Cumulative Risk Assessment at the U.S. Environmental Protection Agency: The Past, The Present and The Future

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Outline

• Definition of Cumulative Risk Assessment (CRA)
• Introduction
  – The United States Environmental Protection Agency (EPA, or “the Agency”)
• Part 1: The Past
• Part 2: The Present
• Part 3: The Future
EPA’s 2003 Definition of CRA (1 of 2)

• **Cumulative risk** is the combined risks from aggregate exposures to multiple agents or stressors, which may include chemicals, biological or physical agents

• **Cumulative risk assessment** is an analysis, characterization, and possible quantification of the combined risks to human health or the environment from multiple agents or stressors

EPA’s 2003 Definition of CRA (2 of 2)

- CRA is population-based with stakeholder emphasis and consideration of Vulnerability Factors:
  - Susceptibility/sensitivity (e.g., genetics, lifestages, disease states)
  - Differential exposure (e.g., homes close to pollutant sources, diet of locally caught fish or game)
  - Differential preparedness (e.g., lack of access to health care)
  - Differential ability to recover (e.g., poor nutrition)

Introduction

• This is going to be a simple, overview presentation of “cumulative risk assessment” in EPA with other related details provided in extra slides

• Many references and links are also provided
The US EPA

Our Mission is to protect human health and the environment.
The US EPA: 16,205 People

Office of Administrator (415 People)

OCSPP (1,078 People)

OSWER (529 People)

OAR (1,177 People)

ORD (1,802 People)

OW (590 People)

Regional Offices – 10 of them (7,702 People)

Where all of EPA’s national laws are carried out; including the “Superfund” Program is implemented.

Where the “Superfund” Program is Administered.

Where the Administrative Part of the Risk Assessment Forum is Located.

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Other Agencies Also…

- Dept. of Health and Human Services (DHHS)
  - Food and Drug Administration (FDA)
  - National Institutes of Health (NIH)
    - National Institute of Environmental Health Sciences (NIEHS)
      - National Toxicology Program (NTP)
    - Centers for Disease Control and Prevention (CDC)
      - Agency for Toxic Substances Disease Registry (ATSDR)
      - National Health and Nutrition Exposure Survey (NHANES)
      - National Institute for Occupational Safety and Health (NIOSH)

- Occupational Safety and Health Administration (OSHA)

- Consumer Product Safety Commission (CPSC)
Government Agencies and CRA

- Individual Groups and Laws
  - Within EPA (air, water, solid waste, pesticides)
  - Across government (pharmaceuticals, chemicals, consumer products, occupational exposures)

- Difficult to have a single, focused approach for something as complicated as CRA
The Reasons to Perform a CRA ("Initiating Factors") – 1 of 2

• Federal Laws
  – Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), 1980 (also known as “Superfund”)
    • Chemical-centric site evaluations including mixtures
  – Safe Drinking Water Act Amendments, 1996
    • Mixtures of contaminants (chemicals, microbes) in drinking water
  – Clean Air Act, 1990
    • Air toxic mixtures, sensitive/differentially exposed populations
  – Food Quality Protection Act (FQPA), 1996
    • CRA of pesticides mixtures with common toxicity
  – Consumer Product Safety Improvement Act, 2008
    • CRA of phthalate mixtures for children’s products
The Reasons to Perform a CRA (2 of 2)

- Executive Order 12898 (February 11, 1994) – (Directive from the President of the US, does not require Congressional approval)
  - Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations
    - At-risk, differentially impacted communities
    - Vulnerable populations (e.g., children, native Americans)
- Other reasons:
  - The existence of sources/releases of pollutants to the environment
  - Disease or illness occurrence/cluster (either human health or eco)
  - Concentration of chemicals in environmental media
Part 1: The (Recent) Past

• Important Reports
  – EPA
  – Outside of EPA

• October 2010 Internal EPA Meeting
U.S. EPA Reports on CRA Theory and Practice

- Methodology for Multipathway Exposures to Combustor Emissions (1998)
- Five CRA’s & Guidance on Cumulative Risk of Pesticides (2002b;2006a,b,c;2007a; 2011)
- Concepts, Methods and Data Sources for Cumulative Health Risk Assessment of Multiple Chemicals, Exposures and Effects: A Resource Document (2007b)

Office of Solid Waste and Emergency Response – Used by Regions
Air Program
Pesticides
Published by Office of Research and Development – “Toolbox”
U.S. EPA Reports on CRA Theory and Practice: Risk Assessment Forum

- Planning & Scoping for Cumulative Risk Assessment (1997)
- Planning & Scoping Lessons Learned (2002a)
- Five White Papers on CRA Published in Open Literature: Directions for CRA, Vulnerability, Combined Effects of Multiple Stressors, Environmental Mixtures, Biomarkers (2007c)

Continuing:
- Expert Panel in 2013

And more to come….
Other Reports (non-EPA)

- NAS and NRC – multiple reports from 1983-2009
- Presidential/Congressional Commission on Risk Assessment /Risk Management - 1997
- DHHS, ATSDR – 2004
- International –
  - World Health Organization (WHO 2007)
  - European Union (EU) 2009 Mixtures Report
US EPA Internal Meeting in October, 2010: Convened to Address Recent NAS Reports (1 of 2)


• EPA should draw on other approaches to incorporate interactions between chemical and nonchemical stressors
  – Ecological Risk Assessment
  – Social Epidemiology
• Increase role of biomonitoring, epidemiologic, and surveillance data
• Develop guidelines and methods for simpler analytical tools
US EPA Internal Meeting in October, 2010: Convened to Address Recent NAS Reports (2 of 2)

*Phthalates & CRA (2008)* Recommendations

- Focus on common health outcomes
- Group chemicals by common adverse outcomes
Part 2: The Present

- The EPA Risk Assessment Forum

- Other EPA Activities
  - Program offices, Regions and research
What is the Risk Assessment Forum (RAF)?

• The Office of the Science Advisor (OSA), provides leadership for cross-Agency science and technology policy and facilitates its integration into the Agency’s programs and decisions.
• The RAF in the OSA is an appointed committee of senior EPA scientists who develop Agency-wide consensus on risk assessment issues and risk assessment guidance.
• The RAF establishes technical panels to undertake substantive initiatives, such as the Cumulative Risk Assessment Technical Panel.
  – The CRA Technical Panel is charged with development of the CRA Guidelines.
The RAF CRA Technical Panel

- Established in 1997
- Current membership is at end of presentation
  - Over 30 scientists from across the agency
  - Important to recognize it is separate from their daily work
- We will talk more about the RAF under “The Future”
But let’s look at the rest of EPA for now

• National, overarching CRA efforts:
  – Pesticides
  – Water
  – Air

• More local (place-based or geographic boundaries)
  – Superfund
  – Regional

• Office of Research and Development – ORD
• Office of Chemical Safety and Pollution Prevention - OCSPP
Example Program Office Applications of CRA Concepts (1 of 2)

- **Office of Solid Waste and Emergency Response (OSWER)**
  - Planning and scoping phase (typically done for site-specific risk assessments)
  - Stakeholder involvement
  - Potentially vulnerable receptors evaluated (e.g., young children, workers) (generally done for site-specific risk assessments)
  - Multiple chemicals/multiple exposure pathways (e.g., soil, water, air)

- **Office of Chemical Safety and Pollution Prevention (OCSPP)**
  - Multiple pesticides, all pathways of dietary and nondietary exposures
  - Toxicity adjustments (e.g., of relative potency factors) for exposures to children
  - Exposure assessments incorporate behavioral and environmental factors
  - Develop approaches for CRA of adverse outcomes (e.g., CRA of phthalates)
  - Begin identifying and compiling case studies and applications of CRA incorporating occupational scenarios
Example Program Office Applications of CRA Concepts (1 of 2)

- **Office of Air and Radiation (OAR)**
  - Chemical mixture risk assessment methods used to assess health risks from multiple air toxics under National Air Toxics Assessment (NATA), Petroleum Refinery Sector Risk and Technology Review (RTR) rules
  - Exposure estimates consider inhalation, and where data permit, ingestion
- **Office of Water (OW)**
  - Regulates some chemical groups as mixtures (e.g., trihalomethanes, haloacetic acids)
Office of Research and Development (ORD)

- Research and Publications
- Annual Course at Society of Risk Analysis (SRA)
CRA Toolbox
(Appendix A of U.S. EPA, 2007)

• Objectives:
  – Consolidate resources for cumulative risk assessors
  – Include notes to help facilitate application
  – Provide coverage for key elements of the assessment process
• Organized into 5 main topic areas:
  – Planning, scoping and problem formulation
  – Environmental fate and transport analyses
  – Exposure analysis
  – Toxicity analysis
  – Risk/uncertainty characterization, presentation of results
• Reflects >70 resources; updates are planned (MacDonell et al. 2013)
• Example resources from the CRA Toolbox are shown at the end
• Online at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=190187#Download
FQPA of 1996 requires EPA to do CRA

- Five common groups have been formed so far - http://www.epa.gov/pesticides/cumulative/common_mech_groups.htm#op:
  - Chloroacetanilides (2006) – formation of nasal turbinate tumors via common tissue reactive metabolites - Three pesticides (plus metabolites)
Office of Pesticide Programs (2 of 2)

• *N*-methyl carbamates (2007) – acetylcholinesterase inhibition (via carbamylation) – **Ten pesticides**

• Pyrethrins/pyrethroids (2011) – shared structural characteristics, disruption of voltage-gated sodium channels leading to alteration of neuronal membranes and ultimately neurotoxicity – **33 pesticides**

• Because pesticide CRA is based on common mechanism, **assumed dose addition (used relative potency factor, or RPF approach)** and because pesticide registration requires much information **no data gaps**.

September 2014
Office of Air – National Air Toxics Assessment (NATA) (1 of 2)

- Is a screening approach
  - Looked at cancer and non-cancer separately
    - Combined cancer effects by summing unit risk estimates (regardless of cancer type or mode of action)
    - Combined non-cancer effects using hazard index method (i.e., the summing of hazard quotients)
      - Did for two endpoints (neuroxicity and respiratory effects)
When no data on cancer/non-cancer were available, a value of zero was used for summation purposes (and no individual chemical evaluation was reported)

http://www.epa.gov/ttn/atw/natamain/index.html
(an overview of the methods – published in 2011)
Other Activities in US

- NIEHS Workshop (September, 2011) - *Advancing Research on Mixtures: New Perspectives and Approaches for Predicting Adverse Human Health Effects*
- International Toxicology of Mixtures Conference (October, 2011) – soon to be special issue of *Toxicology* (Elsevier)
Part III: The Future

The EPA RAF CRA Panel
EPA Risk Assessment Forum (RAF) Cumulative Risk Assessment (CRA) Technical Panel

- Charge to Panel: Write Agency Guidelines for CRA
- Panel History
  - Established in 1997
  - Developed *Framework* Document in 2003
  - Developed case studies via seminar series/workshops in 2007-2009 (end product still being developed)
  - “Re-invigorated” in July 2010
  - Developed outline for Agency Guidelines for CRA in 2011
  - Writing teams established in 2012-13
EPA’s RAF CRA Guidelines Effort

• Current CRA Technical Panel in place since 2010. Efforts include:
  – Draft CRA Guidelines outline
    • Cross-EPA writing teams
  – Draft workshop report on integrating chemical and nonchemical stressors
  – Defining CRA terms (e.g., vulnerability, sensitivity)
  – Draft report on EPA’s use of dose addition in risk assessments
  – Developing CRA tools and approaches for planning, scoping, problem formulation, risk communication, risk analysis, risk characterization
  – Public webinar series on CRA science issues [jointly sponsored with EPA’s National Center for Environmental Research (NCER)]

• Need for Collaborative Efforts
  – Coordinate across EPA program and other offices and regions
  – Address aspects of CRA under the purview of other Federal/State agencies
  – Cultivate partnerships with academia, private industry, tribes, environmental groups, etc.
CRA Guidelines Science Challenges and Research Issues (1 of 2)

- Chemical and nonchemical stressors and vulnerability factors
  - Identify and determine relative importance
  - Grouping and analysis strategies for diverse stressors
- Analysis tiers graded by data availability/quality, resources, need
  - e.g., higher tier analyses may require multiple-route internal doses of chemicals or emergency room visit incidence for a specific disease endpoint
- Joint exposure distributions for stressor combinations
  - Identify local at-risk populations and geographic areas
  - Address problems combining national database information (e.g., NHANES, Census, Toxic Release Inventory)
CRA Guidelines Science Challenges and Research Issues (2 of 2)

- Need methods and data to inform health impacts of stressor combinations
  - Epidemiology studies/methods
  - Traditional / high throughput toxicology
  - Extend chemical mixture risk assessment methods to analyze diverse stressors
- Develop cumulative risk communication strategies for stakeholders and risk managers
- Consider data and resource limitations, statutory requirement constraints
Conclusions on CRA “Readiness” (1 of 2)

• **CRA focus is important for getting environmental health risk assessment “right”**
  - Evaluate “real world” exposures and recognize population vulnerabilities
  - Accurate and complete CRAs should result in improved environmental decision-making and risk management
  - Vulnerable populations (e.g., children, differentially exposed populations) should benefit from the conduct of CRAs

• **Scientific challenges limit EPA’s current ability to implement CRA**
  - EPA research plans and efforts are in place to fill gaps in available data and methods, but some science is immature
    - Primary focus to identify, measure and determine the importance of combinations of chemical and nonchemical stressors, including population vulnerabilities and buffers
Conclusions on CRA “Readiness” (2 of 2)

- CRA Guidelines are needed to span program office and regional responsibilities while keeping EPA activities within legal mandates
  - Some aspects of CRA are already practiced by many organizations within EPA; multi-route/pathways exposures to chemical mixtures are commonly evaluated; vulnerable populations are often considered
References (EPA – 1 of 3)

PESTICIDES:


References (EPA - 3 of 3)

  – Callahan, M.A. and K. Sexton. 2007. If cumulative risk assessment is the answer, what is the question? Environ Health Perspect 115(5):799-806;
• EPA-funded research for 2010-14 (through NCER): http://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/recipients.display/rfa_id/515/records_per_page/ALL
Other References