Chemical Safety for Sustainability Overview

Annette Guiseppi-Elie, Ph D, FAIMBE, Acting National Program Director, CSS

Board of Scientific Counselors Subcommittee Chemical Safety for Sustainability and Health and Environmental Risk Assessment National Research Programs

Virtual Meeting on November 4-5, 2021

The Chemical Safety for Sustainability (CSS) Research Program provides methods, data, information and tools to EPA partners and stakeholders enabling more informed, timely decisions about chemicals, many of which have not been thoroughly evaluated for potential risks to human or ecological health.

BOSC Review of StRAP 3

- 2019 Review of CSS StRAP – Planning Phase
- 2021 Review - Implementation Phase
  - February – Focus on NAMs
  - November – Focus on collaborative, solutions-driven research

BOSC
BOARD OF SCIENTIFIC COUNSELORS

REVIEW OF
U.S. EPA OFFICE OF RESEARCH AND DEVELOPMENT'S
RESEARCH PROGRAMS

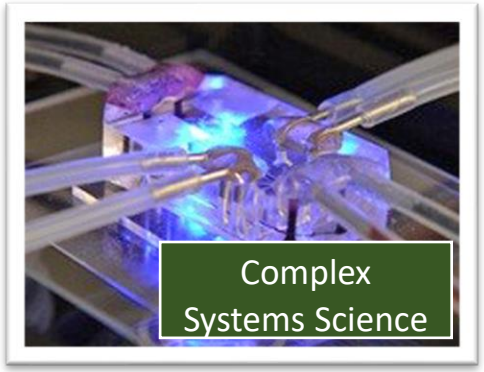
BOSC EXECUTIVE COMMITTEE

Paul Gilman, Ph.D. (Chair) *Covanta*	Shahid Chaudhry, MSc *California Energy Commission*	Joseph Rodricks, Ph.D. *Ramboll Environ*
Lucinda Johnson, Ph.D. (Vice Chair) *University of Minnesota Duluth's Natural Resources Research Institute*	Kari Cutting, MS *North Dakota Petroleum Council*	Leslie Rubin, M.D. *Morehouse School of Medicine*
Viney Aneja, Ph.D. *North Carolina State University*	Courtney Flint, Ph.D. *Utah State University*	Sandra Smith, MS *Retired*
Robert Blanz, Ph.D., PE *Arkansas Department of Environmental Quality*	Charlette Geffen, Ph.D. *Pacific Northwest National Laboratory*	James Stevens, Ph.D. *Paradox Found LLC*
Lance Brooks *Defense Threat Reduction Agency*	Matthew Naud, MPP, MS *adapt.city LLC*	Katrina Waters, Ph.D. *Pacific Northwest National Laboratory*
	Paula Olsiewski, Ph.D. *Alfred P. Sloan Foundation*	

EPA Contact
Tom Tracy, Designated Federal Officer

August 19, 2019

A Federal Advisory Committee for the U.S. Environmental Protection Agency's Office of Research and Development



Research Areas/Priorities:

Topic 1

- High-Throughput Toxicology (HTT)
- Rapid Exposure Modeling and Dosimetry (REMD)
- Emerging Materials and Technology (EMT)

Topic 2

- Adverse Outcome Pathways (AOP)
- Virtual Tissue Modeling (VTM)
- Ecotoxicological Assessment and Modeling (ETAM)

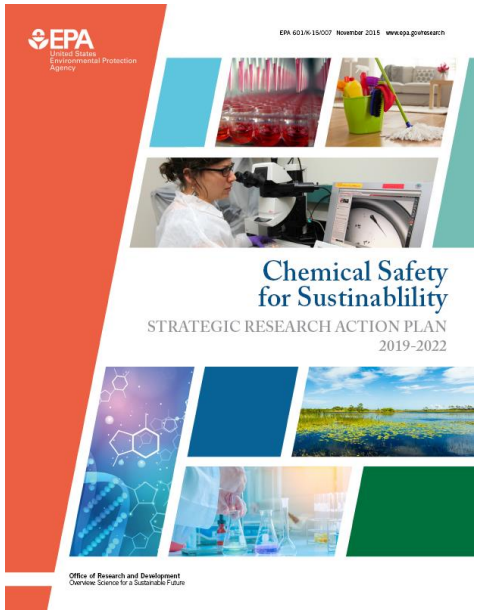
Topic 3

- Chemical Safety Analytics (CSA)
- Informatics, Synthesis, and Integration (ISI)

FY19-22 Strategic Research Action Plan

CSS is guided by its StRAP developed through rigorous engagement with EPA programs and regions, states, and tribes to identify research needs.

Planning



- National Programs Lead
- Strategic Focus
- Resources allocated at Research Area level

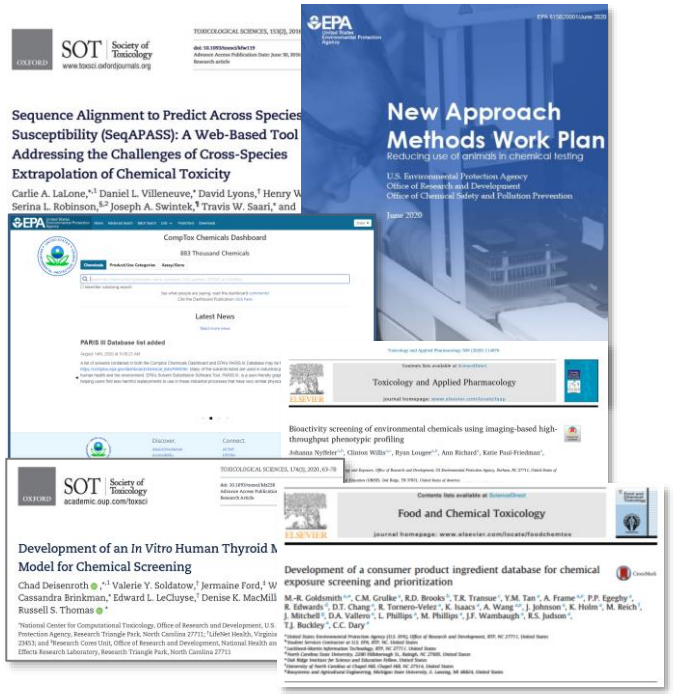
RACTs

Implementation

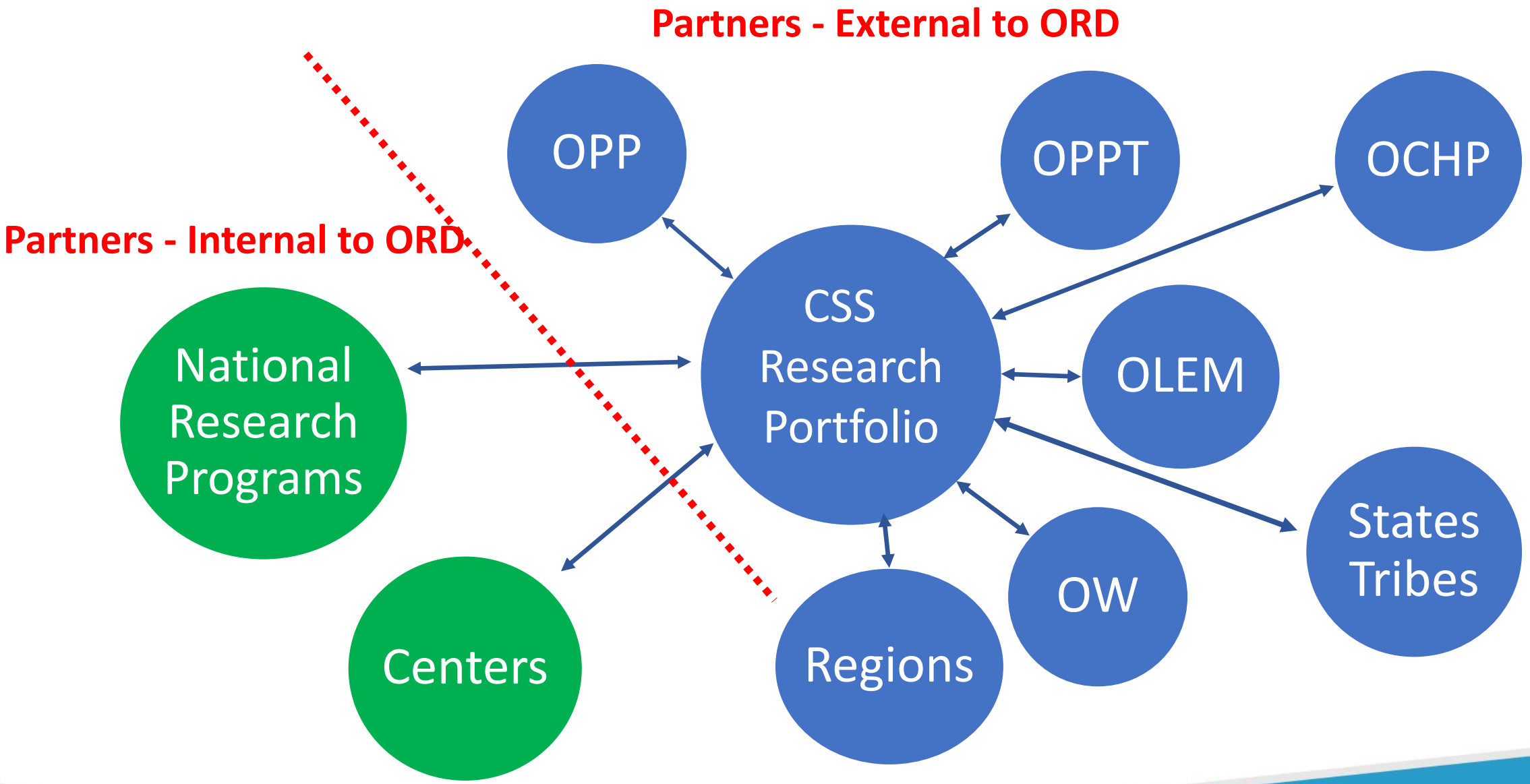
Research Area Implementation Plans

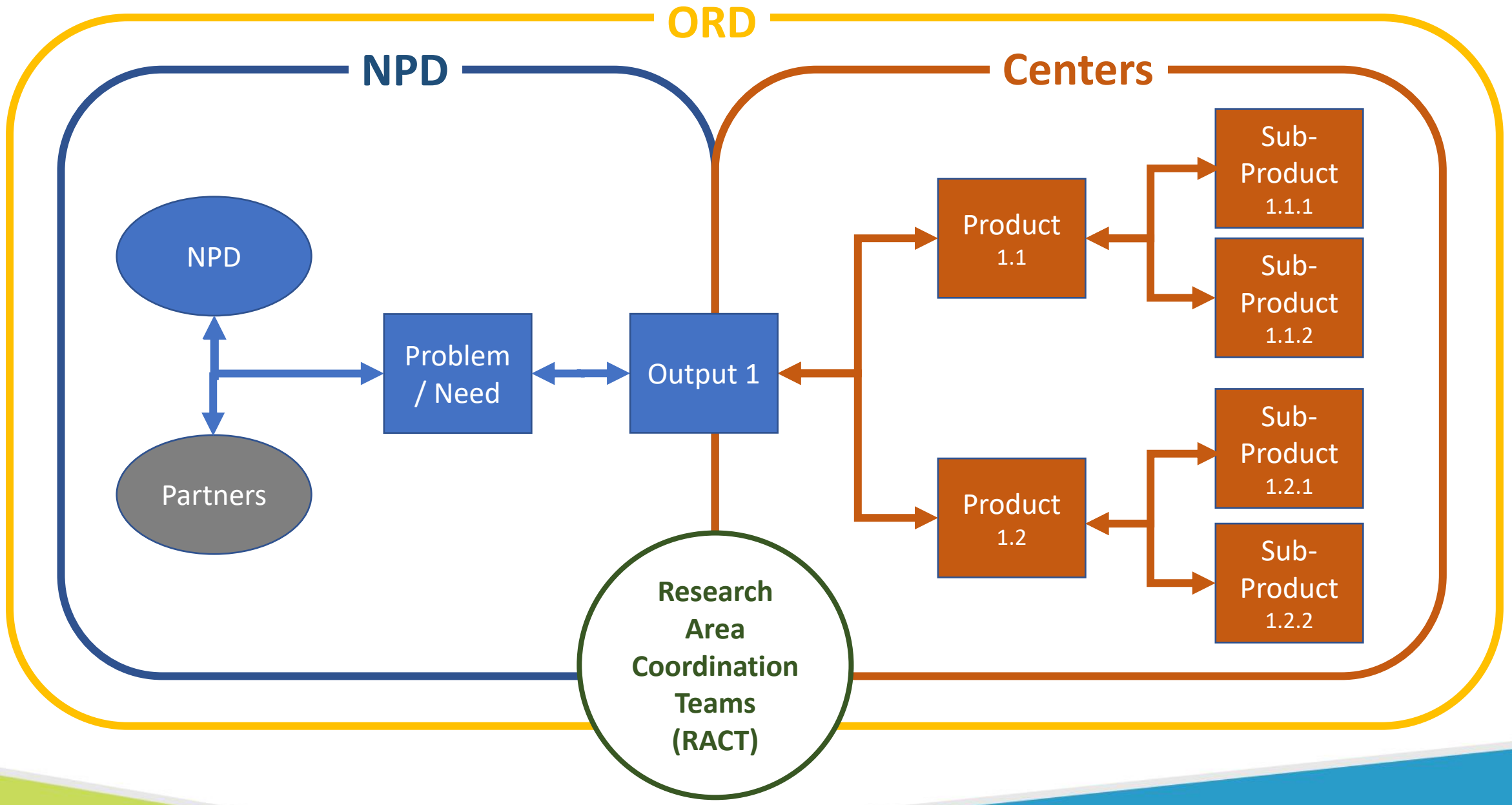
- Center Lead
- Tactical focus
- Resources allocated for specific products

Delivery



- Includes data, models, methods, EPA and journal publications
- Joint activity of National Programs and Centers


Partners - External to ORD
Partners - Internal to ORD
OPP
OPPT
OCHP
National Research Programs
CSS Research Portfolio
OLEM
States Tribes
Centers
Regions
OW


ORD
NPD
Centers
NPD
Partners
Problem / Need
Output 1
Product 1.1
Product 1.2
Sub-Product 1.1.1
Sub-Product 1.1.2
Sub-Product 1.2.1
Sub-Product 1.2.2
Research Area Coordination Teams (RACT)

Objective

- Expand involvement of partners
- Improve understanding needs
- Ensure proposed products are what is needed by partners

Who

- Program Office representative(s)
- Regional Representative(s)
- State Representative
- NPD Representative
- ORD Scientists

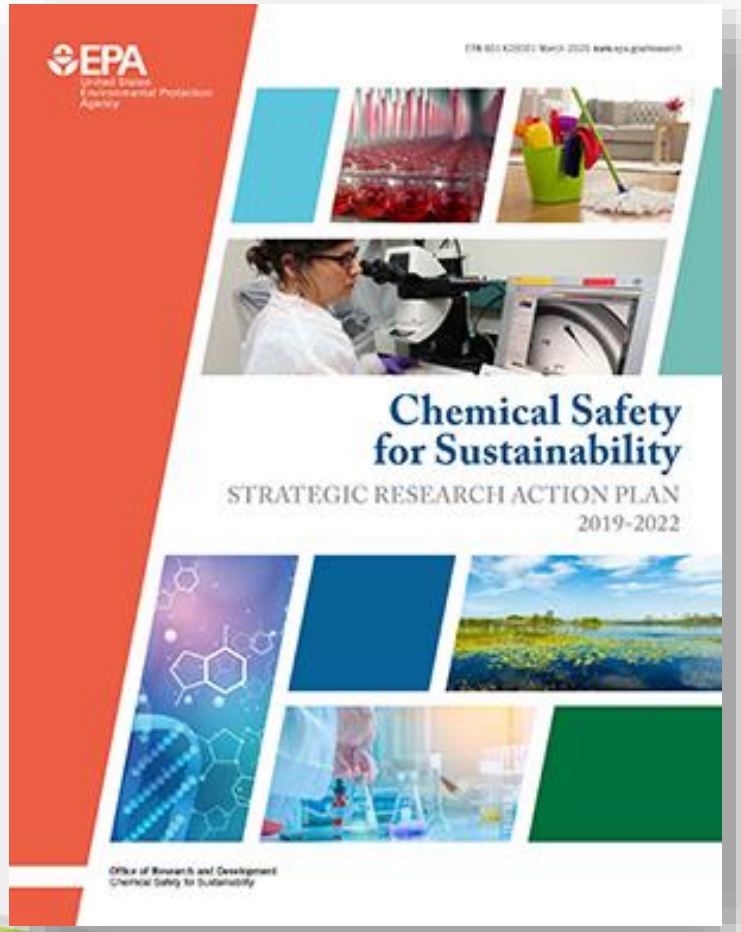
Outcome

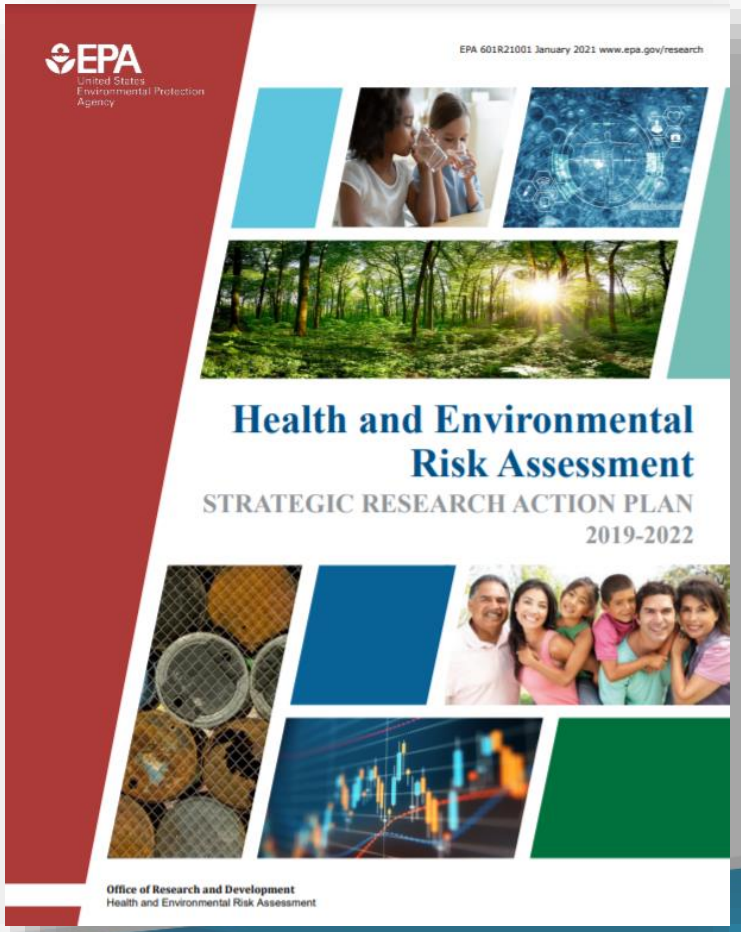
- Products responsive to outputs
- By-in from partners
- Collaboration with partners

Purpose: Define the products that ORD will develop to meet the objectives of the outputs

Research Area Coordination Teams

Relationship between HERA and CSS NRPs





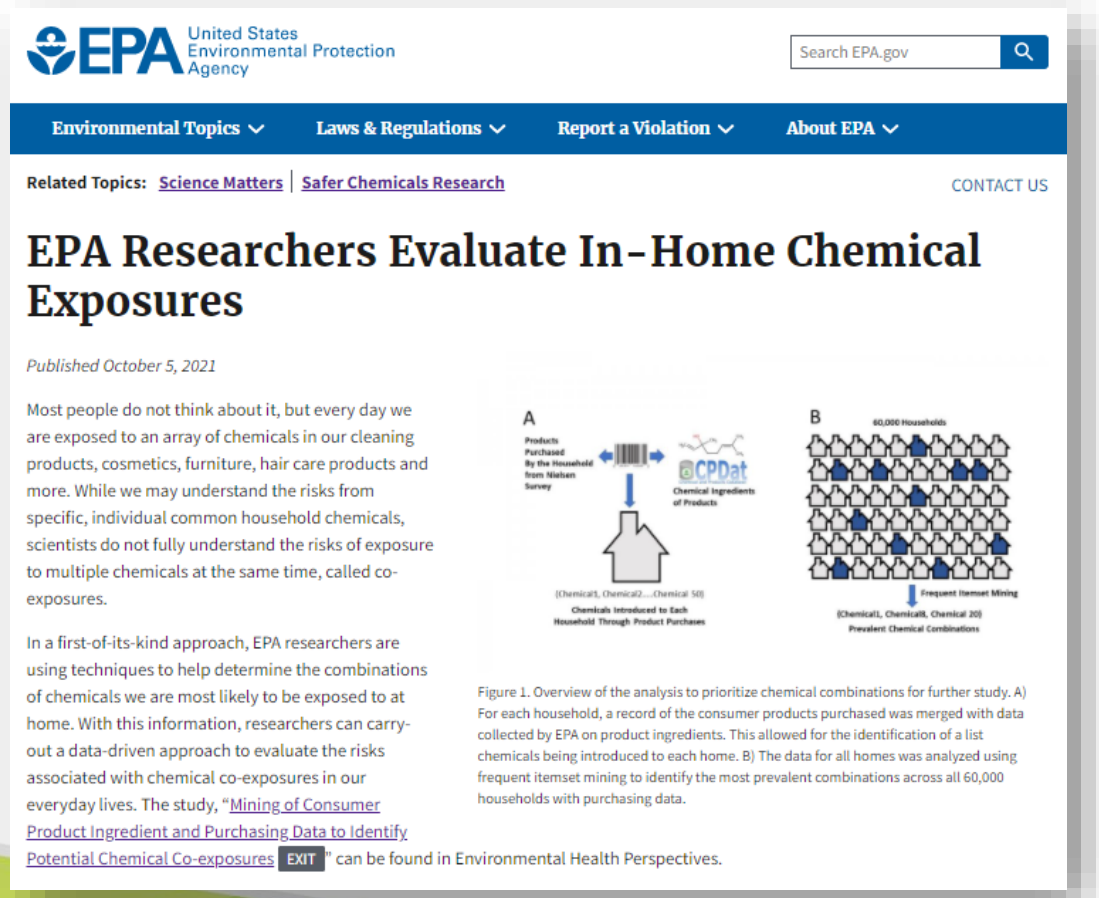
BOSC

BOARD OF SCIENTIFIC COUNSELORS

Incorporating BOSC recommendations into the CSS Research Portfolio

Some Examples

Real-World Scenarios, Complex Mixtures, Sensitive Subpopulations



EPA United States Environmental Protection Agency

Search EPA.gov

Environmental Topics | Laws & Regulations | Report a Violation | About EPA

Related Topics: Science Matters | Safer Chemicals Research

CONTACT US

EPA Researchers Evaluate In-Home Chemical Exposures

Published October 5, 2021

Most people do not think about it, but every day we are exposed to an array of chemicals in our cleaning products, cosmetics, furniture, hair care products and more. While we may understand the risks from specific, individual common household chemicals, scientists do not fully understand the risks of exposure to multiple chemicals at the same time, called co-exposures.

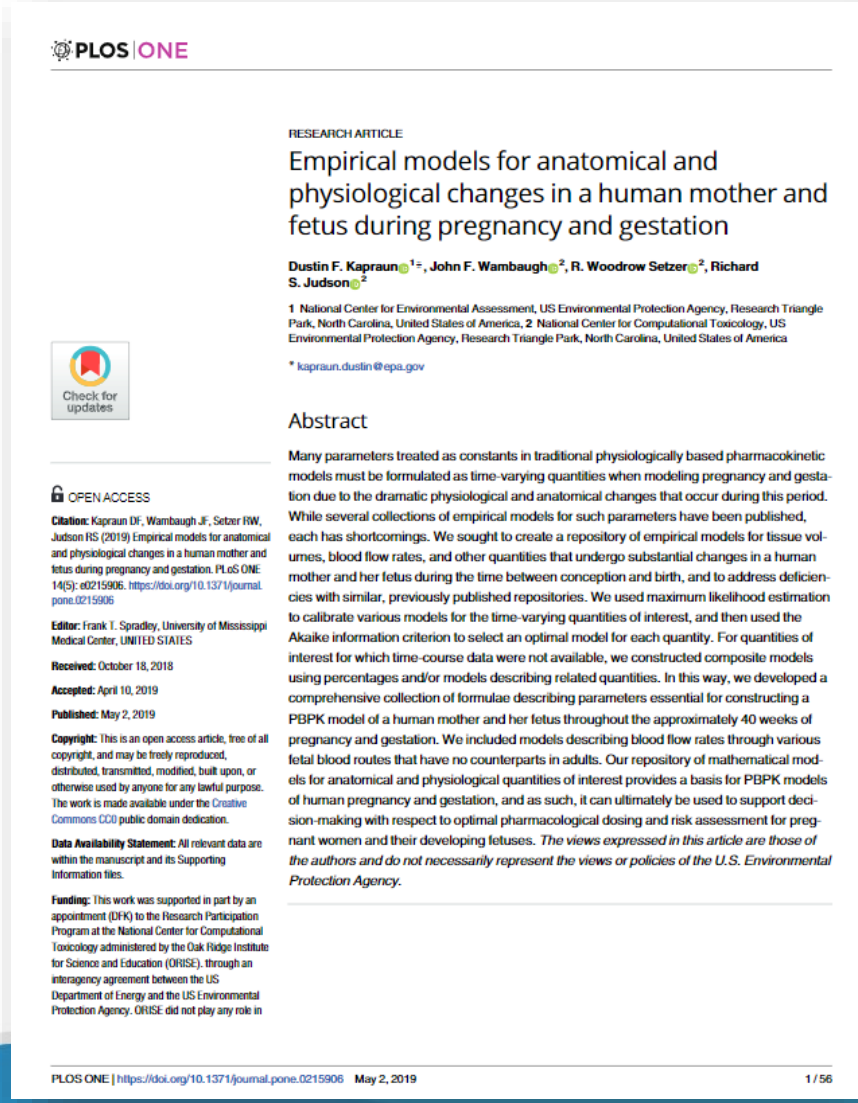
In a first-of-its-kind approach, EPA researchers are using techniques to help determine the combinations of chemicals we are most likely to be exposed to at home. With this information, researchers can carry-out a data-driven approach to evaluate the risks associated with chemical co-exposures in our everyday lives. The study, "Mining of Consumer Product Ingredient and Purchasing Data to Identify Potential Chemical Co-exposures EXIT" can be found in Environmental Health Perspectives.

Figure 1. Overview of the analysis to prioritize chemical combinations for further study. A) For each household, a record of the consumer products purchased was merged with data collected by EPA on product ingredients. This allowed for the identification of a list chemicals being introduced to each home. B) The data for all homes was analyzed using frequent itemset mining to identify the most prevalent combinations across all 60,000 households with purchasing data.

- **CSS.2.1.3** Mining of consumer product and purchasing data to identify potential chemical co-exposures
- Lays the foundation for researchers to determine which household chemical mixtures are the most likely to occur and provides a data-driven pathway to evaluate chemical co-exposures in the home.

Real-World Scenarios, Complex Mixtures, Sensitive Subpopulations

- **CSS.2.2.5** High-throughput exposure models for critical pathways: Implementation and parameterization of models for occupational exposure
- **CSS.2.6.6** Life-Stage and Sensitive Population Characterization and Modeling
- **CSS.4.6.9** Combining cell-based metabolomics and lipidomics with cheminformatics tools for untargeted screening and prioritization of vertebrate-active stressors following exposures to complex mixtures



PLOS ONE

RESEARCH ARTICLE

Empirical models for anatomical and physiological changes in a human mother and fetus during pregnancy and gestation

Dustin F. Kapraun[1]*, John F. Wambaugh[2], R. Woodrow Setzer[2], Richard S. Judson[2]

1 National Center for Environmental Assessment, US Environmental Protection Agency, Research Triangle Park, North Carolina, United States of America, 2 National Center for Computational Toxicology, US Environmental Protection Agency, Research Triangle Park, North Carolina, United States of America

* kapraun.dustin@epa.gov

Check for updates

OPEN ACCESS

Citation: Kapraun DF, Wambaugh JF, Setzer RW, Judson RS (2019) Empirical models for anatomical and physiological changes in a human mother and fetus during pregnancy and gestation. PLoS ONE 14(5): e0215906. https://doi.org/10.1371/journal.pone.0215906

Editor: Frank T. Spradley, University of Mississippi Medical Center, UNITED STATES

Received: October 18, 2018

Accepted: April 10, 2019

Published: May 2, 2019

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Funding: This work was supported in part by an appointment (DFK) to the Research Participation Program at the National Center for Computational Toxicology administered by the Oak Ridge Institute for Science and Education (ORISE), through an interagency agreement between the US Department of Energy and the US Environmental Protection Agency. ORISE did not play any role in

Abstract

Many parameters treated as constants in traditional physiologically based pharmacokinetic models must be formulated as time-varying quantities when modeling pregnancy and gestation due to the dramatic physiological and anatomical changes that occur during this period. While several collections of empirical models for such parameters have been published, each has shortcomings. We sought to create a repository of empirical models for tissue volumes, blood flow rates, and other quantities that undergo substantial changes in a human mother and her fetus during the time between conception and birth, and to address deficiencies with similar, previously published repositories. We used maximum likelihood estimation to calibrate various models for the time-varying quantities of interest, and then used the Akaike information criterion to select an optimal model for each quantity. For quantities of interest for which time-course data were not available, we constructed composite models using percentages and/or models describing related quantities. In this way, we developed a comprehensive collection of formulae describing parameters essential for constructing a PBPK model of a human mother and her fetus throughout the approximately 40 weeks of pregnancy and gestation. We included models describing blood flow rates through various fetal blood routes that have no counterparts in adults. Our repository of mathematical models for anatomical and physiological quantities of interest provides a basis for PBPK models of human pregnancy and gestation, and as such, it can ultimately be used to support decision-making with respect to optimal pharmacological dosing and risk assessment for pregnant women and their developing fetuses. *The views expressed in this article are those of the authors and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.*

Science to Achieve Results

EPA Science to Achieve Results Grant RFA: Development of Innovative Approaches to Assess the Toxicity of Chemical Mixtures

1. Development and application of approaches to establish qualitative membership of chemical mixture components into toxicity pathway groupings in order to quantitatively evaluate their potential joint toxicity.

2. Development of tools useful for the examination of chemical mixture toxicity across different levels of biological organization.

https://www.epa.gov/research-grants/development-innovative-approaches-assess-toxicity-chemical-mixtures-request

Sustainable Chemistry, Life-Cycle Assessment, Circular Economy

- **CSS.2.3.2** Understanding end-of-life U.S. industrial chemical release profiles using data analytics techniques
- This framework can be used to track chemicals, estimate releases, and evaluate potential exposure pathways via various end-of-life scenarios including disposal, recycling, and re-manufacture.

Partner Engagement and Continued Collaborations

Computational Toxicology Communities of Practice

Communications & Outreach

Review CSS Research Area fact sheets, Safer Chemica
Science Matters Articles, and EPA social media pages

Webinars & Meetings

View past and upcoming webinar topics.
- CSS Science Webinar Series
- CompTox Communities of Practice Webinar Series
- Children's Environmental Health PACT Meetings

STATE OF THE SCIENCE ON DEVELOPMENT AND USE OF NEW APPROACH METHODS (NAMs) FOR CHEMICAL SAFETY TESTING

Location: U.S. Environmental Protection Agency
William Jefferson Clinton East Building
Room 1153 (the Map Room)

Date: December 17, 2019
Time: **9:30 am – 5:30 pm***

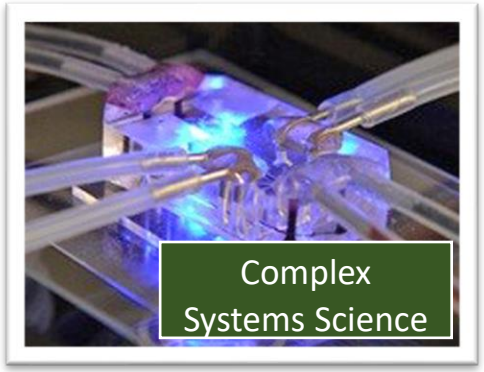
Agenda

8:30 am – 9:45 am	Registration
9:45 am – 10:00 am	Welcome
	Charge to the Group
Establishing Baselines for Animal Use at EPA and Oppo	
10:00 am – 10:20 am	Retrospective analysis of the statutory requirements, study requests, and research utilization in OCSPP and ORD
Variability and Relevance of Current Animal Tests and	
10:20 am – 10:40 am	Concordance of the toxicity of pharmaceuticals in animals and human
10:40 am – 11:00 am	Variability of animal studies for acute toxicity, skin sensitization, and mechanistic responses
11:00 am – 11:20 pm	Qualitative and quantitative variability of repeat dose animal toxicity studies
State of the Science in Development and Applica	
11:20 pm – 11:40 pm	Development of NAMs to predict acute toxicological responses
11:40 pm – 12:00 pm	Application of NAMs for quantitative screening level risk decisions
12:00 pm – 1:00 pm	Lunch
1:00 pm – 1:20 pm	State of the science for predicting developmental toxicity using NAMs

Tox21

Accelerating the Pace of Chemical Risk Assessment

APCRA



We listened -

- **New Approach Methods (NAMS) - in context**
  - Human, ecological, hazard, exposure
  - Generate data, build confidence, tiered approach
- **Tools - Models, databases, other**
  - Relevant, effective design, appropriate application
- **Innovation**
  - Attune to new materials and technologies
  - New ways of looking at intransigent problems
- **Knowledge Delivery**
  - Listen to needs, translate, provide solutions

FY19-22 Strategic Research Action Plan

CSS is guided by its StRAP developed through rigorous engagement with EPA programs and regions, states, and tribes to identify research needs.

BOSC
BOARD OF SCIENTIFIC COUNSELORS

Thank you

Questions

Office of Research and Development | Chemical Safety for Sustainability

Annette Guiseppi-Elie, Acting National Program Director
Kathie Dionisio, Principal Associate NPD
Heidi Bethel, Associate NPD
Kat Compton, Acting Associate NPD
James Smith, Student Services Contractor
Scarlett VanDyke, Student Services Contractor

November 4, 2021