011. Estimation Programs Interface (EPI) Suite, v4.00, AOPWIN v1.92a. U.S. Environmental Protection Agency, Washington, DC

[30] Organisation for Economic Co-operation and Development .(2006). Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3: Part 1- Principles and strategies related to the testing of degradation of organic chemicals. OECD Guidelines for the Testing of Chemicals, Organisation for Economic Co-operation and Development, Paris, France. Adopted 23 March 2006.

American Chemistry Council (ACC)
January 31, 2011

MICHAEL P. WALLS
VICE PRESIDENT
REGULATORY & TECHNICAL AFFAIRS

January 31, 2011

Ms. Libby Sommer
United States Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, N. W.
Mail Code: 7406M
Washington, DC 20460
sommer.elizabeth@epa.gov

RE: Comments of the American Chemistry Council on Draft Alternatives Assessment Criteria for Hazard Evaluation[1]

Dear Ms. Sommer:

The American Chemistry Council (ACC) appreciates the opportunity to comment on the Design for the Environment (DfE) program□s November 2010 draft criteria for hazard evaluation in its Alternatives Assessments (AA). In general, ACC supports the approach to health and environmental hazard criteria outlined in the draft. ACC has a number of concerns with the draft criteria, however, and urges DfE to clarify and modify several elements of the approach.

Alternatives assessment can be an important tool in comparing chemical substances, developing new products and processes, and informing marketplace decisions. Properly executed, alternatives assessment can ensure that key decision elements from the DfE's approach to "Informed Substitution" are evaluated, including technological feasibility, improved health and environmental profiles, equal or better value in cost and performance, and accounting for economic and social considerations.

[1] U.S. EPA Office of Pollution Prevention and Toxics, "Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation," Draft (November, 2010). Available at http://www.epa.gov/dfe/alternatives_assessment_criteria_hazard_eval_nov2010_final_draft2.pdf. .

DfE Should Clarify the Role of Hazard Evaluation in Alternatives Assessment.

The introduction to DfE's proposed hazard criteria appropriately outlines the role of hazard evaluation as a tool for more transparent and meaningful alternatives assessments.[2] The draft notes that in addition to providing a foundation for EPA decisions on alternatives, the criteria "could form the basis for decision-making by other organizations such as manufacturers, retailers, other government agencies, and non-governmental organizations."[3]

In ACC's view, the draft does not go far enough to explain that hazard evaluation is but one component of a complete alternatives assessment as envisioned in the program's approach to "Informed Substitution." Other components necessarily include risk assessment (including an assessment of the magnitude of the exposure, risk of a substance and its possible alternatives, and the likelihood of those respective risks occurring), economic and social impact evaluations, and cost and technological assessments, among others.

DfE□s draft implicitly recognizes that risk-based alternatives assessment is intended. For example, Section 2 of the draft is quite clear that all relevant routes of exposure will be evaluated,[4] and that EPA's risk assessment guidelines will be applied.[5] ACC believes DfE would agree that an alternatives assessment based solely on hazard evaluations would be incomplete, and we encourage the program to clarify that the hazard criteria are not intended to suggest that decisions should be made on the basis of hazard evaluations alone.

Furthermore, DfE has acknowledged that the criteria may well be used by governments, industry, and non-governmental organizations. Without further clarification, the draft may suggest that EPA supports hazard-based decision-making. A hazard-based approach is inconsistent with EPA's statutory responsibility under the Toxic Substances Control Act (TSCA), as well as EPA's recently articulated principles for modernization of the Act.[6]

ACC is particularly concerned that, without further clarification, DfE□s application of the criteria to alternatives assessments for Chemical Action Plan (CAP) chemicals[7] could result in an expectation that potential alternatives to CAP substances would be identified on the basis of hazard alone. This approach would undermine the risk basis for decision-making under TSCA. If taken to its obvious possible conclusion, the approach would constitute an end-run around the regulatory constraints imposed by TSCA and the Administrative Procedures Act (including notice and comment rulemaking) and could allow the Agency to make a determination that substitution of a substance by another is required.

---

[2] Draft Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation at 1.
[3] Id.
[4] Id.
[5] Id.
[6] U.S. EPA, Essential Principles for Reform of Chemicals Management Legislation (September, 2009). Available at http://www.epa.gov/oppt/existingchemicals/pubs/principles.html. EPA□s first principle indicates that "[c]hemicals should be reviewed against safety standards that are based on sound science and reflect risk-based criteria protective of human health and the environment." DfE□s alternatives assessments should do no less.
[7] Announcements section of the Design for Environment Home Page, at http://www.epa.gov/dfe/.

The draft's exclusive focus on hazard is not appropriate. Elsewhere, DfE suggests that where similar product and chemical use patterns are expected, exposure can be considered a constant in alternatives assessments and risk can be lowered by reducing chemical hazard.[8] This view, which focuses decision-making solely on hazard comparisons, is overly simplistic. Not only is such "drop-in substitution" a rare situation, but the substitute materials involved will almost always have different properties, different performance parameters, and different effects on the other material components in the product. These factors will result in differences in the potential for exposure to the chemical and thus a completely different health and environmental risk profile.

ACC supports the concept of developing hazard criteria for use in DfE alternatives assessments. It is incumbent on DfE to be clear, however, that hazard comparison is only one component of such an assessment.

Authoritative Sources as the Basis for Hazard Criteria are Welcome, but Should not be Modified.

ACC strongly supports DfE's use of a number of nationally and internationally accepted "authoritative sources" for the proposed hazard criteria. As these sources and systems have been successfully applied here and abroad, using them as a foundation and building on them makes good sense. ACC members are very familiar with these programs and support their application in DfE's alternatives assessments.

Unfortunately, DfE is proposing to selectively adjust the categorization of several endpoints by creating categories that are not comparable with the U.N. Globally Harmonized System for Classification and Labeling (GHS) or which do not exist in common Pollution Prevention (P2)/Sustainable Futures programs (such as "Very High" and "Very Low," e.g. acute, irritation/corrosivity, aquatic, persistence, bioaccumulation). DfE is also proposing to selectively alter cut-off values for some endpoints (e.g. acute, acute aquatic, reproductive and developmental). ACC strongly disagrees with this approach, as it deviates from well-accepted approaches in safety and green chemistry programs, for example:

- EPA's P2 criteria have been successfully used for many years in setting priorities and taking action in the P2 and New Chemical programs. These criteria have also been applied in EPA□s Sustainable Futures Program[9].
- The Occupational Safety and Health Administration (OSHA) is responsible for implementation of the GHS for the US workplace. OSHA has published proposed regulations to modify its existing hazard communication standard to conform to GHS endpoints and classification criteria.[10]
- The American Chemical Society's Green Chemistry Institute (ACS GCI) initiated the development of an ANSI standard to provide a common set of data

[8] Chemical Alternatives Assessment: Enabling Substitution to Safer Chemicals, *Environ. Sci. Technol.* 2010, 44, 9244-9249

[9] Interpretive Assistance for Sustainable Futures Summary Assessment, updated January 22, 2007.

[10] *See* 74 Fed.Reg 50280 (Sept. 30, 2009). OSHA□s Fact Sheet on aligning the hazard communication program with GHS requirements can be accessed at http://www.osha.gov/as/opa/facts-hcs-ghs.html.

> reporting elements for chemicals, including a set of hazard characteristics for chemicals. Discussions on the standard started in 2009 and have involved stakeholders including EPA, academic, industry and environmental interests. The draft Standard for Greener Chemicals and Processes was released for public comment on September 17, 2010 and it is now in the final revision process. The standard (NSF/GCI 355) proposes to use GHS and P2 hazard endpoints, categories and cut-offs in reporting on "Chemical Characteristics"[11].

Neither OSHA nor the NSF GCI standard altered any of the categories or cut-offs as has been proposed in DfE's draft. DfE's draft criteria contain no justification of the proposed modifications, and without further explanation, seem arbitrary.

For reproductive/developmental endpoints and several others, DfE proposes to employ an approach used in a single instance (chemical categorization under OPPT's Chemical Assessment and Management Program (ChAMP)) that has since been abandoned. This approach, as characterized by EPA□s ChAMP document, states that the criteria are to be used for "...qualitative evaluations that indicate whether OPPT considers an HPV chemical or chemical category as a low, medium or high priority for further assessment."[12] Thus, the ChAMP criteria were not intended for categorization, for which DfE proposes to use them, but rather for prioritization.

ACC strongly recommends that DfE promote harmonization in categories and endpoints by adopting the same cut-off values and categories currently applied in the GHS and P2 programs. Failure to do so will create yet another modification of existing, well-established programs, and the significant potential for misapplication and confusion on the part of those applying the criteria in alternatives assessments.

ACC is also concerned that DfE proposes to adopt the European Union□s classification and labeling categories and risk phrases as an authoritative source for alternatives assessments. DfE should understand that although the EU hazard categories generally conform to the GHS system, chemical classifications under the EU's new Classification, Labeling and Packaging (CLP) Regulation[13] could differ significantly from those resulting from other programs. Current EU CLP classifications are the result of using a crosswalk between previous EU classifications and GHS. The data in current classifications have not been assessed against the GHS criteria, nor have those classifications had input from all stakeholders. It has been recognized by the United Nations Sub-Committee of Experts on GHS that not all experts and countries agree with current EU classifications. In addition, risk phrases for hazards such as carcinogenicity and mutagenicity are derived directly from classifications under the CLP and are not derived from any independent authoritative source. In light of these considerations, the EU CLP and risk phrases should not be designated as sources for DfE's alternatives assessments.

[11] http://standards.nsf.org/apps/group_public/document.php?document_id=9409
[12] http://www.epa.gov/ChAMP/pubs/rbp/RBPMethodology_Web_April%202009.pdf
[13] Classification, Labeling and Packaging Regulation, (EC) No. 1278/2008.

Assessment process needs to provide clarity on how the hazard categorization criteria are evaluated to compare alternatives

There is understanding that the intent of the DFE assessment process is to utilize these criteria to place chemicals on a continuum of relative hazard to inform decision making. ACC understands that, for various endpoints, substances will be categorized as either "High", "Moderate", or "Low" concern and, as a result, for any specific endpoint, one could place substances on a continuum or relative hazard. However, DfE needs to clarify how one would utilize these categorization criteria to compile one continuum of a group of materials being assessed as potential alternatives for an existing material. For instance, it might be implied that "Very High" Acute Toxicity is more important than "High" Carcinogenicity. It would seem that a key objective of the hazard evaluation process has not been addressed. It is important for all stakeholders to have the opportunity to comment on a challenging, yet very important, aspect of the evaluation process. Otherwise, DfE's categorizations could well lead to unintended conclusions.

General Requirements and Toxicological Criteria

ACC supports the scientific principles expressed in the general requirements and data concepts. The evaluation of data for relevant routes of exposure is appropriate.

ACC agrees that EPA risk assessment guidance is the right basis for review of NOAEL and LOAEL values. However, it is not clear which value is to be used in evaluating a chemical against the Criteria for studies in repeated dose toxicity, neurotoxicity, and reproductive and developmental toxicity. In these evaluations, ACC believes that the LOAEL is the proper value. GHS guidance speaks to use of guidance (or cut-off) values for a dose shown to produce a significant health effect:

> 3.9.2.9.4 The decision to classify at all can be influenced by reference to the dose /concentration guidance values at or below which a significant toxic effect has been observed.
> 3.9.2.9.6 Thus for Category 1 classification, significant toxic effects observed in a 90-day repeated-dose study conducted in experimental animals and seen to occur at or below the (suggested) guidance values as indicated in Table 3.9.1 would justify classification[14]

The identical instructions have been carried through into OSHA's implementation of GHS in the US.[15] Thus, as it refers to a dose producing a significant effect, the GHS system both nationally and internationally envisions use of a LOAEL. This utilization of a LOAEL is echoed in the criteria for the ChAMP program, as noted above.[16] EPA should clarify that the LOAEL is the appropriate value for use in comparison against the Criteria.

[14] Globally Harmonized System for Classification and Labeling, of Chemicals, 3rd Revised Edition, Part 3 Health Hazards, page 200 UN, 2009 http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html
[15] Id. At 11
[16] Id. At 13, page 11

The application of EPA HPV Challenge Program and OECD HPV Programme data adequacy guidelines is a critical step in ensuring science-based decisions. ACC supports DfE□s requirement to use "best available data" and a hierarchy that prefers measured data to analogs and analogs to modeled data. To remain relevant and valuable, ACC also recommends that DfE require the replacement of lower tier data with higher tier data as it becomes available, to ensure that assessments are updated to reflect the best data available. Additionally, DfE should clarify the process by which it intends to incorporate updates of new information into existing assessments.

DfE proposes that alternatives assessment include the "no data" designation for situations where there is no suitable measured, analog, or modeled data. There are also situations where an endpoint may not be relevant. For example, the octanol water partition coefficient (LogKow) is not relevant for metals and surfactants, and boiling point is not relevant for solids. ACC recommends that DfE's criteria include the additional designation of "not relevant" in such cases, to better classify these substances.

DfE□s proposal appropriately indicates that a weight-of-evidence evaluation will inform the hazard designation when there is conflicting data. However, it goes on to set an expectation that this should apply a "conservative approach," which is not defined in the draft and the exact meaning of which is ambiguous. ACC believes that DfE's alternatives assessments should adhere to well-accepted and established EPA standards and practices for a weight-of-evidence evaluation, such as that used by the World Health Organization□s International Programme on Chemical Safety (IPCS).[17]

Endocrine Activity as a Criterion

DfE proposes to evaluate endocrine activity in a narrative, which would consist of a characterization of chemicals as having "no data," "no evidence of endocrine activity," or being "potentially endocrine active." Chemicals recognized as "potentially endocrine active" would not be allowed in products recognized by DfE. [18] The proposed approach is inconsistent with scientific understanding of endocrine disruption and is contrary to established Agency policy. This approach is particularly inappropriate as it ignores the Office of Chemical Safety and Pollution Prevention□s (OCSPP) Endocrine Disruptor Screening Program (EDSP) and its definition of "endocrine disruptor" by proposing to apply results of EDSP Tier 1 screening for DfE product stewardship and risk management actions. In the DfE proposed Standard[19], the Agency proposes to make decisions in assessments solely on "interaction" or "perturbation" of the endocrine system:

[17] Boobis, et al. 2008. IPCS framework for analyzing the relevance of a noncancer mode of action for humans. Critical Reviews in Toxicology. 38 (2), 87-96; Seed et al. 2005. Overview: Using mode of action and life stage information to evaluate the human relevance of animal toxicity data. Critical Reviews in Toxicology. 35 (8-9), 664-672.

[18] U.S. EPA Office of Pollution Prevention and Toxics, proposed enhancements to the DfE "Standard for Safer Cleaning Products" (October 2010). Available at: http://www.epa.gov/dfe/proposed_enhancements_to_dfe_standard_for_safer_products.html

[19] Id.

> 4.5.5 Potential endocrine effects. Chemicals that are candidates for endocrine screening will be part of the review. Chemicals found to interact with or perturb the endocrine system—potentially leading to reproductive, developmental, carcinogenic, systemic, hormonal or other effects—will not be allowed based on the toxicological hazards they pose.

This proposed standard is carried through to the proposed AA Hazard Evaluation, which indicates:

> EPA will evaluate endocrine activity rather than characterize hazard in terms of "endocrine disruption". Evidence of a chemical having endocrine activity will be summarized in a narrative.

The DfE proposed approach is wholly inappropriate and inconsistent with EPA's EDSP policy. In the two-tiered EDSP, the assays that comprise the Tier 1 battery have been specifically designed to maximize the sensitivity to detect any interaction with components of the estrogen, androgen and thyroid systems. The EDSP Tier 2 is designed to identify adverse effects and dose response and it is the Tier 2 results that should be used for product stewardship and risk management decisions. The EDSP Tier 1 assays, which determine the potential of a chemical to interact with components of the endocrine system, are not intended to signal a concern for health risks that would lead to bans or substitutions. EPA OCSPP is very clear on this point.

> EPA developed a two-tiered approach to implement the statutory testing requirements. The purpose of Tier 1 screening (referred to as "screening") is to identify substances that have the potential to interact with the estrogen, androgen, or thyroid hormone systems using a battery of assays. The fact that a substance may interact with a hormone system, however, does not mean that when the substance is used, it will cause adverse effects in humans or ecological systems. The purpose of Tier 2 testing (referred to as "testing"), is to identify and establish a dose-response relationship for any adverse effects that might result from the interactions identified through the Tier 1 assays.[20]

The description and proposed actions regarding endocrine in the proposed DfE Standard and Hazard Criteria, as currently written, would base action on Tier 1 EDSP screening results, and would promote product stewardship and regulation based merely on the potential of interactions rather than on adverse effects and risk, thus shifting EPA's well established, scientifically grounded, risk-based chemical management paradigm. This is inappropriate. Even the National Research Council (NRC) panel, which used the term "perturbation," is clear that it did not envision regulatory actions being triggered by any finding of a mere perturbation. NRC□s experts stated in "Toxicity Testing in the 21st Century: A Vision and a Strategy":

---

[20] EPA (2009). Endocrine Disruptor Screening Program; Policies and Procedures for Initial Screening. Federal Register Volume 74, Number 71 (Wednesday, April 15, 2009) Pages 70248-70254. http://www.epa.gov/endo/pubs/revised_pandp_frn_041509.pdf

Biological responses viewed as the result of an intersection of exposures with biological functions. The intersection leads to perturbations of biological pathways. When perturbations are sufficiently large or when host is unable to adapt because of underlying nutritional, genetic, disease or life-stage status, biological function is compromised.[21]

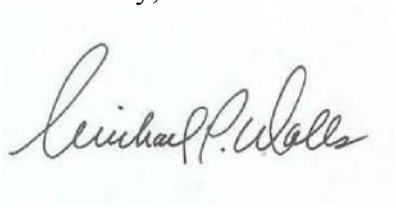
The point is an adverse effect—an effect that warrants use as an endpoint for risk assessment or the basis for determining product stewardship or risk management or consideration for possible substitution of a chemical in a product—is not merely any known biochemical or chemical change, or even any known or measurable precursor along the pathway that could lead to some degree of perturbation. The NRC Committee clearly indicated that consideration of adversity occurs when perturbations are sufficiently large. Evaluation of endocrine disruption requires integration of mode of action screening data with apical test results of adverse effects and dose response. DfE should refer to published approaches, such as that of Boobis et al. (2008) or Bars et al. (2010) [22] for detailed discussion of methods that can be used to accomplish this.

Finally, endocrine activity, as determined by EPA's EDSP Tier 1 screening, is not a distinct toxicological hazard *per se*, but rather a measure of a compound's ability to interact with components of the endocrine system. Interaction with or modulation of endocrine processes may or may not give rise to adverse effects. The DfE has an obligation to ensure that its programs follow EPA science and regulatory policies in describing what EDSP Tier 1 screening results are and are not, and that they use the information generated in the Tier 1 EDSP appropriately. The current proposal does not and therefore should be eliminated from both the Standard and Hazard Criteria proposals.

* * * * *

ACC's looks forward to the opportunity to continue working with DfE in the further development of alternatives assessment approaches. If there are any questions concerning ACC's comments, please contact me, or Brendan Mascarenhas (BrendanMascarenhas@americanchemistry.com, 202-249-6423).

Sincerely,



Michael P. Walls
Vice President
Regulatory & Technical Affairs
cc: Clive Davies, EPA

[21] Toxicity Testing in the 21st Century: A Vision and a Strategy (2007). The National Academies Press, Washington, DC, 20001. Page 49.
[22] Bars et al. 2010. Science based guidance for the assessment of endocrine disrupting properties of chemicals. Regulatory Toxicology and Pharmacology 59: 37-46

American Cleaning Institute® (ACI)
January 31, 2011

January 31, 2011

Ms. Elizabeth Sommer
Design for the Environment Branch
Office of Pollution Prevention and Toxics
USEPA Headquarters
Ariel Rios Building (Mail Code: 7406M)
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460
(via e-mail: sommer.elizabeth@epa.gov)

Dear Ms. Sommer:

The American Cleaning Institute® (ACI) appreciates the opportunity to comment on the EPA's recently-released draft of the Design for the Environment (DfE) *Alternatives Assessment Criteria for Hazard Evaluation.* ACI is the trade association representing the $30 billion U.S. cleaning products market. ACI members include the formulators of soaps, detergents, and general cleaning products used in household, commercial, industrial and institutional settings; companies that supply ingredients and finished packaging for these products; and oleochemical producers. ACI and its members are dedicated to improving health and the quality of life through sustainable cleaning products and practices. ACI's mission is to support the sustainability of the cleaning product and oleochemical industries through research, education, outreach and science-based advocacy.

ACI and its members support the efforts of the agency, and the DfE Program in particular, to seek new and innovative ways to examine and reassess existing chemistries and certain uses of those chemistries in an effort to identify opportunities to shift toward the use of alternative chemicals and processes that might reduce risks to health and the environment. Following are comments concerning the process by which the *Criteria for Hazard Evaluation* is being developed and substantive aspects concerning certain criteria and the manner in which they might be applied in this context.

EPA should comply with the standards of the Administrative Procedure Act (APA) when seeking and considering public comment for the DfE *Alternatives Assessment Criteria for Hazard Evaluation* and the methods by which EPA intends to apply the Criteria both to specific substances and in agency decision making.

It is clear from recent EPA announcements issued in the context of certain "Action Plans" that the agency considers the chemical alternatives assessment process to be a critical component of its program for managing chemical risks for Action Plan Chemicals. Thus, the Criteria that are being developed and will be applied as part of the *Alternatives Assessment Criteria for Hazard Evaluation* will have the effect of providing a basis for agency decisions to regulate or restrict the use of chemicals in the marketplace. Notwithstanding the "voluntary" nature of the DfE Alternatives Assessments Program, the tools and processes used by EPA, and the analytical outcomes that result will have the imprimatur of an EPA safety assessment and preferability of certain chemicals and products containing those chemicals. It is reasonable to conclude that the results of a DfE Alternatives Assessment ultimately will be used within EPA programs and by the states and localities wishing to articulate standards and requirements for the use of certain chemicals by the regulated community. Consequently, in developing procedures and standards for review of chemical substances, EPA should meet the standards for providing all members of the public with notice and the opportunity to provide comment on all aspects of both the development of the AA Criteria and the application of the criteria within the Alternatives Assessments Program as well as EPA's risk-management decision making process. This should, at a minimum, include official notice in the Federal Register of the availability of the draft documents with appropriate comment periods, as well as the consideration of and a response to comments that are received.

EPA should more clearly explain how the Criteria for Hazard Assessment will be used in the Alternatives Assessment process to compare multiple alternatives to each other.

It is clear that the intent of the DfE Alternatives Assessment process is to utilize the AA Criteria to place individual chemicals on a continuum of relative hazard to inform decision-making and presumably alternatives selection. We understand the concept that for particular endpoints, substances will be categorized as either "High", "Moderate", or "Low" concern and, as a result, for any specific endpoint, one could place each substance on a continuum of relative hazard. However, the agency needs to clarify how one would utilize these categorization criteria to compile one continuum for a group of alternative materials being assessed against an existing material. It would seem that a key objective of the hazard evaluation process has not been addressed. It is important for all stakeholders to have the opportunity to comment on perhaps the most challenging, yet most important, aspect of the evaluation process.

EPA should apply broader sustainability criteria when evaluating a particular chemical and its uses against alternative chemicals for each of the same uses.

The *Alternatives Assessment Criteria for Hazard Evaluation* and the process discussed in the publication *Chemical Alternatives Assessment: Enabling Substitution to Safer*

Chemicals[1] demonstrate that EPA intends to rely disproportionately on hazard-based criteria when evaluating the (safe) use of a chemical substance in a product, and when identifying potential alternatives. Such a limited approach can be flawed on several levels especially when hazard-based metrics are applied as the sole criteria for chemical selection. First, this approach presumes that most alternative chemicals are "drop-in" substitutes. However it is very rare that circumstances exist to allow for such seamless substitution. Moreover, an analysis based on hazard factors alone can ignore the effect that differences in physicochemical properties of chemicals can have upon exposures and environmental releases, even when drop-in substitution might be possible. Finding substitutes for established chemistries often requires that an alternative chemical be used at a different concentration than the material it replaces, or with multiple chemicals that are necessary to replace a single substance being de-selected. It is not clear that the DfE AA Criteria can take this into account and compare the relative hazards of one substance with the hazard associated with multiple chemicals or chemicals used in differing concentrations.

The hazard-evaluation-only approach proposed for the DfE AA Criteria also fails to consider other significant factors which influence the health and environmental impacts associated with a product. For many products, such as cleaning products, changes in certain components often can have significant impacts on the energy and water consumption characteristics associated with the use of the products. Therefore, for an alternatives assessment to effectively consider the potential human and environmental impacts of an alternative, consideration must be given to all phases of the product's lifecycle to significantly improve the sustainability profile of a particular product. Minor changes in the formulation of a high volume product can result in significant and unintended impacts on health and the environment. For example, efforts are being made to reduce the environmental impacts of laundering clothes and washing dishes, through the use of more water- and energy-efficient commercial equipment and consumer appliances. If an alternatives assessment fails to take into account non-hazard based factors, such as the compatibility of alternative ingredients for detergent formulations with the current and next-generation equipment that is designed to be less energy- and water-consumptive, then these hoped-for energy and water efficiency improvements might not be achieved due to low consumer acceptance. EPA's proposed hazard-evaluation-only approach for alternative assessment should be modified to more fully assess a product's entire lifecycle and consider the health and environmental impacts of substituting alternative chemistries across the entirety of the product's lifecycle.

The AA Criteria have been released with little context given to the broader Alternatives Assessment program or EPA's AA goal of *informed substitution*. In the past, EPA has stated that, in the context of *informed substitution*, "potential alternatives should exhibit as many of the following characteristics as possible: they should be technically feasible; deliver the same or better value in cost and performance; provide an improved profile for health and the environment; account for economic and social considerations; and have the potential to result in lasting change." None of these other characteristics have been given treatment similar to the AA Criteria for Hazard Evaluation and there is no indication that the agency will provide guidance to the public on how one might evaluate them as part of an alternatives assessment or that more

[1] Emma T. Lavoie, Lauren G. Heine, Helen Holder, Mark S. Rossi, Robert E. Lee II, Emily A. Connor, Melanie A. Vrabel, David M. DiFiore, Clive L. Davies. 2010. *Environmental Science & Technology*. 44 (24): 9244-9249.

comprehensive guidance on conducting an alternative assessment with the goal of informed substitution is forthcoming.

The agency's website on Alternative Assessments[2] includes a description of the key steps to conducting an alternatives assessment including Step 6, Apply Economic and Life Cycle Context. However, the description of Step 6 is quite broad in its coverage. The agency should prepare and communicate to the public a roadmap regarding its guidance on the alternatives assessment process so that no step is given disproportionate or undue weight and so that all characteristics of the goal of *informed substitution* may be satisfied.

EPA should reconsider and enhance the criteria it has selected.

While the toxicological assessment criteria, and environmental toxicity and fate scoring parameters selected for use by EPA in its AA Criteria are familiar and accessible to many in the regulated community, there nevertheless are some important issues that should be taken into consideration with respect to the use of certain of the Criteria in the context of DfE Alternatives Assessments.

Anticipating Potential Changes to the GHS Criteria. EPA proposes to use criteria and endpoints derived from the United Nation's Globally Harmonized System for the Classification and Labeling of Chemicals (GHS). In the U.S., the Occupational Safety and Health Administration (OSHA) is responsible for implementing the GHS system for workplace use. However, OSHA has issued proposed regulations to modify its existing Hazard Communication Standard (HCS) to conform with the GHS [74 FR 50279; September 30, 2009]. The proposed modifications to the standard include revised criteria for classification of chemical hazards. The DfE AA Criteria document does not address whether and how the Criteria can be modified if and when OSHA adopts changes to the GHS. ACI recommends that DfE not adopt GHS criteria for workplace products, but instead wait for OSHA to complete its regulatory development process. Should EPA move ahead with adoption of some GHS components, any criteria that are inconsistent with OSHA final regulations should be revised in order to avoid manufacturers having to assess their products against two different systems.

Also, while the Consumer Product Safety Commission (CPSC) intends to adopt changes to its regulations to implement the GHS, it has not yet proposed those changes. Therefore, in order to avoid inconsistencies between its criteria and CPSC-regulated products, DfE should not implement any GHS-related criteria chemicals used for consumer products.

Consistent to the preceding comments, all references to characterizing chemicals and products according to GHS should be removed. Instead, EPA should refer to the hazard regulations of the respective agencies, which, as they adopt GHS under their respective review and comments procedures, would allow a DfE alternatives assessment program to remain consistent with those requirements.

In addition, EPA has started a public dialogue and record related to the agency's implementation of the GHS. In 2004, the agency received numerous comments on its document *The Globally*

[2] http://www.epa.gov/dfe/alternative_assessments.html

Harmonized System of Classification and Labelling of Chemicals: Implementation Planning Issues for the Office of Pesticide Programs (Environmental Protection Agency (EPA). Pesticides; Implementation of Globally Harmonized System; Notice of Availability, *Federal Register* / Vol. 69, No. 164 / Wednesday, August 25, 2004 [Docket number OPP–2004– 0205]). ACI (under its former name, The Soap and Detergent Association) submitted comments to this record. In addition, the Office of Pesticide Programs held a Public Stakeholder Meeting on the implementation of the GHS in 2006 (October 18-19, 2006), in which the agency received additional input. EPA should consider and respond to the comments it has already received on GHS implementation before proceeding with its proposal to include GHS elements in the Alternatives Assessment Criteria.

Identifying compounds of low hazard. The draft raises the potential for substantial confusion by designating substances where there are negative studies or test results, no structural alerts, etc. as "low" hazard. In such circumstances, the substance should be designated to not present the hazard.

Partial adoption of GHS elements. EPA should avoid incomplete adoption of criteria and approaches to classification presented in the GHS. For example, the proposed adoption of GHS criteria for Specific Target Organ Toxicity – Repeat Exposure (STOT-RE) for neurotoxicity lacks many of the critical elements of the classification criteria for this endpoint that are part of the GHS. EPA should compare the criteria for each endpoint from the GHS that it proposes to adopt against the criteria the agency currently uses, and present its rationale for the GHS elements it proposes to adopt and not adopt for each endpoint.

Use of Criteria from Other Countries Developed Without Opportunity to Provide Input in the U.S. The use of European Union criteria and authoritative lists in Section 4.1.2 and elsewhere in the document is inappropriate. U.S. stakeholders are not a party to the development of the EU lists and EU Risk Phrases. Therefore, unless EPA wishes to first solicit input and comment on the substantive aspects of the EU-based lists and criteria, those criteria should not be used to implement the DfE program in the U.S.

Use of Novel and Untested Criteria. The Endocrine Activity criterion described in the draft (Section 4.1.9) has not been used previously in government programs in the United States or elsewhere in the world. EPA's new testing program for potential endocrine effects is itself in its infancy. By making use of this criterion now, as part of an assessment of alternative chemistries, DfE will be establishing a precedent that suggests the standards being used are considered to be generally acceptable and reliable in the scientific community. Until such time as there is general agreement in the scientific community on the appropriateness of using the method EPA proposes to comment on the potential endocrine effects of a substance, this criterion should be eliminated from the DfE Alternatives Assessment Criteria.

Order of data preference. EPA's proposal states that data will be considered in a specific order of preference ("In general, DfE will use data in the following order of preference: 1) measured data on the chemical being evaluated, 2) measured data from a suitable analog, and 3) estimated data from appropriate models.") and that "available human data will be considered." ACI recommends that EPA clearly give preference to human data and experience, since such

information is most relevant to exposures and effects that could occur in humans. Further, all other data should be considered in a weight-of-evidence evaluation.
Definition of "compound." The term "compound" is used in the document, but is not defined. This could be confusing since terms such as "chemical" and "ingredient" are defined.

Use of Specific Criteria Which Are Inconsistent with Relevant Precedents.
4.1.1 – Acute Mammalian Toxicity: The Table 1. Acute Mammalian Toxicity Criteria for Hazard Designation are stated to have been derived from GHS criteria however these values are not consistent with those proposed by OSHA for the implementation of the GHS in the United States [74 FR 50279; 9/30/09]. We endorse the use of harmonized workplace GHS criteria in the U.S.

4.1.3 – Mutagenicity/Genotoxicity: We urge EPA to remove the Mutagencity/Genotoxicity (M/G) criterion from its proposal. Hazard communication regulations of other agencies, such as OSHA, address mutagenicity/genotoxicity through the reproductive toxicity endpoint (see 29 CFR Parts 1910, 1915, and 1926 Hazard Communication; Proposed Rule; *Federal Register* (Vol. 74, No. 188, September 30, 2009), page 50388: "The GHS has a separate definition for germ cell mutagenicity, which is considered part of reproductive toxicity in the current HCS [Hazard Communication Standard].") In the absence of results from higher-tier more sophisticated studies, the results from genotoxicity assays (i.e., mutagenicity tests) are used by most scientists to predict the potential carcinogenicity of a substance. A material that tests positive for mutagenicity either will be predicted to be a carcinogen or additional higher-tier tests may be undertaken to confirm or over-ride the concern. This is a conservative approach because there are mutagenicity screening tests that yield positive results for substances that are confirmed later not to be carcinogenic. Thus, since EPA proposes covering the Carcinogen and Reproductive toxicity hazard classes in the draft Alternative Assessment Criteria, implementation of M/G hazard would not improve the assessments.

Since the carcinogenicity and reproductive toxicity hazard classes are proposed for the alternatives assessment and they cover the adverse effects of M/G, and there would be a greater impact from the proposal due to the need to provide support applying the M/G criterion, the M/G hazard criterion should not be adopted.

Chronic or target-organ toxicities: For a number of the chronic or target-organ toxicity criteria, GHS hazard criteria for mixtures include both a dose-response value and a product concentration value in deriving the particular classification reflecting the risk-based nature of hazard communication labeling in the United States. If the DfE AA Criteria are going to be consistent with the GHS criteria, they should follow a similar risk-based approach.

4.2.2 Environmental Persistence: The 10-day window should not be incorporated into the criterion; or at least it should be mentioned that this criterion should be applied only for pure/discrete organic substances. Substances which are technical mixtures (e.g., surfactants, polyols, fatty acids and derivatives, etc.) should not be classified on basis of the 10-day window, as specifically stated in the OECD Guidelines.
The attributes that would be associated with a "degradation product of concern" should be stated. Otherwise, almost any degradation product could be of concern for one reason or another, by virtue of its formation.

It is unclear how a "qualitative assessment of atmospheric persistence" will be conducted. EPA should consider that other regulatory programs have employed an atmospheric half-life cut-off of 2 days; where substances which exceed this half-life are considered to have potential for long-range atmospheric transport. Also, the AOPWIN estimation tool should be mentioned as a reliable and semi-quantitative method for assessing atmospheric persistence.

4.2.3 Bioaccumulation: EPA should contemplate and incorporate other data relevant to bioaccumulation and "higher-tier" bioaccumulation studies where appropriate. For example, where measured in-vitro fish metabolism data are available, these data (and associated Km value) could be used to categorize bioaccumulation potential or lack thereof. Similarly, EPA generally accepts that substances of high molecular weight are not accumulating; a cut-off value for molecular weight and/or diameter should be included. Finally, trophic magnification factors (TFM) are considered "gold standard" studies with regard to the potential for a compound to biomagnify up the food chain. Any assessment of a chemicals assessment to bioaccumulation should include the ability to incorporate such data.

* * *

ACI remains committed to working collaboratively with EPA to develop well recognized and reliable criteria for assessing chemicals-related risks and to identifying alternative chemistries which provide an effective means to reduce such risks. Please contact me by phone at 202-662-2516 or by e-mail at pdeleo@cleaninginstitute.org if you would like to discuss our comments and any improvement to the agency's draft that you would like us to help you consider.

Sincerely,

Paul C. DeLeo, Ph.D.
Senior Director, Environmental Safety

Boeing
December 13, 2010

Criteria for Hazard Evaluation – Comment

Morris-Fine, Karen L
To: Elizabeth Sommer
12/13/2010 01:00 PM

History: This message has been replied to and forwarded.

Libby,

The telecon regarding the Hazard evaluation document was informative. I had a couple of follow on comments.

1). Carcinogenicity Criteria: GHS category 2 suspected carcinogen, IARC 2B - possible carcinogen and EU CMR list Category 3 - cause for concern all receive a High Hazard Designation. Has it been considered to give them a moderate ranking instead of high to provide more spread and flexibility in chemical carcinogenicity hazard designations? This same comment applies to the Mutagenicity/Genotoxicity classifications for High hazard designation.

2). In the Hazard Evaluation document I did not see an explanation regarding the methodology for determining the overall Hazard classification of the chemical. Will this be added to the draft document?

3). Since the chemicals being considered for Deca replacements are flame retardants it would be important to consider the toxicity of the thermal decomposition products at the various temperatures of burning. This was not identified in the DFE alternatives assessment criteria for Hazard Evaluation. Is there a plan to include this kind of information? If not, could you considering adding, identifying or considering this information/data in some way.

Thank you for the opportunity to comment.

Regards

Karen Morris-Fine, Ph.D.
Associate Technical Fellow
Enterprise EHS Toxicology, TSCA
Telephone: 425-237-1949; Fax: 425-965-8468
Cell: 206-251-4929; MC 9U4-22
email: karen.l.morris-fine@boeing.com

Chemical Producers & Distributors Association
1730 Rhode Island Avenue, N.W.
Suite 812
Washington, D.C. 20036
202.386.7407
FAX: 202.386.7409

January 31, 2011

VIA E-MAIL

Ms. Elizabeth Sommer
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Ariel Rios Building (MC 7406M)
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

RE: Comments on the Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation

Dear Ms. Sommer:

The Chemical Producers & Distributors Association ("CPDA") appreciates this opportunity to comment on the proposed changes to the above-referenced Design for the Environment ("DfE") alternatives assessment criteria for evaluating hazards ("Criteria Document"). CPDA is the primary advocate on federal legislative and regulatory issues for generic pesticide registrants, adjuvant and inert ingredient manufacturers, and product formulators and distributors.

CPDA supports the U.S. Environmental Protection Agency's ("EPA" or "Agency") DfE initiative and its efforts to "reduce risk to people and the environment by finding ways to prevent pollution." However, we believe that EPA needs to clarify the level of information the Agency requires to "evaluate a chemical of concern and its likely alternatives" in order to "reduce the likelihood of the unintended consequences that might result if poorly understood alternatives are

chosen." We are specifically concerned with EPA's definition of the term "endocrine activity"[1] and subsequent reference to the term in Subsection 4.1.9 of the Criteria Document.[2]

CPDA believes that the proposed definition of "endocrine activity" is not consistent with any other defined toxicological criteria used by the DfE program or EPA in general, and as such is misleading, not useful for assessment and comparison purposes, and not scientifically supported. In fact, the Agency offers no literature reference for the definition set forth in section 3.14 of the Criteria Document or the potential data sources and criteria listed in section 4.1.9 for the evaluation of human health effects of potential endocrine disruptors.[3] With respect to endocrine disruptors, we believe it is scientifically premature to posit criteria by which DfE could compare alternatives and "reduce the likelihood of the unintended consequences that might result if poorly understood alternatives are chosen."

EPA has only recently validated screening assays to gauge a chemical's potential to interact with the endocrine system (Tier 1 screening) and has not yet validated tests to measure dose-response relationships and adverse effects (Tier 2 testing). Therefore, the Agency cannot at this point identify the criteria for "adverse" effects (versus imparting temporary system perturbations) and consequently what alternatives might be "safer." EPA understands this and has repeatedly stated:

> "[B]ased on current information, the public should not presume that the listing of a chemical or substance [on the Tier 1 list] indicates in any way that EPA currently suspects that such chemical or substance interferes with the endocrine systems of humans or other species simply because it has been listed for screening under the EDSP."[4]

These EPA lists for chemicals and substances to be screened under the EDSP are based only on their pesticide registration status and/or because such substances may occur in sources of drinking water to which a substantial population may be exposed. Only when the potential to interact with the endocrine system has been confirmed during the Tier 1 screening will mandatory testing be used to determine any actual endocrine effects.[5] Under the EDSP, EPA has not yet elucidated a weight-of-evidence process by which information of the type listed as potential data sources in section 4.1.9 can be evaluated for potential endocrine system interaction, much less for adverse effects.

Therefore, CPDA recommends that human health endocrine effects criteria not be proposed in the Alternatives Assessment Criteria until such time as 1) a sound, scientifically-based set of criteria can be developed for comparison of alternatives; 2) chemicals or substances have been found to be endocrine disruptors through adequate, reliable, and reproducible scientific studies; and 3) their endocrine-related human health endocrine effects have been elucidated.

---

[1] Criteria Document at p. 6.
[2] Id. at p. 16. (This section addresses endocrine activity as a toxicological criterion for assessing Human Health Effects under section 4.1).
[3] Id. (Section 4.1.9 (A) & (B)).
[4] 75 Fed. Reg. 70248, 70250 (November 17, 2010); see also 74 Fed. Reg. 17579, 17579 (April 15, 2009).
[5] EPA has not yet selected and fully validated the tests needed to determine actual endocrine effects.

Clean Production Action
December 16, 2010

Additional Comments on DfE's DRAFT AA chemical hazard assessment criteria

Lauren Heine
To: Elizabeth Summer
12/16/2010 11:33 AM
Cc: Clive Davies, Caroline Baier-Anderson, Mark Rossi, Alexandra Cc: McPherson, Bev Thorpe

Degradation/Transformation Products

- could DfE provide guidance on identifying degradation/transformation products. How would one know if one has done a comprehensive assessment of feasible transformation products; what are best resources; which transformation pathways need to be considered (oxidation, reduction, pyrolysis; combustion; anaerobic biodegradation, aerobic biodegradation, hydrolysis, photolysis, etc)

- could DFE provide guidance on considering feasible end of life pathways to guide the focus on transformation products; eg looking at aquatic biodegradation for chemicals that go down the drain; or looking at combustion products for products potentially burned for recycling

- Where is the sweet spot between considering ALL transformation products, transient or otherwise and considering only those transformation products that are potentially problematic because they have certain properties (PBT) or otherwise have potential for exposure and toxicity?. Are we dependent only on what has been measured and published in the literature (bio and environmental monitoring studies)?

- Clean Production action believes it is important to keep feasible transformation products front and center in the CHAs because as you know, the transformation products can the source of problematic impacts, even when a parent compound is benign.

Thank you

--
Lauren Heine, Ph.D.
Science Director, Clean Production Action
Bellingham, WA
O: 360-738-4643
M: 360-220-2069
lauren@cleanproduction.org
www.cleanproduction.org

The Dow Chemical Company
Midland, Michigan 48674
USA

1803 BUILDING
January 31, 2011

Ms. Elizabeth Sommer
Design for the Environment Branch
Office of Pollution Prevention and Toxics
USEPA Headquarters
Ariel Rios Building (Mail Code: 7406M)
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460
(via e-mail: sommer.elizabeth@epa.gov)

Dear Ms. Sommer:

The Dow Chemical Company (Dow) appreciates the opportunity to provide comment on the Agency's recently-released draft of the Design for the Environment (DfE) *Alternatives Assessment Criteria for Hazard Evaluation*.

Dow is a diversified company with a portfolio of specialty chemical, advance materials, agrosciences and plastic businesses. Dow delivers a broad range of technology-based products and solutions to customers in approximately 160 countries and in high growth sectors such as electronics, water, energy, coatings and agriculture. Dow is a leader in helping to shape chemicals management improvements across the globe. Further, Dow has more presidential green chemistry challenge awards than any other company. We support the efforts of the Agency, and the DfE Program in particular, in their efforts to seek new and innovative ways to examine and reassess existing chemistries and certain uses of those chemistries in an effort to identify opportunities to shift toward the use of alternative chemicals and processes may pose lower risk to human health and the environment. Following are comments to pass along to you concerning the process by which the *Criteria for Hazard Evaluation* are being developed and substantive aspects concerning certain criteria and the manner in which they might be applied in this context.

Broader elements of sustainability principles need to be incorporated into the alternatives assessment process. Currently the intended differentiation of chemicals for human health and evironmental impact is only based upon the hazard profile (i.e., toxicity) and does not take into account important physical chemistry properties such as molecular weight, vapor pressure, dermal absorption OR the actual use concentrations of the component in a product necessary to

attain a similar efficacy. By the described process it is possible that "safer" alternative chemicals are identified based entirely on the hazard of the pure component but in fact at relevant use concentrations in a product, the identified alternative chemistry could represent a greater risk due to a combination of use concentration, exposure potential and hazard profile. For example, the hazards of individual substances *e.g.* irritation, acute tox, *etc.*, may change when the substances are used in a formulation.

The DfE draft does not go far enough to explain that hazard evaluation is but one component of a complete alternatives assessment. Beyond the consideration of use (referenced above), which feeds into the important risk assessment, the alternatives assessment should also include: life-cycle analyses, economic and social impact evaluations. We assume that the DfE would acknowledge that alternatives assessment can not be based solely on a hazard evaluation. DIE should clarify that decisions on alternatives should not be based on hazard evaluations alone. The Agency should establish criteria and compile guidance documents on these other important elements of an alternatives assessment and allow the public an opportunity to provide comment to ensure the robustness of the assessments.

More guidance and details are needed for the implementation process. There are important areas where very little guidance or details are given for implementation of the process (e.g., selection of appropriate analogs; use of "best" information - experimental or modeled; what is the appropriate model to use?, etc.). Greater details on how EPA intends to implement specific elements of the process as cited above will greatly enhance transparency and ensure consistency of implantation of these process across substances and from reviewer to reviewer.

EPA should consider revisions to the hazard criteria used in the alternatives assessments. GHS criteria - It appears that GHS criteria are used for some endpoints (mammalian, environmental and ecotox) and not others. EPA should consider how it can more consistently apply GHS criteria across its evaluation process and evaluate how it will manage future changes to GHS classification criteria (i.e. those being proposed by OSHA).

Acute criteria - The use of "Low" as a criteria implies there is a potential for toxicity. If a chemical is non-toxic at dose levels ≥2000 mg/kg, "Low" may not be appropriate, especially if exposure paradigms indicate the potential for exposure to exceed 2000 mg/kg to be implausible. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Detection of Toxicity to Reproduction for Medicinal Products & Toxicity to Male Fertility S5(R2) guideline states: (1) "*Under most circumstances 1 g/kg/day should be an adequate limit dose*, and (2) *For compounds causing no lethality at 2 g/kg and no evidence of repeated dose toxicity at 1 g/kg... ... might pose the question ..... whether the compound was an effective medicine*. The interpretation under this pharmaceutical guideline - where humans will be intentionally exposed to a chemical- is that chemicals that do not produce toxicity in animal species at ≥1000 mg/kg will not be toxic to humans, *i.e.*, deserving a criteria score of less than "Low" as defined in the DfE Alternatives Assessment Criteria for Hazard Evaluation. EPA should consider the guidance outlined above and consider adding a category of "non-toxic" based on the above criteria.

Other relevant criteria – The EPA should take into account other relevant information that can help inform the alternative assessment. For example, no consideration is given for environmentally-friendly alternatives where the intermediates, manufacturing process, and/or waste stream *etc*. is much less "green" than the chemical being replaced. It could be that the process involved in the manufacture of the replacement makes the replacement a less suitable alternative to the environment than the chemical being replaced.

As another example, when supplemental data are available for a substance, EPA should have a means to include these data into the alternatives assessment. For instance, supplemental data such as pharmacokinetic/metabolism data can inform the assessment by helping to determine which species are closest in sensitivity to human. A chemical that produces the same toxicity in rats and rabbits but at vastly differing dose levels due to differences in ADME illustrates this point. The this case the classification should be based on the data most relevant to humans in their ADME response and not on the lowest NOEL value. Basing classification only on dose level is an oversimplification of basic biological responses that can lead to error in the classification process, an error that may result in exclusion of truly environmentally-friendly option.

Specific Comments to the proposed draft of the Design for the Environment (DfE) Alternatives Assessment Criteria for Hazard Evaluation

Page 1: Can EPA provide clarification about the impact of the following statement on timing for finalization of its criteria: *Lessons learned from the application of the criteria during those assessments will be incorporated into a finalized version*. Does the Agency intend to update these criteria on some reoccurring basis as you have real experience with their use?

Page 3: Introduction: There is understanding that the intent of the DfE assessment process is to utilize specific criteria to place chemicals on a continuum of relative hazard to inform decision making. We understand the concept that for particular endpoints, substances will be categorized as either "High", "Moderate", or "Low" concern and, as a result, for any specific endpoint, one could place substances on a continuum or relative hazard rating. However, the Agency needs to clarify how one would utilize these criteria to compile one continuum of a group of materials being assessed as potential alternatives for an existing material. How will categories be ranked in relative importance for the overall assessment process (e.g. how do you define a continuum when one chemical is high for a human health endpoint and another is high for excotoxicity or phy/chem. properties). Does the agency then take into account use pattern, application etc.? Will stakeholders to have the opportunity to have inpout on this important aspect of the evaluation process?

Page 4 General Requirements:
2.1 – "Data for all relevant routes of exposure will be evaluated." In order for "relevant route of exposure" to be determined and used in the process, the product use characteristics must be known. For example, if a substance is only used in a surface-applied spray cleaner, oral toxicity data may not be relevant. Are data from non relevant exposure routes eliminated in the classification process?

2.2- As first mentioned in this section and used throughout the document, NOAELs and LOAELs are given equal weight when placing a test result based on dose into either High , Moderate or Low categories. EPA should note that these endpoints are entirely a function of dose selection for a study and could reward studies that are intentionally tested at higher doses with the intent of obtaining a relatively high LOAEL and not determining a NOAEL. For example, if one material tested in a reproduction study at doses of 30, 100 and 300 mg/kg/day has a LOAEL of 100 and a NOAEL of 30, it would be classified as "High" Reproductive hazard (NOAEL < 50 mg/kg/day), whereas if the same compound was tested at 100, 300 and 1000, with a LOAEL of 100, it would be would be classified as "moderate" (LOAEL between 50-250). It does not seem scientifically valid to give the same weight to NOAELs and LOAELs in determining classification category.

"All reviews will include an assessment of potential impact to vulnerable populations and life stages." Can EPA please provide more details on how this will be done? There was no further mention of it in the document.

Pg. 9 Terms:
3.37: Transparency of the process will be improved if EPA can provide a much more thorough discussion on what constitutes a "suitable analog" and how such a determination is made.

What is the process and what are the models that will be used in determining toxicity for compounds without data?

Toxicological Criteria:
Page 10
4.1.2 Carcinogenicity and Mutagenicity:
The list of different Authoritative bodies' classification systems should be revised. First -the Dangerous Substances Directive (DSD) in the EU is now replaced by the Classification Labelling and Packaging (CLP) directive; Thus, the list should refer to CLP and not DSD. It is redundant to include the CMR categories and also a separate line for the Risk phrases as they are directly linked in EU directives. Plus, the EU implementation of GHS is consistent with the Global version so probably only need to include GHS at the top. One important point is that there is no harmonised list of GHS classifications for all countries implementing it. Rather each country or region has their own lists of 'agreed' classifications and these are not always consistent. Given this point, does EPA suggest use of the classification from the country with the most conservative classification? Does EPA suggest that the GHS system be used to decide if something should be classified?

Cat 2 CMRs, according to GHS, should be considered as 'moderate' hazard as these are generally considered to be of low risk to humans and Cat 2 carcinogens according to GHS are normally non-genotoxic, threshold etc.

Page 12
4.1.4 Reproductive and Developmental Toxicity
Can EPA discuss why the GHS system is not included here or why relevance to effects to humans or severity of effects is not taken into account? For example, a rat- or rabbit-specific

reproductive toxicants, i.e., developmental toxicity due to metabolite that is not produced by humans, should not be classified as Moderate or High if NOEL is <250 mg/kg.

Page 13
4.1.5 Neurotoxicity
Can EPA provide a definition of what constitutes a neurotoxic effect?

Page 14
4.1.6 Repeated Dose Toxicity
How will the 'similarly modify' criteria be used for studies of duration longer than 90 days? NOELs in 90-day studies and 28 day studies are not always going to be as little as or as much as 3 times lower? The NOELs could even be the same for both studies.
Will the severity of the toxicity be considered? In GHS, it is noted that when considering repeated dose toxicity it is important to assess the severity of effects observed when deciding if something really poses a significant repeated dose toxicity threat. The document should refer to the STOT RE classifications for repeated dose toxicity.

Page 16
4.1.8 Eye and Skin Irritation/Corrosivity
What criteria are being used to determine what is mildly/moderate/severe irritating? It would be helpful provide a clear definition.

Page 16
4.1.9 Endocrine Activity
The Endocrine Activity criterion described in the draft is not a distinct toxicological hazard but rather a measure of a substance's ability to interact with the endocrine system; interaction may not give rise to effects. EPA's new testing program for potential endocrine effects is itself in its infancy and has not been used in other government programs or elsewhere in the world. By making use of this criterion now, as part of an assessment of alternative chemistries, DfE will be establishing a precedent that suggests the standards being used are considered to be generally acceptable and reliable in the scientific community. Until such time as there is general agreement in the scientific community on the appropriateness of using the method EPA proposes to comment on the potential endocrine effects of a substance, this criterion should be eliminated from the DfE Alternatives Assessment Criteria.

If the Agency determines that Endocrine Activity should be maintained as a criterion, then DFE is encouraged to consider the following points.
Will *in vitro* receptor binding assays be enough to classify as having "endocrine activity"? *In vitro* receptor binding is not evidence of in vivo receptor binding OR in vivo biological endocrine activity. If only *in vitro* receptor binding data is available, it may be considered, but only in light of ADME, exposure paradigms and results of reproductive toxicity tests.

Page 17
4.2 Environmental Toxicity and Fate
4.2.1 Aquatic Toxicity
It is hard to find other regulatory framework or classification schemes where LOEC is used to classify aquatic toxicity. REACh, OECD, GHS, etc. all employ classification schemes for chronic toxicity which are on the basis of NOEC (or ECx) values.

Page 18
4.2.2 Environmental Persistence
The relevant modes of degradation, in addition to biodegradation, should be noted (e.g. hydrolysis, photolysis, oxidation/reduction).

The 10-day window should not be incorporated into the criteria; or at least make mention that this should be applied only for pure/discrete organic substances. Substances which are technical mixtures (e.g. , surfactants, polyols, fatty acids and derivatives, etc.) should not be classified on basis of the 10-day window, as specifically stated in the OECD Guidelines.

It should be stated as to what attributes would be associated with a "degradation product of concern". Otherwise, almost any degradation product could be of concern for one reason or another, by virtue of its formation.

It is not clear how a "qualitative assessment of atmospheric persistence" will be conducted. Other regulatory programs have employed an atmospheric half-life cut-off of 2 days; where substances which exceed this half-life are considered to have potential for long-range atmospheric transport. Also, the AOPWIN estimation tool should be mentioned as a reliable and semi-quantitative method for assessing atmospheric persistence.

Page 18
4.2.3 Bioaccumulation
In cases where measured in-vitro fish metabolism data are available, it should be stated how these data (and associated Km value) could be used to categorize bioaccumulation potential or lack thereof. Similarly, as EPA generally accepts that substances of high molecular weight are not accumulating, perhaps a cut-off value for molecular wt. and/or diameter could be included.

In summary, Dow supports the Agency efforts to develop well recognized and reliable criteria for assessing chemicals-related risks and to identify alternative chemistries that can provide effective means to reduce risks to human health and the environment. Please contact me if you would like to discuss our comments.

Sincerely,

Pamela J. Spencer, PhD., D.A.B.T
Toxicology Consultant Leader
Phone: 989-636-9797
Email: pjspencer@dow.com

ENVIRONMENTAL HEALTH RESEARCH FOUNDATION
A NONPROFIT RESEARCH FOUNDATION SPECIALIZING IN HEALTH AND ENVIRONMENTAL SCIENCE

January 31, 2011

Comments on the DfE Alternatives Assessment Criteria for Hazard Evaluation

The Environmental Health Research Foundation (EHRF) is pleased to have this opportunity to provide comments on the EPA DfE draft Alternatives Assessment Criteria for Hazard Evaluation. EHRF is a nonprofit, nonpartisan scientific research foundation seeking to improve the analysis and communication of health and environmental science. Its goal is to further the understanding of science related to health and the environment, and especially the interaction between the environment and human health.[1]

EHRF comments will be centered on two themes. First, our comments will focus on the criteria as they apply to the Bisphenol A (BPA) alternatives in thermal paper as this is the chemical for which we have the greatest scientific expertise. Secondly, we will offer specific suggestions to improve the transparency and clarity of the Alternatives Assessment Hazard Criteria.

1. Recent Assessments and Studies Affirm that BPA Thermal Paper Does Not Pose a Health or Environmental Risk

EPA began the Alternatives in Thermal Paper project as part of the BPA Action Plan (3/29/2010), which states that EPA is initiating immediate actions to address levels of BPA in the environment based on concerns for potential effects in aquatic species (p.1). It further states (p. 14) that there is agreement among international regulatory authorities, using accepted approaches to human health, that human exposures to BPA are below levels that would be associated with health effects, leading to determination that current uses of BPA do not present human health risks.

[1] For more information on the Environmental Health Research Foundation, see www.ehrf.info

International Health Assessments

Since the publication of the action plan, several assessments and studies have reaffirmed the safety of BPA below the 0.5 mg/kg bw and that thermal paper is not expected to significantly contribute to human exposure. These conclusions have been recently confirmed by the European Food Safety Authority (EFSA).[2] The EFSA assessment, published in September 2010 evaluated new studies published since the previous EFSA review, completed in 2008. Additionally, it scrutinized, in detail, the Stump et al. neurobehavioral toxicity study that was a cause for concern to FDA and the biomonitoring studies claimed by some scientists to demonstrate a link between BPA exposure and human health effects.

After considering these new studies, the EFSA panel of independent scientific experts:

- Concluded that the data currently available do not provide convincing evidence of neurobehavioral toxicity of BPA.
- Noted that human epidemiological studies do not support the conclusion that BPA is the cause of any health effects.
- Concluded they could not identify any new evidence which would lead them to revise the current Tolerable Daily Intake (safe level) for BPA of 0.05 mg/kg body weight set by EFSA in its 2006 opinion and re-confirmed in its 2008 opinion.

In short, the European Food Safety Authority, after reviewing the latest science on BPA, concluded that there is no reason to change its safety standards on BPA.

Even more recently, an international panel of experts convened by the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO)[3] reported that after reviewing all the evidence on the potential of BPA to affect human health, "There is considerable uncertainty regarding the validity and relevance of [low dose] observations," and suggested that more research is necessary to better characterize the potential hazards, especially in regard to regulatory purposes. Also of note, the panel concluded that food was "by far the main source of BPA exposure" and other sources, including thermal paper, were likely of "minor relevance."

Health Studies

In addition, new studies have shed light on the safety of thermal paper since the publication of the action plan. We have not identified any scientific evidence to suggest adverse human health effects from the small amounts of BPA that may migrate from thermal paper.

A significant recent study on dermal absorption (February 2010), by the Centre for Xenobiotic Risk Research (XeRR) at the University of Zurich,[4] concludes that dermal absorption is at most a secondary absorption route for Bisphenol A. The primary absorption route is still dietary intake.

[2] European Food Safety Authority, http://www.efsa.europa.eu/en/press/news/cef100930.htm
[3] http://www.who.int/foodsafety/chem/chemicals/bisphenol_release/en
[4] http://www.xerr.uzh.ch/news/bisphenol01.html. An English translation is available from EHRF.

For this route, daily total amounts of BPA around 10,000 times higher are considered harmless for adults."

XeRR's conclusions that human exposure to BPA from thermal paper is likely to be quite low were affirmed by various laboratory experiments. Recent data from Biedermann et al (2010)[5] indicate that roughly 0.5 µg is transferred from receipt paper per finger under normal skin conditions. Experiments demonstrate only 4%-15% of BPA on the skin is absorbed into the body in 24 hours[6,7,8]. Biedermann's data demonstrates that fingers become rapidly saturated with BPA, so that repeatedly touching receipts will not quickly change the amount of BPA on the fingers. Importantly, BPA can be washed off the skin decreasing the chance of absorption. Together these data, along with WHO and EFSA's 2010 assessments, demonstrate that thermal paper does not represent a significant source of exposure.

Another recent, widely publicized report, published by Daniel Zalko et al. in the journal Chemosphere,[6] reports for the first time that BPA is efficiently converted to water soluble metabolites in the skin. These metabolites are known to be completely lacking in estrogenic activity[9] and to be efficiently excreted from the body in the urine.

Biomonitoring studies also reveal little concern for exposure from thermal paper. Braun et al (2010)[10] measured total urinary BPA in 389 pregnant women (includes all metabolites). Cashiers had the highest exposure in the study, while teachers and industrial workers had the lowest exposure, but when normalized for socioeconomic differences, the effect was attenuated (ratio: 1.15; 95% CI: 0.84, 1.57).

- The 17 cashiers in the study had geometric mean (GM) concentration of 2.8 µg/g creatinine, GSE 1.1.
- Teachers had a GM: 1.8 tg/g; GSE: 1.1, and
- Industrial workers had a GM: 1.2 tg/g; GSE: 1.2.

While these data indicate that BPA levels in cashiers were higher than in the other populations, it is important to note that the cashiers in the study fall within the 50th percentile of exposure (2.3-2.8 µg/g creatinine) of the entire US population based on 2003-2004 NHANES data[11]. Furthermore, these levels of total BPA in urine are still below the TDI.
In addition, the authors point out several caveats regarding the data:

---

[5] Biedermann, S., Tschudin, P. and Grob, K., Transfer of bisphenol A from thermal printer paper to the skin. Anal. Bioanal. Chem., published on-line 11 July 2010.
[6] Kaddar N, Harthe C, Dechaud, H, Mappus E, Pugeat. 2008. Cutaneous penetration of bisphenol A in pig skin. J. Toxicology and Environmental Health. 71: 471-3.
[7] EU risk assessment 2008.
[8] Zalko D, Jacques C, Duplan H, Bruel S, Perdu E. 2010. Viable skin efficiently absorbs and metabolizes bisphenol A. Chemosphere, doi:10.1016/j.cheosphere.2010.09.058
[9] Matthers, J.B., Twomey, K. and Zacharewski, T.R., In vitro and in vivo interactions of bisphenol A and its metabolite, bisphenol A glucuronide, with estrogen receptors alpha and beta. Chem. Res. Toxicol. 14 (2): 149-157, 2001.
[10] Braun, J.M. et al., Variability and predictors of urinary bisphenol A concentrations during pregnancy, Environmental Health Perspectives, online 8 October 2010.
[11] Calafat, A.M., et al. Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. Environmental Health Perspectives 116: 39-44, 2008.

1. The subset of 17 cashiers is not statistically robust enough to draw conclusions.
2. Serial urinary BPA concentrations were highly variable, had a low degree of reproducibility, and varied according to time of day of sample collection in the latter two-thirds of pregnancy"; thus, they were not able to get an accurate, long-term estimate of exposure.
3. Since BPA is rapidly metabolized by the skin and excreted and there is no data about when the cashier worked in relation to the sample collection, their potential occupational exposure could bear little significance on their measured urinary BPA metabolites.

Environmental Working Group (EWG)[12] recently authored a report on the exposure to BPA from thermal paper; they examined NHANES data to look at potential occupational exposure. They report that 195 retail workers had 28% higher levels of BPA than 916 people in other occupations. 4 out of 5 occupations with the highest exposure may have contact with thermal paper (Department store retail, Communications, Food store retail, Eating & drinking establishments). However, these data do not take into account that education and socioeconomic status are good predictors of exposure. Since most of the reported occupations are relatively low wage, this is likely to confound the EWG findings.

Environmental Assessments

Importantly, BPA in thermal paper poses negligible risk to the environment. The European Commission risk assessment (2008) used new data from the European Thermal Paper Association to calculate the amount of BPA released to surface water, sediment, and sludge during thermal paper recycling7. They separately examined two paper recycling processes; those that de-ink the pulp and those that do not. The assessment demonstrates that the predicted environmental concentration (PEC) is lower than the predicted no-effect concentration (PNEC) in fresh and marine water and in land-applied sludge. Even if the conservative, Canadian value (as noted in the EPA action plan) for the PNEC is used, in almost all cases, the PEC/PNEC ratio indicates that there is little to no ecological risk from recycling of thermal paper.

Conclusions

The review of recent literature has found significant scientific support for the ecological and human safety of thermal paper in commercial use, as in cash register receipts. No evidence was found of any credible risk to human health or safety from the commercial use of thermal paper, which was found by the WHO international panel of experts to be of only "minor relevance" for BPA exposure. BPA in thermal paper can be absorbed into the skin, but slowly and incompletely. Hand washing can significantly reduce exposure. BPA is not accumulated in the body and is rapidly eliminated through urine. Risk calculations put exposure to BPA from paper as low as 10,000 times lower than the TDI. Finally, biomonitoring studies suggest that cashiers fall into the median exposure category and their exposure is still below the TDI, which already have built in margins of safety. All these data indicate that BPA in thermal paper is safe for human health and the environment.

[12] Environmental Working Group - http://www.ewg.org/bpa-in-store-receipts.

2. Comments on DfE Hazard Criteria

EHRF believes that the DfE criteria, which are based entirely on hazard properties, not risk assessment, could be made more transparent and more effective with the inclusion of the changes listed below.

1. The criteria could be improved by the clarifying how the Alternatives Assessments programs will deal with endpoints that have no data. Lack of data should not be considered any more favorably than the worst endpoint on the continuum. This point is crucial, so that there is no misrepresentation that uncharacterized alternatives are safer than chemicals where the hazard is known and understood.
2. DfE should clarify whether and how it intends to weight each endpoint. Are all the endpoints in the criteria given equal weight or are some endpoints more important than others?
3. Clarification on the weight of evidence (WOE) approach is merited. The criteria states that published, peer-reviewed and guideline studies will be preferentially considered; however, DfE should consider clarifying their approach to the interpreting the strength of evidence and how that fits with DfE's "conservative approach".
4. Information on how DfE plans to implement the evaluation of endocrine activity is needed, especially in regard to preferred tests and interpretation guidelines.
5. There are a number of additional unresolved issues regarding use of endocrine activity as an alternatives criterion.

These points are discussed in more detail below.

Treatment of chemicals that lack data. The criteria could be improved by clarifying how the Alternatives Assessments programs will deal with chemicals and/or endpoints that lack data. Use of the term, "informed substitution" implies that lack of data, lack of suitable analog data, or lack of accurate model data should merit the same treatment as the worst failing endpoint (either very high or high concern). Lack of data should not be considered any more favorably than the worst endpoint on the continuum. This point is critical to ensure that uncharacterized alternatives cannot be represented as safer than chemicals whose hazard is known and quantified.

> From 4. Toxicological Data (our suggestion in italics).
>
> In the absence of measured data on the chemical being evaluated, measured data from a suitable analog and/or estimated data from computer models will be used. In the event that there are no suitable analogs, that suitable analogs lack measured data, and the substance, or its analog cannot be modeled, the hazard endpoint cannot be evaluated and will be designated *"no data" and will be regarded as equivalent to the highest level of concern of the category (very high or high).*

Equal weight of quantitative endpoints. The DfE program should clarify whether it intends to weigh each endpoint equally or if some endpoints will be considered more important than others.

If endpoints are assigned a different weight, how would that decision be made? We support a model where each defined endpoint is given equal weight; endpoints addressed by narrative or equivocal data should receive less weight. For example, we can envision a scenario where endocrine activity may trump the well-defined endpoints given the debate regarding whether endocrine effects can occur at environmentally-relevant or consumer-use type doses. However, given the controversy over the accuracy and reproducibility of low dose experiments, we suggest that all quantitative endpoints be assigned equal weight and the endpoints where the data is so contradictory that a quantitative measure cannot even be designated, should be given a lesser weight.

> From 4. Toxicological Data (perhaps as a new third paragraph).
>
> *In terms of the ultimate evaluation of the chemical, each quantitative endpoint will be considered of equal importance. Because of the equivocal nature of the endpoints that receive a*
> *qualitative review, these endpoints should carry less weight than the well-defined ones in determining the overall "grade" of the chemical.*

Along these lines, we also have questions regarding how the narrative on endocrine activity will fit on this otherwise, fairly quantitative scale. How can there be a fair comparison of endocrine activity when one chemical receives an entire narrative but the alternatives have no data. This lack of data may be much harder to convey in a narrative format, where "no data" does not receive an obvious failure designation.

Clarification on the weight of evidence approach. Clarification regarding the implementation of the WOE is merited. The criteria states that published, peer-reviewed and guideline studies will be preferentially considered; however, questions still remain regarding how the strength of the evidence will be considered? Will studies that do not follow GLP be considered? We suggest that a ranking system, such as the one used to evaluate studies for OECD SIDS (ranking of 1-4 based on the reliability) or the more qualitative approach used by NTP to review BPA. NTP included a few short paragraphs evaluating the utility, strengths and weaknesses of the study. Additionally, we seek clarification on the meaning of a "conservative" WOE approach.

Standard endocrine activity protocols and interpretation. In the endocrine activity criterion, DfE lists a number of protocols and outcomes that might fall under the auspices of endocrine activity; however, for each of the other endpoints, OECD or EPA standard testing protocols are listed as the preferred test method. We suggest that for endocrine activity testing, DfE list OECD or EPA standard testing protocols as the preferred test methods. These would include for, in instance, OECD Guideline 455 (Stably transfected human estrogen receptor-a transcriptional activation assay of estrogenic agonist-activity of chemicals, 2009) and the protocols developed for the EPA's Endocrine Disruptor Screening Program (EDSP). These offer standard, replicable protocols to assay a chemical interference with the endocrine system.

An advantage of standardized testing protocols is that they include clear guidelines for the interpretation of positive and negative results. Unfortunately non-standard studies often do not include such guidelines. Based on EPA's experience in evaluating tests for the EDSP, EPA should recommend guidelines for interpreting the results of these studies, including use of positive and negative controls, reproducibility, validation, etc. These will ensure internal consistency for DfE and consistency for companies, states, or other entities that might like to conduct an Alternatives Assessment. For example, it would be unfortunate if a 2-year multigenerational rat study was given less credence than a single, non-repeatable, sub-cutaneous injection of chemical investigating the methylation of an obscure gene.

Issues with endocrine activity as an alternatives criterion.

1. Endocrine activity is a mechanism of action rather than a measure of toxicity per se and as such is not directly related to hazard or to risk assessment. While there is considerable uncertainty regarding "low-dose" toxicity, ultimately it is the toxicity that is of importance to a safety assessment. The statement on endocrine activity provides no information on how endocrine activity relates to actual hazard or risk. For the public, identifying a substance as having endocrine activity suggests that it has serious hazard properties and risk, when in fact this might not be the case. This has been quite clearly illustrated for BPA, which has endocrine activity, but does not present human health risks according to international regulatory agencies. In short, the inclusion of endocrine activity among the alternatives criteria poses severe communications challenges that the Alternatives Assessment Criteria do not, but should address.

2. The criteria used to evaluate endocrine activity are much less well defined than those for the other endpoints. For instance, are the criteria weighted? Furthermore, the criteria do not seem consistent with EPA's criteria for evaluating data from Tier 1 of the EDSP. In view of this apparent inconsistency, either the criteria need to be considerably strengthened to be consistent with EDSP, or alternatives that meet the criteria will suffer from numerous data limitations that will require extensive explanation.

3. The summary description of endocrine activity for each alternative chemical is very briefly defined, especially considering the importance of these statements both for the alternatives assessment and for public communications. DfE should elaborate on what will be included, how conflicting results will be dealt with, how the strength of evidence will factor in and finally, how DfE will distinguish between endocrine activity at high doses (low risk) and low doses.

4. How is endocrine activity evaluated versus other endpoints? One might argue that given the scientific limitations reviewed above that it shouldn't be included, or should be given less weight in the assessment that the other criteria, which are much better defined and based on standard test methods. If that is not possible, then it is important that communications put those results into the context of the limitations discussed above - most notably that endocrine activity does not necessarily imply a health risk.

We thank you for this opportunity to provide comments on the EPA DfE draft Alternatives Assessment Criteria for Hazard Evaluation.

John E. Heinze, Ph.D.
Executive Director

Environmental Working Group
January 31, 2011

Libby Sommer
US EPA, Design for the Environment Washington DC
Sommer.elizabeth@epa.gov

January 31, 2011

Ms. Sommer,

Environmental Working Group (EWG) appreciates the opportunity to comment on the Design for the Environment (DfE) draft "Alternatives Assessment Criteria for Hazard Evaluation" (EPA 2011). This document outlines the criteria that DfE plans to use to evaluate and differentiate chemicals of concern for their impacts to human health and the environment.

The DfE program has been publicly presented as one of the flagship EPA efforts to reduce consumer exposures to hazardous or concerning chemicals. DfE evaluations have historically focused on products where there is concern for human exposure including household cleaners, fire retardants used in foam furniture, and most recently alternatives to bisphenol A in thermal paper. As such several additions to the proposed Alternatives Assessment tool could make the process an even more useful method of shifting industries away from highly toxic chemicals and reformulating products that have been shown to pose risks to consumers and/or the environment.

It is widely acknowledged that the 1972 Toxic Substances Control Act provides few tools for EPA to address the hazards posed by harmful chemicals. As EPA Administrator Lisa Jackson writes today in USA Today, "[TSCA] is insufficient for managing exposure to chemicals in the products and environment of the 21st century (Jackson 2011). EWG supports reform of federal chemical policies to require that companies prove that chemicals meet a risk-based standard to protect children and other vulnerable groups, before chemicals are added to products that fill American homes. While these reforms are put in place, we recognize the role the DfE program plays in guiding companies toward safer alternatives. We offer three basic points about strengthening the DfE alternative assessment process.

#1 DfE should examine production alternatives instead of limiting scope to drop-in technologies.
In many cases the DfE assessments are [highly] compromised by focusing exclusively on "drop-in" replacements instead of a broader examination of alternative technologies. An example is a multi-year effort to assess the varying toxicity of chemical fire retardants used in upholstered foam furnishings, which devoted just 3 of more than 200 pages to the fact that adding chemical fire retardants to foam was not necessarily the only, nor the most preferable method for achieving fire safe furniture (DfE 2004). In fact there is still no evidence that fire retarding foam

furniture improves consumer safety and ample evidence that historic uses of fire retardants in foam pose serious risks to human health and the environment (EPA 2010a). DfE is attempting to remedy this in the DecaBDE partnership, where the identification of "inherently fire-safe alternative technologies" is listed as a project milestone (EPA 2010b). We suggest this approach be required in all DfE assessments.

Unfortunately the current effort to find replacement chemicals for use in thermal paper neglects to examine any alternative ways of printing store receipts or transmitting purchasing data to customers. As thermal paper has been shown to contain and shed large amounts of Bisphenol A (EWG 2010), we believe that EPA should frame its alternatives assessment broadly. An exhaustive evaluation of alternatives may not be necessary. But EPA should consider a handful of present or near-future technologies that could avoid, for example, the need to coat paper with poorly studied chemicals as alternatives to BPA. Many retailers currently use ink-jet printers for store coupons, and an increasing number offer to email sales records averting the need for thermal receipts.

EWG suggests that the Alternatives Assessment document be modified to require an upfront assessment of the performance goal of the product in question (i.e. fire safe foam furniture or achievable sales records) and to identify any alternative processes that could achieve these goals while reducing the volume or toxicity of chemicals additives, or reducing the potential for human exposure.

#2 DfE should improve its characterization of hormone disruption.
EWG is encouraged by the proposal to include information on endocrine disruption as part of DfE assessments of chemical toxicity. Many of EPA's Action Plan chemicals affect reproductive and neurological signaling, making hormone disruption a key toxicological concern for DfE chemical assessments.

DfE currently proposes to review available evidence and classify chemicals as "potentially endocrine active" or "no evidence of activity" with appropriate documentation of the confidence level and the presence of equivocal or conflicting data. EWG recommends that the information be synthesized into a qualitative determination of "high," "medium" or "low" concern level for chemicals relative to other alternatives studied. This would be limited to chemicals with adequate toxicity information, and should consider generally the potential for human exposure. Those with inadequate information can be characterized as having "no data," which is different than low concern. DfE should update its alternatives assessment criteria as tiered strategies for identifying and categorizing hormone disrupting chemicals are validated.

#3 DfE must clearly summarize and synthesize the information gathered in its assessment documents.
The current proposal indicates 9 separate human health endpoints, and 3 environmental endpoints that shall be considered. DfE assessments can produce summary documents that evaluate a dozen or more chemicals and include hundreds of pages of detail. Previous DfE reports gather these data into a single massive, summary table as a "quick reference." However it is difficult if not impossible for a non-technical reader to clearly discern better and worse choices, which limits the utility of DfE reports to affect market changes.

The Foam Furniture evaluation did not include clear conclusions about the relative merits of the 15 chemical fire retardants studied, stating: "The Partnership designed this report to provide stakeholders with the ability to impose their own values on which chemicals to select and weigh information based on multiple considerations, focusing on environmental and human health attributes" (EPA 2004). However in actuality the lack of clear conclusions makes the overall report far less useful for downstream users who may lack the technical ability to interpret the data and for consumers seeking out better products.

EPA should modify the assessment approach to require a summary that distinguishes better and worse alternatives based on toxicity and potential for human contact, and/or environmental toxicity. This would be based on EPA expert evaluation of the available data, and must be clearly presented in a summary table. While qualitative in nature, these judgments should address the impact evaluate data gaps and scientific uncertainties to ensure that readers are guided to the most preferable alternatives.

In conclusion we appreciate the substantial efforts of the DfE program, including the draft criteria for evaluating the relative concerns posed by chemicals in DfE alternatives assessments. We propose three straightforward steps that will strengthen the DfE assessments, make better use of the data they gather, and improve the ability to sway markets and protect health.

Sincerely,

Sonya Lunder MPH
Senior Analyst
Environmental Working Group 1436 U Street, Suite 100
Washington DC 20009

References:

EPA. 2004. Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam. US Environmental Protection Agency, Design for the Environment Program.
http://www.epa.gov/dfe/pubs/flameret/ffr-alt.htm

EPA. 2010a. Polybrominated Diphenyl Ethers (PBDEs) Action Plan Summary. US Environmental Protection Agency, Office of Pollution Prevention and Toxics.
http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/pbde.html

EPA. 2010b. Flame-Retardant Alternatives for DecaBDE Partnership. US Environmental Protection Agency, Design for the Environment Program.
http://www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

EPA. 2011. Draft Alternatives Assessment Criteria for Hazard Evaluation. US Environmental Protection Agency, Design for the Environment Program. http://www.epa.gov/dfe/alternatives assessment criteria hazard eval jan2011 final draft3.pdf

EWG. 2010. Synthetic estrogen BPA coats cash register receipts, Environmental Working Group. http://www.ewg.org/bpa-in-store-receipts

Jackson L. 2011. "EPA concerned about chemical risks" Letter to the Editor, USA Today, January 31, 2011. http://www.usatoday.com/news/opinion/letters/2011-0 1 -3 1 - letters3 1 _ST1_N.htm

Global Automakers, Inc.
January 31, 2011

GlobalAutomakers

Aston Martin • Ferrari • Honda • Hyundai • Isuzu • Kia • Mahindra • Maserati
McLaren • Mitsubishi • Nissan • Peugeot • Subaru • Suzuki • Toyota

Delivered via email

January 31, 2011

Elizabeth Summers
EPA Design for the Environment
Washington, DC

Dear Ms. Summers,

Enclosed are the comments from Association of Global Automakers, Inc. (Global Automakers) on EPA's Design for the Environment (DfE) draft Alternatives Assessment Criteria for Hazard Evaluation.

Global Automakers is a trade association that represents international motor vehicle manufacturers, original equipment suppliers and other automotive related associations. We provide our members with information, analysis and advocacy on a wide range of legislative and regulatory issues impacting the auto sector. Our goal is to enable our members to provide high quality, environmentally sound products and services. We strive to assist members in continuous product improvement and, wherever possible, to not only meet but exceed safety and environmental standards. It is in that spirit that we provide the following comments and recommendations.

Please contact me at (202) 650-5562 of you have any questions or concerns.

Sincerely,

John M. Cabaniss
Director, Environment & Energy

Association of Global Automakers, Inc.

Comments on the Environmental Protection Agency's (EPA's)
Design for the Environment (DIE)
Draft Alternatives Assessment Criteria for Hazard Evaluation

January 31, 2011

The Association of Global Automakers, Inc.[1] appreciates the opportunity to provide comments to the Environmental Protection Agency (EPA) regarding the Design for the Environment (DfE) draft Alternatives Assessment Criteria for Hazard Evaluation. Global Automakers is a trade association that represents international motor vehicle manufacturers, original equipment suppliers and other automotive related associations. We provide our members with information, analysis and advocacy on a wide range of legislative and regulatory issues impacting the auto sector. Our goal is to enable our members to provide high quality, environmentally sound products and services. We strive to assist members in continuous product improvement and, wherever possible, to not only meet but exceed safety and environmental standards. It is in that spirit that we provide the following comments and recommendations.

Global Automakers and its members have been strong advocates for the DfE program and have worked collaboratively with the EPA via the Suppliers Partnership for the Environment to identify and adopt the best practices in the automotive industry. We believe strongly that working through such partnerships we can ensure safe work environments and safe products for consumers.

As drafted, the criteria presented in the November, 2010 draft "Design for the Environment Program: Alternatives Assessment Criteria for Hazard Evaluation" have a number of strengths we would like to recognize. Specifically, we applaud EPA's commitment to harmonization with existing schemes, including the United Nation's Globally Harmonized System (GHS); existing EPA schemes for both new and existing chemicals, and current EPA risk assessment guidance. Assuring a consistent and predictable approach for hazard evaluation both domestically and internationally is critical to facilitating common understanding and cooperation, maximizing positive outcomes, and making the best use of limited resources.

We would also like to recognize EPA's commitment to transparency by publishing these draft criteria for comment and for committing to evaluate the final criteria in a "lessons learned" approach after they have been used with upcoming DfE Alternatives Assessments. We understand that assessments are currently under way or will be conducted for bisphenol A (BPA), phthalates, decabromodiphenyl ether (decaBDE), hexabromocyclodecane (HBCD), and

[1] Global Automakers' members are American Honda Motor Co., American Suzuki Motor Corp., Aston Martin Lagonda of North America, Inc., Ferrari North America, Inc., Hyundai Motor America, Isuzu Motors America LLC, Kia Motors America, Inc., Mahindra & Mahindra Ltd., Maserati North America, Inc., McLaren Automotive Ltd., Nissan North America, Inc., Mitsubishi Motors North America, Inc., Peugeot Motors of America, Subaru of America, Inc., Toyota Motor North America, Inc ., ADVICS North America, Inc., Delphi Corporation, Denso International America, Inc., and Robert Bosch Corporation.

nonylphenol and nonylphenol ethoxylates (NP and NPE's). We look forward to the opportunity to review both the assessments and the "lessons learned" documents.

Recognizing the importance of selecting the right criteria for hazard evaluation, Global Automakers would like to offer the following recommendations. In light of EPA's recognition that these criteria "could form the basis for decision-making by other organizations" [page 3 of the draft] it is even more important that, when applied, these criteria guide the user to make selections that will result in optimal public health and safety protections. We believe there are three areas where additional clarification or explanation is essential to understanding the Agency's approach and selected criteria. Specifically, we are concerned about:

1. The lack of clarity regarding assessments of different types of hazards and guidance on how EPA will balance choices between safety and performance with human health and environmental effects.
2. The apparent move from a Precautionary Approach to adoption of the European Union's (EU) Precautionary Principle
3. Misleading or Overly Conservative Category labels

The lack of clarity regarding assessments of different types of hazards and guidance on how EPA will balance choices between safety and performance with human health and environmental effects

Global Automakers understands that the scope of the DIE hazard assessment process is limited to identification of concerns related to human health and environmental hazards. We recognize the importance of this focus as EPA strives to encourage the design and development of safer chemicals and technologies. A significant drawback to this approach, however, is the limited scope of types of hazards that are evaluated and factored into a substitute's identification. As EPA points out on page three of the draft criteria document, "the assessments are intended to reduce the likelihood of the unintended consequences that might result if poorly understood alternatives were chosen." Given the limited scope of the hazards assessed, it is highly likely that manufacturers and consumers will move away from chemicals that fall into the High, Medium and Low hazard categories and substitute chemicals that may have (or appear to have) a more benign environmental profile; however,such a shift may also result in inferior performance and/or sub-standard safety profiles. For example, some flame retardants may have a more benign environmental profile than others. Simply identifying those with high, medium and low hazards may cause manufacturers and consumers to move to the low hazard category in an effort to be "greener." That choice, if not informed by data and information on performance and safety characteristics of the low hazard options could well result in an increased risk of fire-related deaths and injuries. The same issues may apply to de-icing agents used in the airline industry, and brake friction products for the automotive sector, to name just a few.

Global Automakers strongly encourages EPA to be careful as they move forward with this hazard assessment scheme and to ensure that a full array of right-to-know data is made available to the public. If the DfE program is to have a positive impact on influencing safer and better manufacturer and consumer choices, then EPA must bear the responsibility of presenting a complete hazard profile; one that includes performance and safety assessments of alternatives in

addition to the human health and environmental hazard profile. However, one precautionary note is that EPA must remain diligent in recognizing the need to protect confidential business information. We appreciate that EPA recognizes the potential for unintended consequences and strongly support a more comprehensive assessment of hazards. Global Automakers recognizes that in order to provide this type of complete hazard assessment, industry stakeholders will need to be actively engaged in the process. Global Automakers is prepared to participate on issues related to the automotive sector.

The apparent move from a Precautionary Approach to adoption of the European Union's (EU) Precautionary Principle

Global Automakers is concerned about the statement under General Requirements, section 2.2 of the draft that states, "In reviews that include conflicting data, a weight of the evidence evaluation will inform the hazard designation with a **conservative approach...**" (emphasis added). In the absence of a more complete explanation or description of what a "conservative approach" means, it appears that EPA may be moving away from its traditional sound science and public policy approach to one more driven by rhetoric than science.

We recommend that a more complete explanation of what this new policy means and how it will be applied be included in the Alternatives Assessment document. If in fact the Agency does intend to move toward the Precautionary Principle, then this signals a significant, potentially counter-productive policy shift for EPA and the U.S. government in terms of environmental regulatory policy. To date, the U.S. has adhered to a precautionary approach when regulating chemicals, pesticides, products of biotechnology, etc. Sound science, weight of evidence, and concern for demonstrated public harm has driven the development of regulations. A comprehensive assessment of hazards and exposures has been the underlying basis for risk determinations. The U.S. has not in the past adopted the Precautionary Principle, which we believe is a more reactive regulatory approach that calls for regulation even in the absence of sound science and compelling evidence. Global Automakers recognizes that the DfE program is not a regulatory program nor is it driven by requirements of the Toxic Substances Control Act (TSCA). It can however be a precursor to identifying chemicals for future regulatory action. In light of this concern as well as potential TSCA reauthorization or TSCA amendments, we are concerned about the precedent this "conservative approach" could set for future EPA actions.

Misleading or Overly Conservative Category Labels

Global Automakers recognizes the need to have simple, easily understandable hazard categories. Moreover, we believe that the terminology of High, Medium, Low, etc. is appropriate. However, what appears to be missing is a category that recognizes that a chemical has undergone a series of tests and has shown no positive results. If this assessment process is to provide accurate information to the industrial sector and the public in order to allow them to make more informed choices, then the categories' headings or labels need to be as clear and specific as possible. For example, in the draft document, for the carcinogenicity category, a chemical that has been tested and has had negative results and no structural alerts would be classified as Low Hazard, and a chemical with equivocal results would be listed as a Moderate Hazard. For a program that intends to reach a broad audience, these categorizations are at best confusing and at worst

misleading. Global Automakers recommends that EPA develop category headings or labels that are more in keeping with plain English meanings. For example, a chemical that has undergone testing for carcinogenicity and has shown negative results and no structural alerts would more appropriately be listed as "No Concern," "No Concern at this Time," etc. Likewise, a chemical that exhibited equivocal results would more appropriately be listed as "Low concern at this Time." These same issues apply to subsequent toxicity categories identified in the draft document.

Global Automakers would like to emphasize that we are not seeking to undermine an aggressive approach to hazard evaluation, but rather we are trying to assure that as an industry that must meet the highest of performance and safety standards, that all relevant hazards, exposures, and risks are evaluated as "safer" choices are selected. Green chemistry and DfE programs are accelerating progress in the design and development of chemicals and component products that are environmentally benign and meet stringent safety and performance specifications. However, we know that there are many chemicals, some of which are being assessed for environmental and human health effects that are still essential to meet flammability standards, impact standards, and braking standards to name just a few. Trading one public health risk for another is a complicated undertaking and one which requires a complete understanding of all the downstream implications. The unintended consequences of shifting from one chemical to another need to be fully explored and vetted before major public policy choices are made. Inherent in that vetting process is ensuring that the public has all the data and information necessary to understand clearly the trade-offs that are being made.

Thank you for the opportunity to comment on this draft document and for the opportunity to share some serious concerns. We would welcome the opportunity to meet with you to discuss these concerns and look forward to a continued collaborative process as the DfE program is developed.

IBM Corporation
January 13, 2011

EPA Announces Mew Tool to Promote Safer Chemicals and Products
Arthur T Fong
to:
Elizabeth Sommer
01/13/2011 02:58 PM
Cc:
Lauren Heine, Shari Franjevic, Clive Davies, "Stone, Alex (ECY)"
Show Details

History: This message has been forwarded.

Hello Libby,

Happy New Year.

Couple of things jumped out as I was reading (skimping really) through the new Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation (http://www.epa.gov/dfe/alternatives_assessment_criteria_hazard_eval_nov2010_final_draft2.pdf).

May I trouble you to give me a better understanding of the decision to deviate from the more common practice of considering possible carcinogen, i.e., GHS Category 2, EPA Suggestive Evidence of Carcinogenicity, IARC 2B, EU CMR Category 3, EU Risk Phrases R40, as a "MODERATE" hazard level, to the November draft of the Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation, which ranks such possible carcinogens into the "HIGH" carcinogenicity hazard category.

Might cause confusion for industry users (or other users), as the EPA DfE carcinogenicity hazard ranking differs from other alternatives assessments tools, such as the Green Screen, Quick Screen, etc., which generally considered such substances to be in a "MODERATE" carcinogenicity hazard level. Don't want to see that become a roadblock for industry buy-in to the excellent DfE tool. Industry like harmonization, common practices/platforms. I think industry may look at this more carefully than usual because Steve Owens has said the DfE tool will be used as a guide for regulatory decisions for Chemical Action Plan chemicals, yes? But just my speculation on what interests industry.

Thank you very much for your courtesy.

Table 3. Criteria and Authoritative List Used to Designate **High** Hazard for Carcinogenicity

Authoritative Body	Classifications for High Hazard Designation
Globally Harmonized System (GHS) [6]	Category 1A – Known to have carcinogenic potential for humans Category 1B – Presumed to have carcinogenic potential for humans Category 2 – Suspected human carcinogens
National Toxicology Program (NTP)	Known to be Human Carcinogen Reasonably Anticipated to be Human Carcinogen
U.S. Environmental Protection Agency (EPA)	(2005/1999) Carcinogenic to humans, Likely to be carcinogenic to humans, or Suggestive evidence of carcinogenic potential (1996) Known/Likely (1986) Group A – Human Carcinogen, Group B – Probable human carcinogen, or Group C – Possible human carcinogen
International Agency for Research on Cancer (IARC)	Group 1 – carcinogenic to humans Group 2A – probably carcinogenic to humans Group 2B – possibly carcinogenic to humans
EU CMR List [21]	Category 1 – Known to be carcinogenic to humans Category 2 – Should be regarded as if carcinogenic to humans Category 3 – Cause for concern for humans owing to possible carcinogenic effects
EU Risk Phrases [21]	R45: May cause cancer R49: May cause cancer by inhalation R40: Limited evidence of a carcinogenic effect *And all combination risk phrases containing one or more of the above.*

Cordially,
Art

Arthur Fong, PhD
Toxicology and Chemical Management Corporate Environmental Affairs
IBM Corporation
925-277-5258 (t/l 8-227-5258)
fonga@us.ibm.com

ICL-IP America Inc.
January 7, 2011

New hazard criteria for DfE Alternatives Assessments ex
Hanna Silberberg
to:
Elizabeth Sommer
01/07/2011 03:35 PM
Cc:
Emma Lavoie, Caroline Baier-Anderson
Show Details

History: This message has been replied to and forwarded.

Hello Libby,

Happy New Year!

Our environmental specialist reviewed the environmental hazard criteria outlined in the draft document and have the following comments:

1. Persistency: section 4.2.2 first paragraph and also repeated in section 5.9: Environmental monitoring data may modify how a persistence designation is determined" . This is quite a vague sentence that is not transparent. We would appreciate receiving an explanation on the criteria to be used for evaluating monitoring data.

2. Persistency, same section as in (1): We would appreciate a clarification on the last sentence in the first paragraph: " If ready biodegradability test data are available but the chemical did not pass, the chemical is evaluated based on measured data for half life". Which data will be used for the half life evaluation, the ready degradation data? If yes, this doesn't seem appropriate, especially for hydrophobic substances, not to mention the very stringent conditions which are not representing real environment.

3. Bioaccumulation: section 4.2.3 first paragraph and repeated in section 5.10: "Environmental monitoring data will be considered when available". Please indicate how the data will be considered, what will be the rational and criteria used for the evaluation of the bioaccumulation. Without setting this criteria, the evaluation process is not transparent.

4. Bioaccumulation, page 19, second bullet under the section "When experimental BAF or BCF data are available". The paragraph is analyzing the situation when log BCF or BAF are below 2, which means the potential for bioaccumulation is below the "low" level criterion. However, the conclusion of "no bioaccumulation" is not accepted but rather an additional analysis is done using the model. This seems rather strange that so much

weight is given to a model when actual measurements are available. However, if the model is requested, for the case of measured BCF we can see the rational of using the model to take into consideration BAF. But, it is not clear why in the case of a measured log BAF (which is more conservative than BCF) that is below 2, it cannot be concluded that the substance is not bioaccumulative without consideration on a case to case basis.

5. Bioaccumulation, page 19, first bullet under the section "When experimental BAF or BCF data are not available". Both log Kow and log Koa are discussed. It is not clear why a measured log Kow that is less than 2 is not enough to agree that the substance is not bioaccumulative. Such a low log Kow falls under very low BCF or BAF (see Arnot and Gobas review). A measured log Koa is usually not available and to our best knowledge there are no guidelines for this kind of study. If there is an approved guideline, please include it in the list of test methods. Otherwise, some guidance is needed for the performance of such studies that will be accepted for evaluating the bioaccumulation potential.

Thanking you in advance for your response and clarification. Best Regards,

Hanna

Hanna Silberberg
Regulatory Affairs Manager ICL-IP America Inc.
Tel: (301) 765-1918
Fax: (301) 983-1917
Email: silberbergh@icl-ip.com

Institute of Scrap Recycling Industries, Inc.
December 10, 2010

From: "David Wagger" <DavidWagger@isri.org>
To: Emma Lavoie/DC/USEPA/US@EPA
Date: 12/10/2010 02:38 PM
Subject: RE: Postponement of todays Partnership meeting until Tuesday Dec 7 at 3pm

Thanks, Emma.

What happened at the conference call today? I had a conflicting meeting.

I read through the draft hazard assessment document. While I am not an expert in that field, a couple of things puzzled me.

1. Some of the units on the criteria were "mg/kg/day" while others were "mg/kg-bw/day". Are these the same or different? Doesn't "kg" refer to body mass?

2. The “very high” designation for acute aquatic toxicity is <1 mg/L. That seems to be a huge threshold. Most AAT values of importance to my work are much smaller.

If you could comment, I would appreciate it.

Thanks,

David

Intelligent Global Pooling Systems (iGPS)
January 31, 2011

January 31, 2011

Elizabeth Sommer
Design for the Environment Branch
Office of Pollution Prevention and Toxics
US Environmental Protection Agency
Ariel Rios Building (Mail Code 7406M)
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Ms. Sommer:

Intelligent Global Pooling Systems (iGPS) appreciates the opportunity to submit these comments in response to the U.S. Environmental Protection Agency's (EPA's) request for comments concerning its draft DfE *Alternatives Assessment Criteria for Hazard Evaluation*. iGPS is a leader in its field as the operator of a shipping pallet rental pool that is comprised of a revolutionary, lightweight, discretely traceable and 100% recyclable plastic pallet which provides an alternative to platforms made of wood. The iGPS pallet has shifted the paradigm for the pallet pooling industry because of the iGPS pallets' many positive attributes, not the least of which is the way in which the iGPS pallet has significantly enhanced the environmental profile of plastic pallets. Among the many positive features of the iGPS pallet is its ability to meet the strict technical standards for performance during both use and storage, including flammability standards. The iGPS pallet historically has incorporated low-levels of decaBDE to provide the flame retardancy necessary for a plastic pallet to meet those standards. Thus, iGPS has been an active and supportive stakeholder in EPA's on-going DfE Alternatives Assessment for decaBDE.

As discussed during the Stakeholder's meetings, iGPS is concerned that the draft Assessment Criteria, when applied, will give persons who make use of any assessments performed using the Criteria an overly simplistic understanding of the potential risks associated with assessed chemicals and the possible alternatives. Moreover, the limited nature of the draft Criteria will ensure that persons making use of the Criteria, and reviewing Hazard Assessments performed while using the Criteria, will fail to gain insight into other factors that affect risk associated with use of assessed chemicals and the possible alternatives; specifically, factors such as exposure during use and the impacts that other alternatives may have by potentially diminishing the performance and functionality of a product in which the alternative are used. In any final version of the Criteria, the Agency should clearly articulate the importance of a more robust assessment (that goes beyond mere hazard ranking comparisons) when evaluating

potential chemical substitutions. Further, EPA also should publish and seek comments on the manner in which the Agency intends to implement the results of assessments performed using its DfE Assessment Criteria. These concerns are described more fully below.

Undue Emphasis on Hazard Implies Hazard is the Sole Criteria in Selecting Substitutes

iGPS supports efforts to consider critically and carefully alternative chemicals when evaluating potential substitutes for another chemical in a specialized use. There are a multitude of factors that should be considered carefully, in order to avoid an outcome whereby a substitute is selected that does not serve to improve the safety and environmental profile of the end product in which it will be used. This requires careful consideration of all aspects of the potential impacts of use of a substitute chemical throughout the lifecycle of the product in which it would be used -- commencing with the product's manufacture, and carrying through its use and ultimately its disposal.

The Hazard Assessment Criteria proposed by EPA instead focuses primarily on 9 health effects end-points and 3 environmental fate and effects observations and assigns rudimentary scores to the various chemicals under consideration on the basis of these 12 hazard-based criteria. Thus, by applying the Hazard Assessment Criteria, crude comparative "rankings" of various alternatives might become possible (especially comparisons within the Criteria of a specific end point or group of endpoints). In many cases, such as with decaBDE, the hazards posed by many proposed alternatives have never been as comprehensively tested as decaBDE. In which case, Structure Activity Relationships will be used and other professional judgments made to provide estimates of results for certain hazard endpoints. This allows for the possibility that an alternative chemical, which has not been as thoroughly tested, might appear to be a "favorable" alternative to a well-studied chemical with known toxicity -- even one for which exposures can be safely controlled during use (e.g., by limiting its content in a product, thereby limiting its potential for release). The use of ranking systems and estimates means that imprecision is inherently built in to the draft Criteria. Care must be taken that the Hazard Assessment Criteria are not misinterpreted as being a definitive risk assessment or the results might be used erroneously to justify or encourage substituting untested alternatives for well-studied chemicals.

Adding to the inherent imprecision of the Hazard Assessment Criteria rankings is the fact that the current protocol was developed to evaluate only organic chemicals. Since many proposed alternatives to decaBDE are inorganic in nature, using a ranking system that fails to consider the unique attributes of inorganic substances may lead to ill-founded conclusions regarding the suitability of alternatives as safer chemicals.

The Agency apparently has not, however, provided similar simplified ratings for other factors that affect risk, such as the likelihood of there being greater or lesser exposure to an alternative during the manufacture, use and disposal of a product containing an alternative. It also is not clear from the draft document that was made available for comment how the Hazard Assessment Criteria will be balanced against and factored into what EPA previously has stated are the seven steps in conducting a full Alternatives Assessment. http://www.epa.gov/dfe/alternative_assessments.html. By failing to make reference to or acknowledge these other factors and their equal importance to a Hazard Assessment when

evaluating substitutes, EPA might unintentionally mislead users of Hazard Assessment documents who may conclude that hazard is the key area of focus for the Agency when determining the appropriateness of a potential chemical alternative. Along these lines, the Agency has also neglected to articulate how it might compare or prioritize all the relevant attributes of sustainability that are impacted by use of a chemical and its substitutes (e.g., Will human health risk be weighed more heavily than ecological risks? Will climate change effects such as greenhouse gas generating potential be considered? How will the impacts of substitution or solid waste production be weighed?).

The draft Hazard Assessment Criteria inadvertently implies that all potential substitutes will perform similarly, and are equally "viable". However, use of the Hazard Assessment Criteria alone will fail to assess fully other potential impacts of each substitute. For example, if the use of a particular substitute will make an end use product inherently weaker than the predicate product, or heavier (thus more energy consumptive during shipment and use), these factors also will have a potential health, safety, and environmental impact that should be considered and evaluated before use of the substitute is commenced. Significantly, the use of certain chemicals in a product might enhance or discourage the product's ability to be re-used repeatedly and perhaps even be recycled. EPA's final Criteria document should be written such that users are made aware that failing to take other important attributes (e.g., performance) into consideration could lead to decisions about substitutes that have unintended consequences that would run counter to the basic aspirations of the pollution prevention ethic that drives an alternatives evaluation such as the DfE program.

iGPS encourages EPA to enhance the Criteria to add references to such other factors and to publish for comment similar tools for assessing and taking them into account in the context of an overall Alternatives Assessment. Previously, EPA has stated that alternatives must satisfy a number of criteria that are not mentioned or referenced in the draft Criteria EPA has released. These include:

a) commercial availability;
b) technological feasibility;
c) delivery of the same or better value in cost and performance;
d) the potential for an improved health and environmental profile;
e) economic and social factors;
f) ability to provide lasting change; and
g) being of interest stakeholders.

iGPS believes such a list of criteria also should include consideration of: comparison of any impacts on worker and consumer exposures to a particular chemical and the alternatives under consideration if substitution were to occur; comparisons of energy consumptiveness; end-of-life and recycling impacts; and additional "life cycle" factors that should be evaluated.

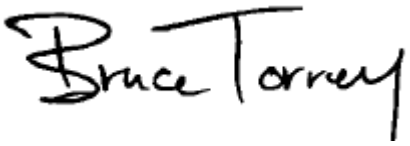
Procedural and Implementation Concerns

Seeking input on the draft Hazard Assessment Criteria is an important mechanism for improving Agency efforts. iGPS encourages EPA to make clear and solicit comments on the ways in which EPA intends to make use of the results of the various Alternatives Assessments

that are being performed using the Hazard Assessment Criteria. The Agency has acknowledged that Alternative Assessment results will carry great weight both within the Agency and with interest groups, consumers, as well as state and local governments. Moreover, reference to such Assessments as critical components of EPA regulatory undertakings announced in various "Action Plans" conveys the Agency's apparent intent to rely on the results of such Assessments to inform regulatory decision making. Notably, actions taken pursuant to Section 6 of TSCA require that an assessment of substitutes be made by the Agency in the course of determining appropriate options for regulatory actions to mitigate chemical-related unreasonable risks. However, the unsophisticated nature of the Hazard Assessment Criteria is likely to generate results that might provide false impressions about the viability and availability of substitutes to Agency staff and others who seek to make use of the results in critical regulatory efforts. Before implementing the Criteria in the context of an overall Alternatives Assessment, iGPS requests that greater effort be given to discussion in public, and with the opportunity for review and comment, of the ways in which the Criteria and any results of their use will inform EPA decision makers in the context of Risk Management Programs.

iGPS intends to remain an enthusiastic participant in the DecaBDE Alternatives Stakeholders' Process, and to work with EPA to develop appropriate criteria for fully assessing chemicals-related risks and to identifying alternative chemistries which provide an effective means to reduce such risks. Please contact me at 407-367-4459 if you would like to discuss these comments.

Sincerely,



Bruce Torrey
Vice President, Technology

National Institute of Environmental Health Sciences (NIEHS)
December 10, 2010

From: "Dunnick, June (NIH/NIEHS) [E]" <dunnickj@niehs.nih.gov>
To: Emma Lavoie/DC/USEPA/US@EPA
Date: 12/10/2010 02:59 PM
Subject: Review of alternative criteria

Emma,

Comments on today's review:

1. put BAF or BCF in the "terms" list; what are the units in Table 15?
2. put in the document how are epigenetic mechanisms will be captured
3. give a more detail example of how neurotox endpoints will be modified for studies of longer or shorter durations (for example if a chemical dose causes neurotox at 100 mg/kg in a 28 day study and in a 90 day study how will the "potency" be determined for each study?
4. More explanation is needed as to why a hazard call will not be made on endocrine disruption activity.
5. High throughput screening = ToxCAST. EPA considers these data to be "research" and will not integrate into the EfD reports (a note should be added on this).

Best regards. June
--
Dr. June K. Dunnick
NIEHS
P. O. Box 12233
Research Triangle Park, NC 27709
919 541 4811

National Resources Defense Council (NRDC)
January 31, 2011

NATURAL RESOURCES DEFENSE COUNCIL

January 31, 2011

Office of Pollution Prevention and Toxics (OPPT), EPA
Submitted via email to Libby Sommer, sommer.elizabeth@epa.gov

Re Comments on "Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation." January 2011, Draft

On behalf of the Natural Resources Defense Council (NRDC), we submit the following comments on the Design for the Environment (DfE) draft criteria for chemical hazard evaluation.

NRDC uses law, science, and the support of more than 1.2 million members nationwide to protect the planet's wildlife and wild places and to ensure a safe and healthy environment for all living things. NRDC has no direct or indirect financial or fiduciary interest in the manufacture or sale of any industrial or HPV/Inert chemicals that may be selected for review using these hazard criteria. More information is available at the NRDC website www.nrdc.org.

NRDC supports the goals of EPA's DfE to identify safe alternatives to chemicals of concern such as BPA, phthalates and flame retardants. The DfE label gives consumers confidence that they are choosing products that are safe for their families and the environment, provides important information for retailers and manufacturers, and creates an incentive to place a priority on health and environmental concerns in chemical alternatives. The criteria chosen for hazard evaluation of these alternatives forms the foundation of the DfE program and it is critical that these criteria are robust and comprehensive to be truly protective of human health and the environment.

Therefore, the process of developing the criteria for hazard evaluation is very important and we appreciate the opportunity to give comments.

General comments on Criteria for Hazard Evaluation.
We support the inclusion of carcinogenicity, genotoxicity/mutagenicity, reproductive and developmental toxicity, neurotoxicity, dermal toxicity and sensitization as endpoints to be evaluated. We also strongly support the inclusion of endocrine activity as an endpoint for inclusion in the hazard evaluation but rather than a qualitative assessment, a quantitative assessment should be applied which would create high, moderate and low criteria for endocrine activity. Until EPA's Endocrine Disruptor Screening Program is producing results, the potential for endocrine activity can be determined from existing scientific literature and structural similarities.

Though we agree with the inclusion of these endpoints, as it is now written, U.S. EPA's proposal is overly narrow and omits significant hazards. There are several other toxicological endpoints which should be added to the hazard criteria, including a broader definition of respiratory toxicity to include endpoints beyond irritation or sensitization, hepatotoxicity, nephrotoxicity, hematotoxicity, immunotoxicity, cardiotoxicity, reactivity and the development of oxidative stress, and epigenetic changes. The environmental hazard traits should also be more comprehensive to include domestic animal toxicity; impacts on wildlife growth, survival, development and reproductive toxicity; loss of genetic diversity/biodiversity; and mobility in environmental media.

It is important to note that the creation of hazard criteria is a framework for the types of data that could be considered or included for each of the endpoints. Notably, once finalized this document does not create any requirements for businesses or industries. They do not require testing or submission of data. There is no regulatory impact. They simply address the kinds and categories of data which should be considered when determining the safety of an alternative chemical. Therefore, this document should be broad and more comprehensive than it is currently drafted.

In particular, U.S. EPA should consider incorporating many of the same hazard traits and endpoints which have been designated by California's EPA, Office of Environmental Health Hazard Assessment (OEHHA) in their draft "Identification of Hazard Traits, Endpoints, and Other Relevant Data for Inclusion in the Toxics Information Clearinghouse in Green Chemistry Initiative."[1] These rules proposed by California EPA were based on review of the existing scientific literature and are broader and more scientifically up to date and consistent with recent recommendations by the National Academy of Sciences (NAS).

U.S. EPA should use an approach which defines early indicators of harm by considering early changes or perturbations as an adverse effect. This will be more consistent with recommendations of the NAS and will have the potential to decrease the amount of animal testing, while allowing for a better assessment of multiple chemicals and sensitive life stages.

Finally, the draft criteria do not include explicit considerations for metabolites or degradation by-products. Many chemical compounds have greater toxicity after metabolism or degradation and an evaluation which does not consider this likely scenario could result in regrettable substitution.

[1] Division 4.5, Title 22, California Code of Regulations, Chapter 54. Green Chemistry Hazard Traits. The public notice with links to the current draft of the rules is at http://oehha.ca.gov/multimedia/green/gc121710.html

The metabolism or degradation of a chemical into another form which meets the criteria for any of the endpoints in the hazard evaluation should be included in any assessment of alternatives.

Specific comments on Criteria for Hazard Evaluation.

1. *Routes of exposure.*

Section 2.1 of the draft states "Data for all relevant routes of exposure will be evaluated." However, the only routes of exposure discussed for specific endpoints, such as reproductive and developmental toxicity, are oral, dermal, and inhalation. Additional relevant routes of exposure which should be included are transplacental transport, lactational transfer, as well as experimental animal models which use injection either as intraperitoneal or subcutaneous administration. All of these routes of exposure are relevant for fetal and neonatal exposure to chemicals during critical periods of development.

For example, in the case of bisphenol A (BPA), laboratory studies that have found evidence of a predisposition to cancer or brain and behavioral abnormalities have dosed the animals via subcutaneous injection during critical windows of development such as in the womb (prenatal) or early in life (neonatal). Independent peer-reviewed research has demonstrated that during these critical windows of development, the capacity to breakdown or metabolize BPA is not developed and therefore, the route of administration has not been found to change circulating levels of BPA.[2]

In the 2008 report of the National Toxicology Program's (NTP) Center for Evaluation of Risks to Human Reproduction on BPA, the NTP wrote the following regarding route of administration of BPA in animal studies:

> "Taken together these data indicate that, compared to adults at a given dose, neonatal rats (and presumably mice) metabolize bisphenol A more slowly and suggest that differences in circulating levels of free bisphenol A arising from oral and subcutaneous routes of administration as a result of "first-pass metabolism" are reduced in fetal or infant animals compared to adults." and "While more research in this area is warranted, data from studies where bisphenol A was given by subcutaneous injection were considered as useful in the NTP evaluation as oral administration when treatment occurred during infancy when the capacity to metabolize bisphenol A is low."[3]

2. *Define adverse effect.*

EPA should define what an "adverse effect" is in Section 3, "Terms". California's EPA has adopted the following definition, which we support:

[2] Taylor, J. A., W. V. Welshons, et al. (2008). "No effect of route of exposure (oral; subcutaneous injection) on plasma bisphenol A throughout 24h after administration in neonatal female mice." Reprod Toxicol 25(2): 169-76.
[3] Chapin, R. E., J. Adams, et al. (2008). "NTP-CERHR expert panel report on the reproductive and developmental toxicity of bisphenol A." Birth Defects Res B Dev Reprod Toxicol 83(3): 157-395.

"Adverse effect" for toxicological hazard traits and endpoints means a biochemical change, functional impairment, or pathologic lesion that negatively affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge. "Adverse effect" for environmental hazard traits and endpoints means a change that negatively affects an ecosystem, community, assemblage, population, species, or individual level of biological organization."[4]

3. *Carcinogenicity.*

The definition of carcinogenicity should include the development of malignant, benign, and pre-neoplastic lesions and should also include considerations for non-genotoxic and non-mutangenic mechanisms of carcinogenesis such as hyperplasia, decreased apoptosis or epigenetic changes in gene expression. The International Agency for Research on Cancer (IARC) deems an agent carcinogenic if it is "capable of increasing the incidence of malignant neoplasms, reducing their latency, or increasing their severity or multiplicity."[5] The IARC preamble should be used to update carcinogenic criteria.

Additional authoritative lists used to designate hazard should include Chemicals known to the State of California to cause cancer, in Title 27, California Code of Regulations, Section 27001.

4. *Reproductive and Developmental Toxicity.*

A table listing authoritative bodies and criteria for high, moderate and low hazard should be created in section 4.1.4, "Reproductive and Developmental Toxicity". Additional authoritative lists should include:

i. Chemicals known to the State of California to cause reproductive or developmental toxicity, in Title 27, California Code of Regulations, Section 27001;
ii. The U.S. National Toxicology Program;
iii. The U.N. Globally Harmonized System for Classification and Labeling;
iv. The National Institute for Occupational Safety and Health's Pocket Guide to Chemical Hazards;
v. identification in a report published by the National Academy of Sciences' National Research Council or Institute of Medicine;
vi. IARC designation for transplacental carcinogenicity and
vii. Recognition by California, other states, the United States or other nations of the chemical substance posing a reproductive or developmental toxicity hazard.

5. *Environmental Toxicity and Fate considerations*

The proposed criteria only consider aquatic toxicity and do not consider effects of chemicals on domesticated animals or wildlife. There is also no consideration of loss of genetic diversity or

[4] Division 4.5, Title 22, California Code of Regulations, Chapter 54. Green Chemistry Hazard Traits. Page 4. http://oehha.ca.gov/multimedia/green/pdf/GC_packett121710.pdf
[5] International Agency for Research on Cancer (IARC), Preamble to the IARC Monographs: A. General Principles And Procedures: Objective and scope. http://monographs.iarc.fr/ENG/Preamble/currenta2objective0706.php (accessed August 25, 2009)

biodiversity. Whenever this information is available, it should be included in any analysis of the safety of alternatives.

Thank you for the opportunity to comment and for your careful consideration of these comments.

Sincerely,

Sarah Janssen, MD, PhD, MPH
Senior Scientist
Natural Resources Defense Council

North American Metal Packaging Alliance, Inc. (nampa)
January 31, 2011

NORTH AMERICAN METAL PACKAGING ALLIANCE, INC.
1203 19th Street NW, Suite 300 · Washington, DC 20036-2401 · 866-522-0950 · www.metal-pack.org

January 31, 2011

Via E-Mail

Ms. Elizabeth Sommer
Design for the Environment Program
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460-001

Re: Alternatives Assessment Criteria for Hazard Evaluation

Dear Ms. Sommer:

The North American Metal Packaging Alliance, Inc. (NAMPA)[1] is pleased to submit these comments on the draft alternatives assessment criteria for hazard evaluation to be used in the U.S. Environmental Protection Agency's (EPA) Design for the Environment (DfE).

NAMPA applauds EPA's efforts in developing the draft DfE alternatives assessment criteria document. It clearly identifies how EPA will utilize various study data in evaluating and differentiating chemicals based on their concern for human health and environmental hazard. We fully support EPA's weight of evidence approach and its intent to rely on studies conducted under good laboratory practices with recognized, validated test protocols.

While we appreciate the need to consider available data on all routes of exposure, NAMPA urges EPA to recognize that studies conducted using relevant exposure routes should provide the primary basis for assessment. For example, studies in which test animals are directly injected with a test substance, which bypasses normal metabolic processes, are not directly relevant in hazard assessment. Likewise, NAMPA recommends that the document reflect *that in vivo* studies should be given greater weight than *in vitro* or studies conducted on cellular levels. NAMPA also suggests that EPA's criteria include consideration of study adequacy, including studies that may be published and/or peer reviewed. Study size, replication of study results, and availability of raw data should be factors in EPA's consideration of a study in its assessment approach.

[1] NAMPA is a not-for-profit corporation committed to protecting health through the safety of metal packaging and metal packaged foods. NAMPA's membership includes companies and associations representing various sectors along the supply chain for the food and beverage packaging industry.

Finally, while NAMPA recognizes that EPA's intent is to apply these assessment criteria for hazard evaluation for potential alternatives for chemicals of concern, we urge EPA to apply the same deliberative process to the purported chemicals of concern. We would note that various regulatory agencies across the globe have conducted thorough assessments of bisphenol-A (BPA), one of the chemicals included in EPA's DfE program, and repeatedly have found that low levels of BPA do not present a health risk to children or adults. NAMPA recommends that EPA conducts its own assessment of BPA, using the same robust and scientifically sound criteria it would intend to apply to BPA alternatives, as a preliminary step.

Thank you for this opportunity. If you or your staff has any questions regarding this letter, please do not hesitate to contact me. I can be reached at kroberts@metal-pack.org or (443) 964-4653.

Regards,

Kathleen M. Roberts
Executive Director

The Proctor & Gamble Company (P&G)
January 31, 2011

The Procter & Gamble Company
NA Regulatory & Technical Relations
One Procter & Gamble Plaza (C-6)
Cincinnati, OH 45202
www.pg.com

January 31, 2011

Ms. Libby Sommer
US EPA Headquarters
Ariel Rios Building
1200 Pennsylvania Avenue, N. W.
Mail Code: 7406M
Washington, DC 20460
sommer.elizabeth@epa.gov

Re: Comments on Design for the Environment Program Draft Alternatives Assessment Criteria for Hazard Evaluation[1]

Dear Ms. Sommer:

The Procter & Gamble Company (P&G)[2] appreciates this opportunity to comment on the draft document, *Alternatives Assessment Criteria for Hazard Evaluation* ("Alternatives Document") that was recently offered for comment by the Design for the Environment (DfE) Program. P&G values the importance of aligning protection of health and the environment with the pursuit of sustainable innovation. We believe some of the world's toughest sustainability challenges will be solved through innovation, and we are committed to developing technologies, operations and products that will assist in this goal.

Alternatives assessment can be an important tool in comparing chemical substances and developing new products and processes, especially as new information emerges about health and environmental risk. Our interest in alternatives assessment and the policies of the DfE program led us to participate in the Safe Detergent Stewardship Initiative, in which we achieved the "Champion" status in the product formulator category. P&G supports the proper execution of

[1] U.S. EPA Office of Pollution Prevention and Toxics, "Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation," Draft (November, 2010). Available at http://www.epa.gov/dfe/alternatives_assessment_criteria_hazard_eval_nov2010_final_draft2.pdf

[2] The Procter & Gamble Company is the world's leading consumer products company operating in more than 80 countries worldwide. Our strong portfolio of recognized, quality and leadership brands includes numerous household, industrial and personal care products. Procter & Gamble is fully committed to helping solve sustainability challenges, which is embedded in our Company Purpose "to improve the lives of the world's consumers, now and for generations to come." Please visit http://www.pg.com for the latest news and in-depth information about P&G and its brands.

alternatives assessment that evaluates the key decision elements from the DfE's approach of "Informed Substitution," including technological feasibility, health and environmental profiles, equal or better performance, and the risks, costs and benefits of existing substances and possible alternatives.

As we understand the role of the Alternatives Document, it is intended to "inform substitution" when individual companies make decisions about what might be a safer alternative to an existing chemical used in a particular application. We understand that EPA also intends to use the DfE approach for Chemical Action Plans for specific substances[3]. Specifically, the Alternatives Document would be used to "place chemicals on a continuum of relative hazard to inform decision making."[4] The Alternatives Document generally defines "High", "Medium" and "Low" concern levels, based on quantitative or qualitative hazard classifications drawn from a variety of policy and regulatory contexts.
In general, the criteria set forth in the Alternatives Document build upon hazard classification schemes and testing protocols that have been used by EPA and other regulatory agencies for several years. Accordingly, P&G believes that most of the criteria provide a reasonable basis for evaluating the hazards of chemicals in the DfE program. However, these classifications do not attempt to address exposure factors that are necessarily part of the health and environmental risks associated with particular technologies. We continue to assert that the lack of emphasis on exposure considerations is a weakness of the DfE approach that fails to provide a well informed, holistic view of alternatives assessment and informed substitution.

We encourage the addition of clear explanation in the Alternatives Document that the hazard criteria are not intended to suggest that decisions should be made on the basis of hazard evaluations alone. Rather, hazard evaluation is but one component of a complete alternatives assessment. Other components necessarily include risk assessment (including an assessment of the magnitude of the exposure and risk of a substance and possible alternatives and the likelihood of those respective risks occurring), economic and social impact evaluations, and cost and technological performance assessments, among others. P&G is particularly concerned that, without further clarification, DfE's application of the criteria to alternatives assessments for Chemical Action Plan chemicals could result in an expectation that potential alternatives would be identified on the basis of hazard alone.

With that said, P&G supports the concept of developing hazard criteria for use in DfE alternatives assessments. In these comments we offer suggestions for modifying the hazard classification criteria in the Alternatives Document.

1. *Harmonization of classifications and endpoints*

DfE is proposing to selectively adjust the categorization of several endpoints by creating categories that are not comparable with the U.N. Globally Harmonized System for Classification and Labeling (GHS) or which do not exist in common pollution prevention (P2) programs (such as "Very High" and "Very Low"). DfE is also proposing to selectively alter cut-off values for some endpoints (e.g. acute, acute aquatic, reproductive and developmental). With this approach,

[3] Announcements section of the Design for Environment Home Page, at http://www.epa.gov/dfe/
[4] Alternatives Criteria, at pg. 3.

DfE's proposals will deviate from well-accepted approaches in safety and green chemistry programs. P&G strongly recommends that DfE promote harmonization in categories and endpoints by adopting the same cut-off values currently applied in the GHS and P2 programs. Failure to do so will create a modification of existing, well-established programs, and the significant potential for misapplication and confusion on the part of those applying the criteria in alternatives assessments.

2. Approach to Equivocal Data

For two of the endpoints in the document – carcinogenicity (4.1.2) and mutagenicity/genotoxicity (4.1.3) – a "Moderate" risk characterization has been assigned when available data yield "equivocal results." By its very nature, "equivocal" data are information that is subject to two or more interpretations and thus carries substantial uncertainty. Such data would not tend to support any conclusion about the hazard of a substance. There certainly is no reason to apply a "Medium" hazard label where available data cannot support a reasoned evaluation of the chemical. We recommend that OPPT consider including additional descriptor categories to the Alternatives Document to recognize situations where there are no data on a particular endpoint or where existing information suffers from some inadequacy that does not call for a reliable assignment of a "High," "Medium" or "Low" label.

3. Cancer Criteria

The carcinogenicity criterion (4.1.2) indicates that a "High" level of concern is assigned where there are "positive results" regarding cancer. This description is further defined by reference to cancer weight of evidence descriptors that have been used in a variety of contexts, including the Globally Harmonized System, the National Toxicology Program, the EPA Cancer Guidelines, the International Agency for Research on Cancer, the European Union's Carcinogenic, Mutagenic or Toxic to Reproduction List, and the European Union's Directive regarding Risk Phrases. While the cancer classification criteria issued in these contexts vary, all of these systems recognize that the strength of evidence for human cancer among chemicals varies over a continuum.

We are concerned that the Alternatives Document has assigned a "High" concern level to classification categories that were intended, in their original source framework, to reflect a relatively low concern about the potential for human cancer. Specifically, the cancer criterion in 4.1.2 is grouping together chemicals for which there is compelling evidence of human cancer with chemicals for which there may be only one animal study that does not show a statistically significant increase in tumors.

The Alternatives Document has included in the "High" concern category any chemical that falls into the "Suggestive Evidence of Carcinogenic Potential" descriptor category under the Agency's own March 2005 final Cancer Guidelines[5]. EPA reserves this classification in its cancer policies for situations where an animal study shows a small increase in tumors, but the increase is not statistically significant or there is evidence that background factors, rather than

[5] EPA, "Guidelines for Carcinogen Risk Assessment," EPA/630/P-03/001F (March 2005). The explanation of the cancer descriptors used by EPA is found at p.2-54 of the Guidelines.

the tested chemical, may be causing the tumors. Chemicals in this category have such a weak base of evidence to support a cancer determination that EPA does not try to set cancer-based health benchmarks for these chemicals. P&G believes that chemicals carrying the "Suggestive Evidence" descriptor should be categorized, at most, in the "Medium" concern category.

We urge EPA to reconsider its approach to the cancer criterion to provide better alignment between "High," "Medium" and "Low" concern levels and the gradations of cancer evidence in the EPA Cancer Guidelines to ensure consistency for application in "informed substitutions" and possibly in the Chemical Action Plan regulatory context.

* * *

In closing, we thank you for the opportunity to offer comments on the Alternatives Document. As noted at the beginning of these comments, P&G has collaborated with the DfE program through ongoing partnership on the Safe Detergent Stewardship Initiative. We offer our comments in the interest of advocating a more holistic approach to alternatives assessment that will better inform EPA's chemical assessment activities and support technological innovation that leads to meaningful improvements in environmental performance.

Should you have any questions about these comments, please contact me at (513) 983-2531 or froelicher.jm@pg.com.

Sincerely,
Julie Froelicher
NA Regulatory & Technical Relations Manager
The Procter & Gamble Company
One Procter & Gamble Plaza
Cincinnati, OH 45202
(513) 983-2531
froelicher.jm@pg.com

STATE OF WASHINGTON
DEPARTMENT OF ECOLOGY
PO Box 47600 • Olympia, WA 98504-7600 • 360-407-6000
TTY 711 or 800-833-6388 (for the speech or hearing impaired)

January 31, 2011

Ms. Libby Sommer
Design for the Environment (DfE)
US Environmental Protection Agency
1200 Pennsylvania Avenue, NW, Mail Code 7406-M
Washington, DC 20460

RE: DfE Draft Alternatives Assessment Criteria for Hazard Evaluation

Dear Ms. Sommer:

The Washington State Department of Ecology (Ecology) is pleased to provide comments on the U.S. Environmental Protection Agency's (EPA) Draft Alternatives Assessment Criteria for Hazard Evaluation. Ecology would like to take this opportunity to thank EPA for its work to continue to advance the science of alternatives assessment.

The DfE criteria are used by Ecology to conduct our alternative assessment evaluations. We urge EPA to continue to support and promote the DfE methodology, since it provides the states and other organizations with a consistent framework to conduct chemical hazard assessments.

Attached are Ecology's comments on the proposed criteria that are suggestive of work that EPA could do which would make the criteria even more useful. One of the challenges faced by state and local governments is how to interpret a wide range of technical sources to meet these criteria. EPA could expand upon its fundamental work to include additional sources of information and provide an even more beneficial product to assist organizations using the criteria.

If you have any questions on our comments, please contact Dr. Alex Stone (alex.stone@ecy.wa.gov) of my staff.

Sincerely,

Ken Zarker, Manager
Pollution Prevention and Regulatory Assistance Section
cc: Dr. Alex Stone, Ecology

Washington State Department of Ecology comments on EPA's Design for the Environment (DfE) Alternatives Assessment Criteria for Hazard Evaluation

General Comments:

Washington State Department of Ecology (Ecology) supports DfE's efforts to quantify important hazard criteria and to coordinate its efforts with international requirements such as the Global Harmonization System. Because of DfE's efforts in this area, Ecology has decided to use these hazard criteria as the basis for the hazard evaluation portion of any alternative assessments conducted by Ecology. Ecology has conducted alternative assessments as directed by the Washington Legislature and will conduct further assessments over the upcoming years. Ecology appreciates DfE's efforts to provide guidance on how to conduct a hazard assessment and to make its methodology open, transparent and scientifically defensible.

Ecology further supports and thanks DfE for its efforts to assist others interested in conducting alternative assessments by providing clear and useful guidance. One of the strongest benefits of the DfE protocol is its efforts to standardize the approach to hazard assessment. This enables different organizations to reach similar conclusions based upon the same criteria when using this standardized methodology. This strengthens the benefits of conducting a hazard assessment when such uniformity and consistency is available.

The only major addition Ecology would recommend is that DfE considers extending its guidance on several hazard criteria by including ranking of method results other than those currently appearing in the methodology. One the strongest benefits provided by this work is the manner in which DfE assigns a relative severity for toxicity data in each hazard criteria. DfE, however, limits this work to commonly available toxicity values such as LD50 (the concentration at which 50% of the population dies) or LOAEL (lowest observed adverse effect level). However, many toxicity studies are available using other toxicity endpoints. DfE can make this guidance more useful to users such as Ecology who may not have the resources and technical expertise available to DfE if it expands upon these ranking criteria to include these other toxicity endpoints. Additional information will be provided in subsequent comments on specific toxicity criteria.

Skin/Eye Irritation:

The Standard Draize Test has been a widely used method to determine level of skin and eye irritation. Although it may not exist as one of the standard methods used by GHS or OECD, considerable data exists from these tests and it may help to fill in any gaps in chemical hazard data until the results from newer methodologies become more prevalent. Any guidance that DfE could provide on evaluating the results from a Standard Draize Test would help implementing a hazard assessment for those organizations which do not have access to experts in this field.

Acute Mammalian Toxicity, Multiple Dose Toxicity, Reproductive and Tumorigenic Data:

Many scientific journal articles and some databases such as the Registry of Toxic Effects of Chemical Substances (RTECS) include extensive data on toxicity endpoints such as TDLo (the Lowest published Toxic Dose), LDLo (the lowest published lethal dose), TCLo (the Lowest

published toxic concentration, LCLo (lowest published Lethal Concentration), TD (toxic dose) and TC (toxic concentration) as alternative values for evaluating these toxicity criteria. The DfE guidance would be greatly improved if DfE could either provide similar ranking for these toxicity results as was done with LD50 and other toxicity results included in the methodology or provide some guidance on how to compare these results with the criteria already established.

Mutagenicity:

As with skin/eye irritation results, considerable historic data exist from the results from testing methods not currently included in GHS and OECD sources. Until data are available using these more recent methodologies, the DfE criteria would be improved if DfE could provide some guidance on how to interpret these results or to compare them with existing methodologies. For example, RTECS reports results under headings such as 'DNA damage' or 'cytogenic analysis'. If these results can be used in a hazard assessment, DfE should include information in the guidance on how to interpret the results. If they should not be used for technical reasons, their omission should also be explained.

Endocrine Disruption

Ecology supports the addition of endocrine activity to the list of DfE criteria. Recent scientific developments have indicated the impact endocrine disruptors may be having upon human health and the environment. Therefore, although the science of endocrine disruption or endocrine activity is only in the infancy, the inclusion of endocrine activity among the list of DfE criteria emphasizes the importance of this hazard criteria and the need for chemicals to be evaluated for their impact upon the endocrine system. No hazard assessment is complete without evaluating endocrine activity and Ecology is pleased to see that DfE recognizes this serious data gap.