Sustainability and Microconstituent Management What Are the Big Questions?

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NEWEA Conference, Bentley University, Waltham, MA

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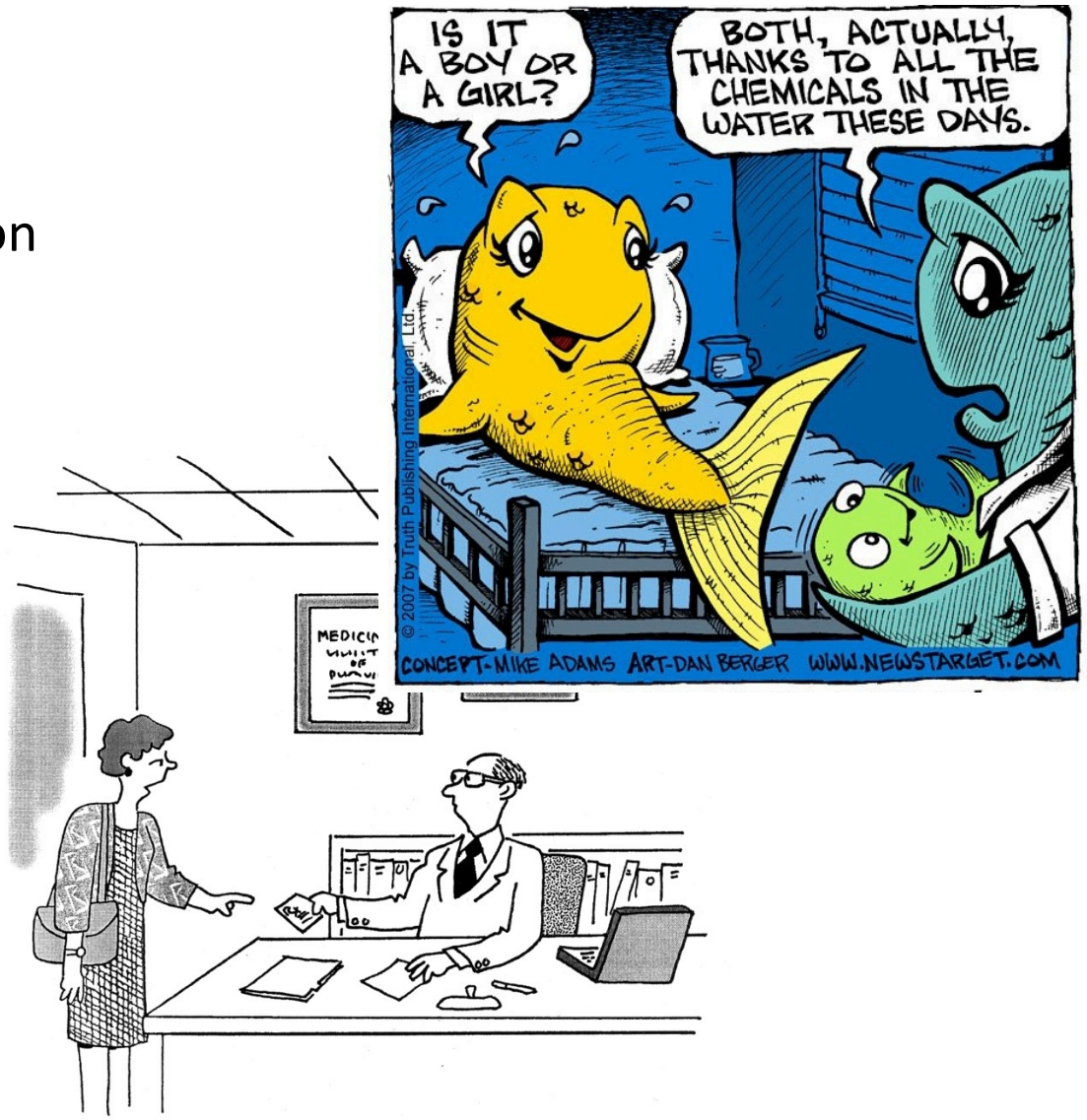
Web of Science: “pharmaceutical” OR “personal care product” OR “medicine” AND “surface water” OR “soil” OR “wastewater”

Issues

- Biodegradation
- Environmental attenuation
- Transformation products
- Biosolids
- Aquifer impacts
- Monitoring
- Antibiotic resistance
- Human health risks
- …



"Will this prescription interact with the meds already in my drinking water?

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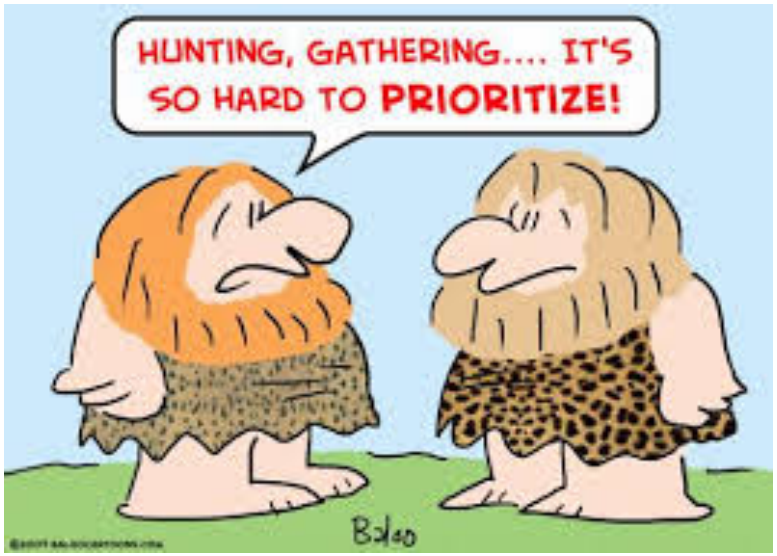

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"Key Question" Exercise

- SETAC Global Pharmaceutical Advisory Group
- Horizon scanning method
- Systematic way to identify major research and policy directions
- Involves people from a range of sectors
- Previous exercises on ecology, conservation, biodiversity, and agriculture

The top 100 questions of importance to the future of global agriculture

Jules Pretty[1]*, William J. Sutherland[2], Jacqueline Ashby[3], Jill Auburn[4], David Baulcombe[5], Michael Bell[6], Jeffrey Bentley[7,8], Sam Bickersteth[9], Katrina Brown[10], Jacob Burke[11], Hugh Campbell[12], Kevin Chen[13], Eve Crowley[14], Ian Crute[15], Dirk Dobbelaere[16], Gareth Edwards-Jones[17], Fernando Funes-Monzote[18], H. Charles J. Godfray[19], Michel Griffon[20], Phrek Gypmantisiri[21], Lawrence Haddad[22], Siosiua Halavatau[23], Hans Herren[24], Mark Holderness[25], Anne-Marie Izac[26], Monty Jones[27], Parviz Koohafkan[28], Rattan Lal[29], Timothy Lang[30], Jeffrey McNeely[31], Alexander Mueller[11], Nicholas Nisbett[32], Andrew Noble[33], Prabhu Pingali[34], Yvonne Pinto[35,36], Rudy Rabbinge[37], N. H. Ravindranath[38], Agnes Rola[39], Niels Roling[37], Colin Sage[40], William Settle[11], J. M. Sha[41], Luo Shiming[42], Tony Simons[43], Pete Smith[44], Kenneth Strzepeck[45], Harry Swaine[46], Eugene Terry[47], Thomas P. Tomich[48], Camilla Toulmin[49], Eduardo Trigo[50], Stephen Twomlow[51], Jan Kees Vis[52], Jeremy Wilson[53] and Sarah Pilgrim[1]

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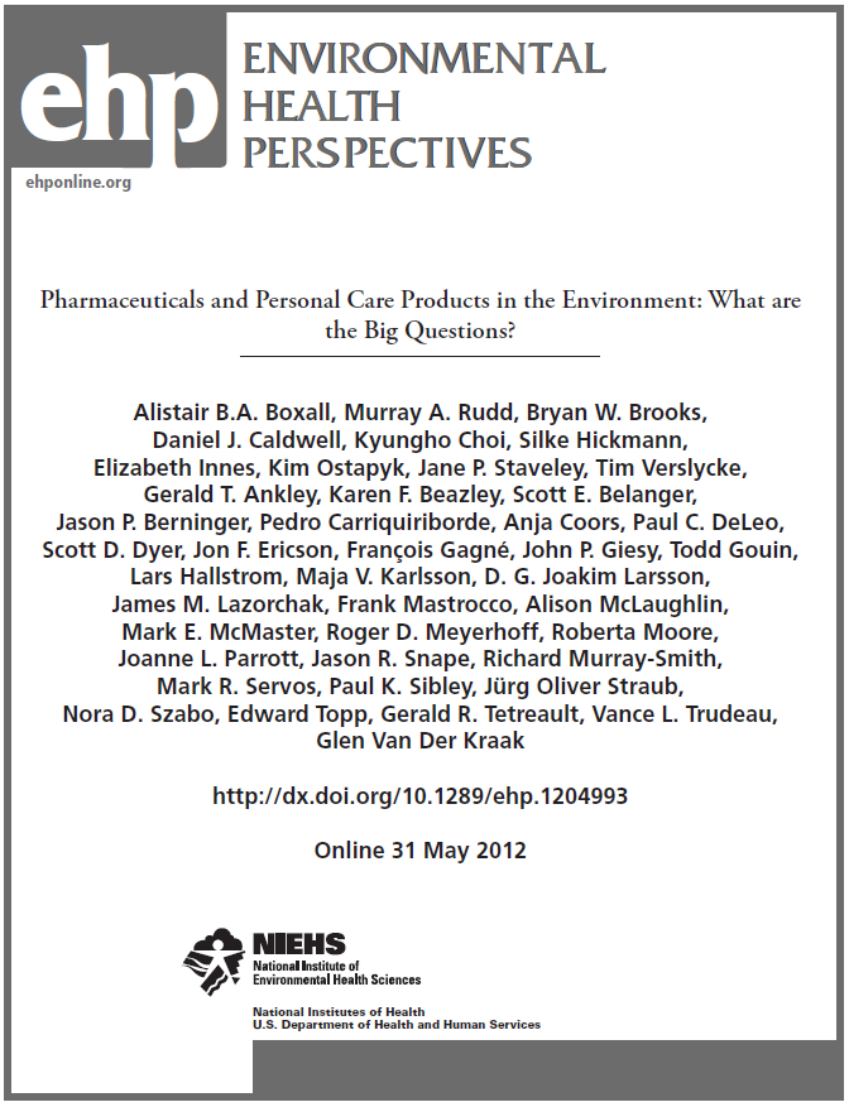
"Key Question" Exercise

- Initial, broad selection of questions
- Refine based on aspirational criteria
- Discuss refined questions among experts at two-day workshop
  - Grouped questions into themes
  - Breakout groups, tasked with culling down to two "top 20" questions and one alternate
  - Plenary session to distill 26 "top" questions down to top 20
- Post-workshop collaborative editing and ranking



ehp ENVIRONMENTAL HEALTH PERSPECTIVES

ehponline.org

Pharmaceuticals and Personal Care Products in the Environment: What are the Big Questions?

Alistair B.A. Boxall, Murray A. Rudd, Bryan W. Brooks, Daniel J. Caldwell, Kyungho Choi, Silke Hickmann, Elizabeth Innes, Kim Ostapyk, Jane P. Staveley, Tim Verslycke, Gerald T. Ankley, Karen F. Beazley, Scott E. Belanger, Jason P. Berninger, Pedro Carriquiriborde, Anja Coors, Paul C. DeLeo, Scott D. Dyer, Jon F. Ericson, François Gagné, John P. Giesy, Todd Gouin, Lars Hallstrom, Maja V. Karlsson, D. G. Joakim Larsson, James M. Lazorchak, Frank Mastrocco, Alison McLaughlin, Mark E. McMaster, Roger D. Meyerhoff, Roberta Moore, Joanne L. Parrott, Jason R. Snape, Richard Murray-Smith, Mark R. Servos, Paul K. Sibley, Jürg Oliver Straub, Nora D. Szabo, Edward Topp, Gerald R. Tetreault, Vance L. Trudeau, Glen Van Der Kraak

http://dx.doi.org/10.1289/ehp.1204993

Online 31 May 2012

NIEHS National Institute of Environmental Health Sciences

National Institutes of Health
U.S. Department of Health and Human Services

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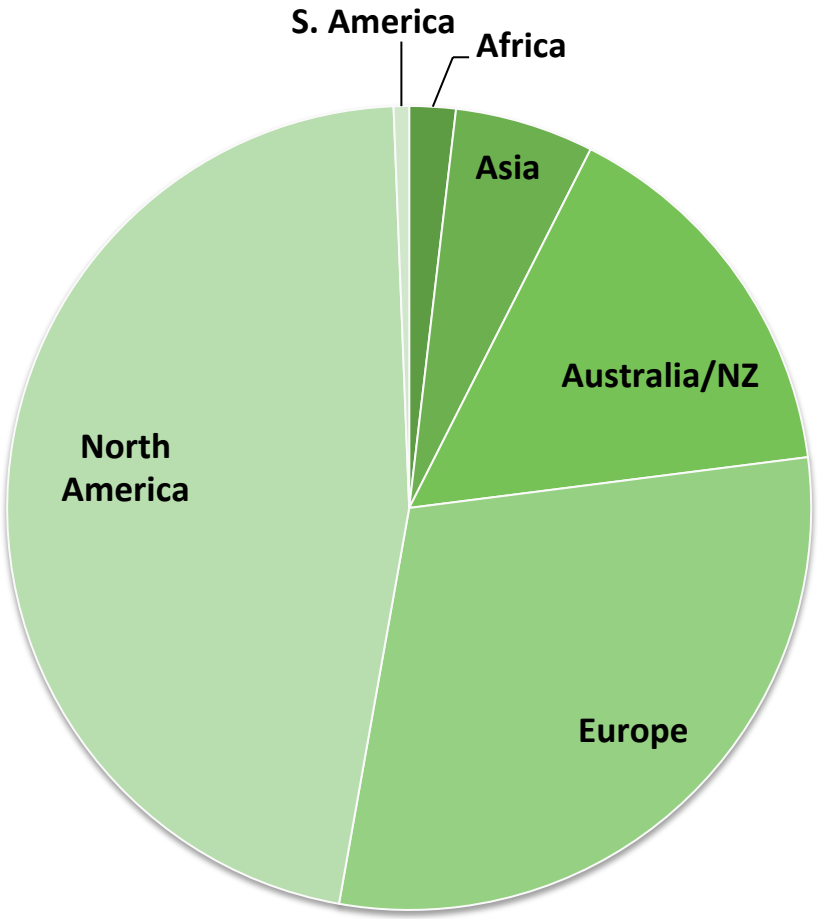
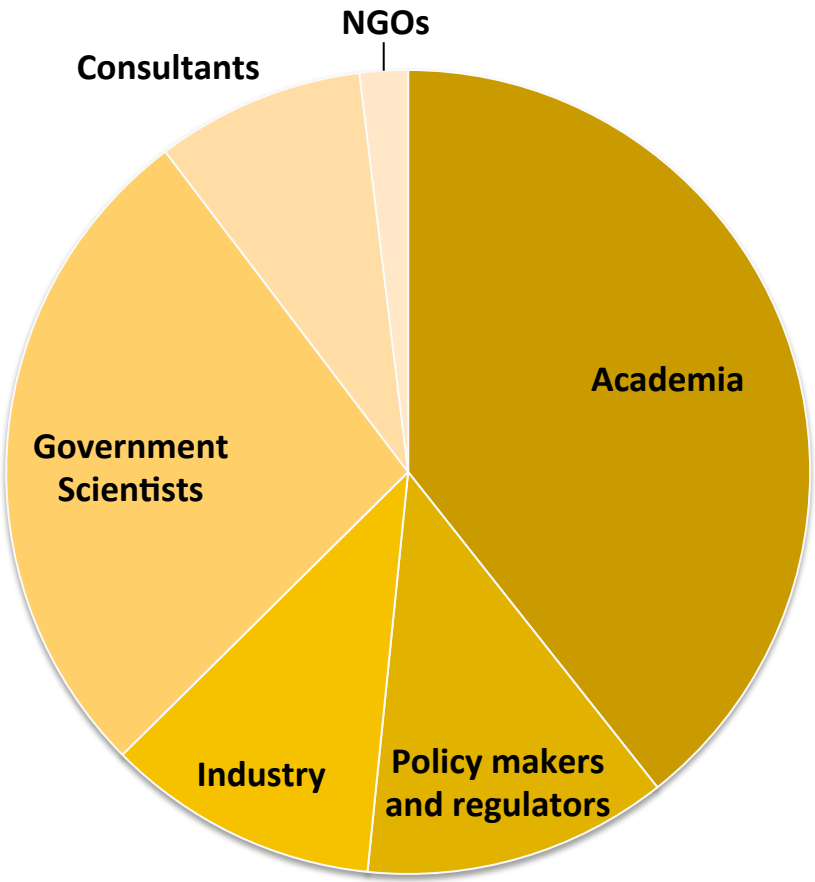
Candidate Questions

403 questions – 161 submissions



Geographical input



Sector input

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Workshop

- Sponsors
  - SETAC
  - Health Canada
- Steering Committee
  - University of York, UK
  - Baylor university, USA
  - Seoul National University, South Korea
  - Health Canada
  - UBA, Germany
  - Johnson & Johnson, USA
  - Exponent, USA
  - Gradient, USA
  - SETAC, Belgium
- Participants
  - 41 Participants from North America, South America, Europe, and Asia
  - Academia (17), business (13), and government (11)
  - Ecologists, environmental chemists, ecotoxicologist, pharmacologists, risk assessors

Top 20 Questions Categories

- Risk and relative risk
- Prioritization of PPCPs
- Pathways of exposure
- Bioavailability and uptake
- Effects characterization
- Antibiotic resistance
- Risk management

Ranking

Workshop attendees were sequentially presented with sets of 4 questions and asked to select the highest and lowest range question from the group. Using this process, all the 20 questions were ranked. Related questions were identified.

Risk and Relative Risk

"How important are PPCPs relative to other chemicals and non-chemical stressors in terms of biological impacts on the natural environment?" *[#1]*

"Do PPCPs pose a risk to wildlife such as mammals, birds, reptiles and amphibians?" [#11]

"How can retrospective analyses be used to validate prospective risk assessments?" [#14]

"How can regions where PPCPs pose the greatest risk to environmental and human health, either now or in the future, be identified?" [#16]

"How can the environmental risks of metabolites and environmental transformation products of PPCPs be assessed?" [#17]

Prioritization of PPCPs

"What approaches should be used to prioritize PPCPs for research on environmental and human health exposure and effects?" *[#2]*

>4000 pharmaceuticals

Compounds of most concern

- Properties
- Usage
- Mode of action
- Side effects
- QSAR predictions
- Therapeutic dose, etc.

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Pathways of Exposure

"What are the environmental exposure pathways for organisms (including humans) to PPCPs in the environment and are any of these missed in current risk assessment approaches?" *[#12]*

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Bioavailability and Uptake

"How can the uptake of ionizable PPCPs into aquatic and terrestrial organisms and through food chains be assessed?" [#15]

"What is the bioavailability of non-extractable residues of PPCPs?" [#20]

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Effects Characterization

"How can pharmaceutical preclinical and clinical information be used to assess the potential for adverse environmental impacts of pharmaceuticals?" [#3]

"How can effects from long-term exposure to low concentrations of PPCP mixtures on non-target organisms be assessed?" [#4]

"What can be learned about the evolutionary conservation of PPCP targets across species and life stages in the context of potential adverse outcomes and effects?" [#5]

Antibiotic Resistance

"Does environmental exposure to PPCP residues result in the selection of antimicrobial resistant micro-organisms and is this important in terms of human health outcomes?" [#6]

"How can the risks to human health, arising from antibiotic resistance selection by PPCPs in the natural environment, be assessed?" [#9]

Risk Management

"How can the efficacy of risk management approaches be assessed?" [#10]

"If a PPCP has an adverse environmental risk profile what can be done to manage and mitigate the risks?" [#13]

"What effluent treatment methods are effective in reducing the effects of PPCPs in the environment while at the same time not increasing the toxicity of whole effluents?" [#18]

Hazard *versus* Risk

Perception and Communication

Feasibility and Effectiveness

Solution

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Examples

- **Industry Examples/Product Stewardship**
  - **Personal care products**
  - **Hydraulic fracturing products**
- **Regulatory Example**
  - **Endocrine disrupting chemicals**

Surfactants in PCPs

	Approach	Category	Scoring Basis	Significance
HAZARD	1A	Persistence (P)	Biodegradability	No differentiation within a category
	1B	Bioaccumulation (B)	Bioconcentration Factor (BCF)	
	1C	Aquatic Toxicity (T)	Fish 96h LC50 , invertebrate 48h EC50, and algae 72h or 96h EC50	Only acute aquatic toxicity
	1D	(P+B+T)	P+B+T	Only hazards
RISK	2	(P+B+T) × Rel UV	Combined P, B, and T weighted by Relative Use Volume	"Quasi" risk-based ranking
	3	Rel HQ	Relative Hazard Quotient (HQ)	Only risks due to direct "aquatic" effects not indirect effects (*e.g.*, *via* bioaccumulation)
	4	P+B+100 × Rel HQ	P + B + 100 × Relative HQ	"Overall" relative risks for all receptors

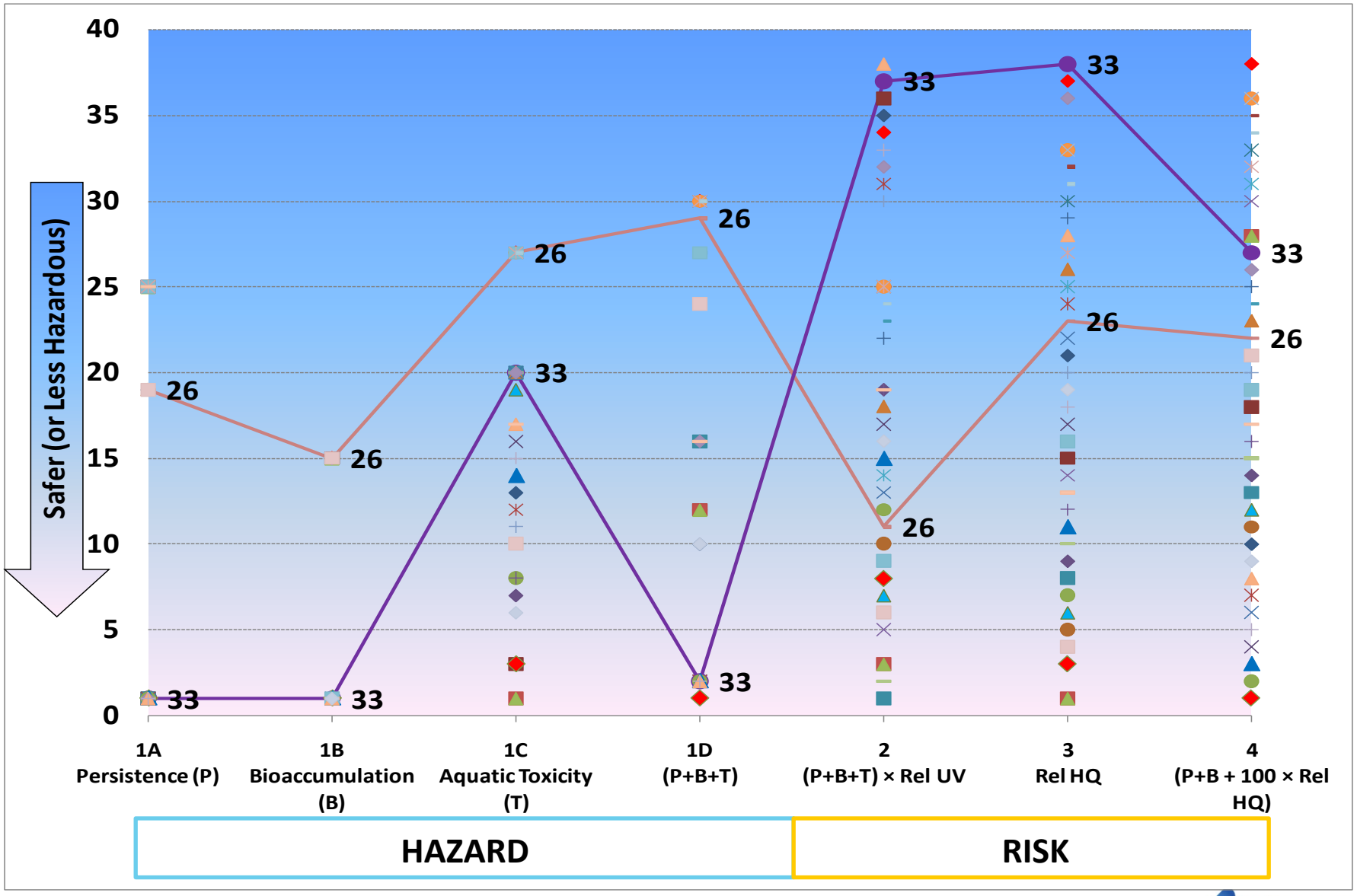
Surfactants in PCPs

Category	Score	Definitions
Persistence (P)		
Persistent	50	Not Readily Biodeg.
Inherently not Persistent	10	Readily Biodeg., but not meeting the 10-day window
Not Persistent	0	Readily Biodeg. and meeting the 10-day window
Data NA P	*50*	*Data Not Available*
Bioaccumulation Potential (B)		
Bioaccumulative	50	BCF ≥ 500 (or if absent, log K_{ow} ≥ 4)
Not Bioaccumulative	0	BCF < 500 or log K_{ow} < 4)
Data NA B	*50*	*Data Not Available*
Acute Aquatic Toxicity (T)		
Category 1	100	L/EC50 ≤ 1 mg/L
Category 2	75	1 mg/L < L/EC50 ≤ 10 mg/L
Category 3	50	10 mg/L < L/EC50 ≤ 100 mg/L
Not Acutely Toxic	0	L/EC50 > 100 mg/L
Data NA T	*100*	*Data Not Available*

Surfactants in PCPs

Predicted No (Adverse) Effect Concentration (PNEC) = Min{EC}/AF		
Min{EC}	Lowest Effect Concentration (EC)	Minimum of L(E)C50
AF	Assessment Factor	1,000; 5,000; or 10,000
Predicted Environmental Concentration (PEC) = V_{USE}/DV x Purity		
V_{USE}	Annual Use Volume (kg)	Chem-specific; 100,000 kg (when not available)
DV	Dilution Volume (L)	1.5×10^{11} L (EU, 2007)
Purity	Surfactant Purity (fraction)	Chem-specific (0 to 1); 1 (when not available)
Hazard Quotient (HQ) = PEC/PNEC		
The lowest PNEC for use group (when not available)		

Surfactants in PCPs



The Chemistry Scoring Index (CSI)

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Article

The Chemistry Scoring Index (CSI): A Hazard-Based Scoring and Ranking Tool for Chemicals and Products Used in the Oil and Gas Industry

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CSI – Hazard Criteria

- Human Health
- Physical Safety
- Environment

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CSI – Hazard Categories

Environment	Human Health	Physical Safety
Acute Aquatic Tox (Cat. 1-3)	Carcinogenicity (Cat. 1-2)	Explosive
Chronic Aquatic Tox (Cat. 1-4)	Mutagenicity	Pyrotechnic
Bioaccumulation	Reproductive Toxicity	Flammable Gas
Biodegradation (persistent/inherent)	Sensitizer	Oxidizing Gas
Ozone Depleting Substance	Acute Toxicity (Cat. 1-4)	Gases Under Pressure
Endocrine Disruptor	Corrosivity (Cat. 1- 2)	Flammable Liquid (Cat. 1-4)
Volatile Organic Compound (VOC)	Acute Target Organ Toxicity	Flammable Solid
Hazardous Air Pollutants	Chronic Target Organ Toxicity	Self-Reactive Substance
Hazardous Water Pollutants	Aspiration Hazard	Pyrophoric (Liquids and Solids)
		Self-Heating Substance
		Emit Flammable Gases in Contact with Water
		Oxidizing Liquid
		Oxidizing Solid
		Organic Peroxide
		Corrosive to Metals

Globally Harmonized System of Classification and Labeling of Chemicals (GHS)

CSI – Product Scoring

- **CSI scoring matrix**
  - Specifies scores for each assigned hazard category based on the percentage of that chemical in the product
  - Also assigns scores to components for which data are not available
- **CSI Product Score**
  - **Environmental Score** + **Physical Score** + **Health Score**
  - Allows for hazard comparison between products within the same **product use group** (*e.g.,* emulsifiers, foaming agents, proppants, surfactants, corrosion inhibitors…)
  - Products that score lower within a product use group are considered to have a lower intrinsic hazard compared to other products within the same use group that have higher scores

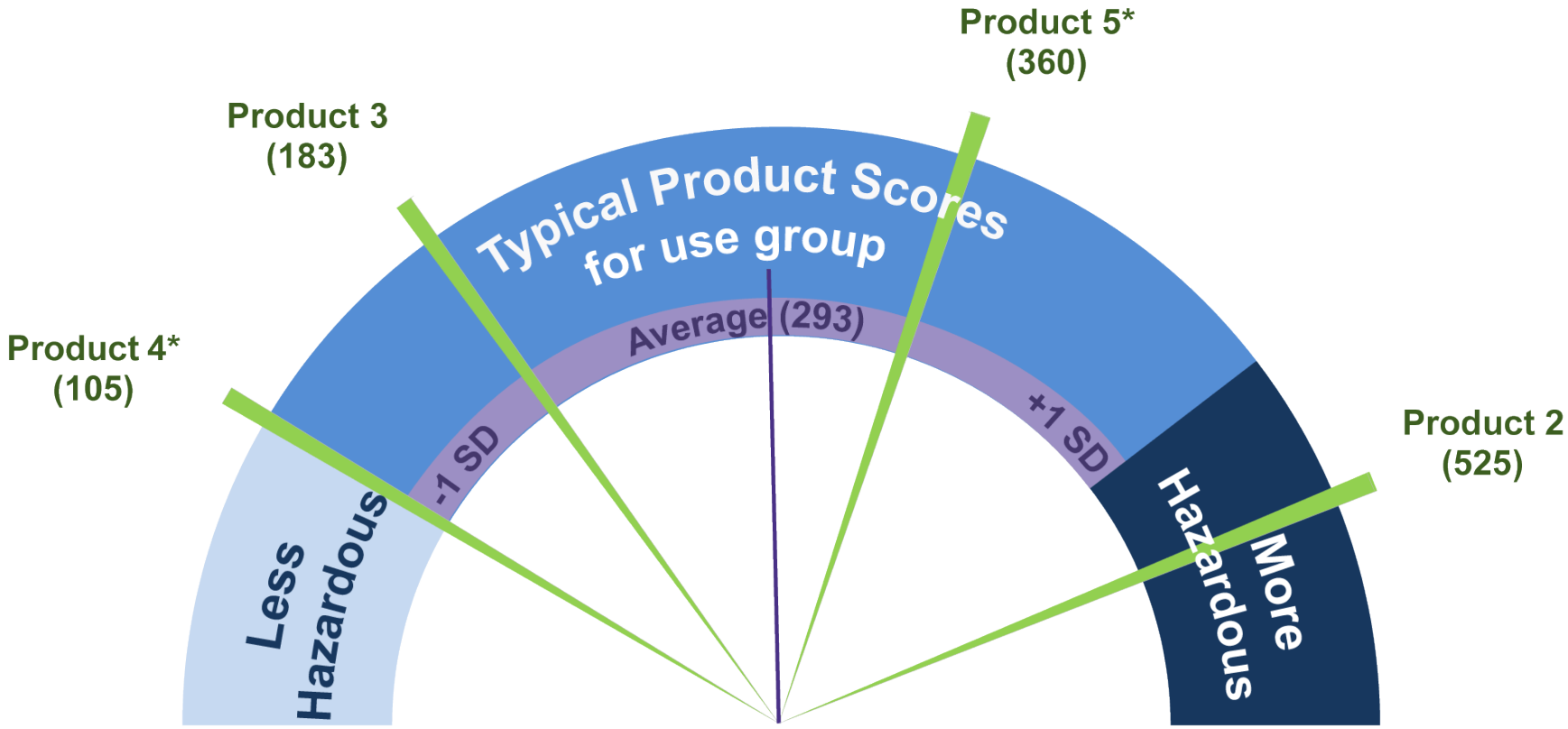
CSI – Product Scoring – Matrix

Hazard Criteria	Hazard Categories	Max. Score	Product Component Percent Range						
			>0 - 0.09%	0.1 - 0.9%	1- 4.9%	5 - 9.9%	10 - 29.9%	30 - 59.9%	60 - 100%
ENVIRONMENTAL	No Data Available	100	10	25	50	75	100	Do not evaluate	Do not evaluate
	Acute Aquatic Toxicity Cat. 1	100	1	5	10	25	50	75	100
	Acute Aquatic Toxicity Cat. 2	75	0	1	5	10	25	50	75
	Acute Aquatic Toxicity Cat. 3	50	0	0	1	5	10	25	50
	Ozone Depletion	50	5	10	50	50	50	50	50
	Volatile Organic Compounds	50	5	10	50	50	50	50	50
	Hazardous Air Pollutants	50	1	5	10	25	40	50	50
	Hazardous Water Pollutants	50	1	5	10	25	40	50	50
	Biodegradation - Persistent	50	5	10	50	50	50	50	50
	Biodegradation - Inherent	10	1	10	10	10	10	10	10
	Bioaccumulation	50	5	10	50	50	50	50	50
	Endocrine Disruptors	50	10	25	50	50	50	50	50
	No Hazard	0	0	0	0	0	0	0	0

CSI – Product Scoring – Example

Prod	Comp	% Mass	Environmental Hazards	Physical Hazards	Health Hazards	CSI Scores
1	A	1- 4.9%	No Data Available (50)	No Data Available	No Data Available (50)	ENV = 250 PHY = NA HEA = 200 **TOTAL = NA**
	B	60 - 100%	Acute Aq Tox Cat. 1 (100) Biodegradation - Persistent (50) Bioaccumulation (50)	No Data Available	Acute Tox Cat. 2 (75) Corrosivity Cat. 1 (25) Chronic Target Organ Tox (50)	
2	C	60 - 100%	Acute Aq Tox Cat. 1 (100) Biodegradation - Persistent (50) Bioaccumulation (50)	Flammable Solid (75) Self-Reactive Substance (50)	Acute Tox Cat. 2 (75) Corrosivity Cat. 1 (25) Acute Target Organ Tox (50) Chronic Target Organ Tox (50)	ENV = 200 PHY = 125 HEA = 200 **TOTAL = 525**
3	D	1- 4.9%	Acute Aq Tox Cat. 3 (1)	Corrosive to Metals (1)	Acute Toxicity Cat. 4 (1) Corrosivity Cat. 1 (5) Acute Target Organ Tox (10)	ENV = 101 PHY = 26 HEA = 56 **TOTAL = 183**
	E	10 - 29.9%	Acute Aq Tox Cat. 1 (50) Bioaccumulation (50)	Oxidizing Liquid (25)	Acute Toxicity Cat. 4 (5) Corrosivity Cat. 1 (10) Acute Target Organ Tox (25)	
4	**F**	5 - 9.9%	No Data Available (75)	No Data Available (25)	Corrosivity Cat. 1 (5)	ENV = 75 PHY = 25 HEA = 5 **TOTAL = 105**
5	G	10 - 29.9%	Acute Aq ToxCat. 3 (10) VOC(50) Hazardous Air Pollutants (40)	Flammable Liquid Cat. 2 (25)	Reproductive Tox (50) Acute Tox Cat. 3 (25) Corrosivity Cat. 2 (5) Acute Target Organ Tox (25) Chronic Target Organ Tox (25)	ENV = 175 PHY = 50 HEA = 135 **TOTAL = 360**
	F	5 - 9.9%	No Data Available (75)	No Data Available (25)	Corrosivity Cat. 1 (5)	

CSI – Product Scoring – Example



*Product contains components that lack hazard data

Regulations – EDCs

- EU Water Framework Directive
  - 2012 proposal: 0.035 ng EE2/L in EU waters by 2021
  - Would require significant upgrades to WWTPs
  - Estimated compliance cost in England/Wales was estimated at more than $30 billion (Owen & Jobling. *Nature* 2012)
  - Significant opposition from pharma industry, water industry, many governments, etc.
  - 2013: diclofenac, EE2, E2 added to "Watch List"
- EU is currently defining criteria for identifying EDCs
  - Will have significant impacts on plant protection products, biocides, cosmetics, chemicals regulated under REACH
- US Endocrine Disruptor Screening Program
  - Purpose and use of EDSP have been poorly communicated
  - Cost for 1 chemical (Tier 1 + 2): >$3 million

Questions?

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