



NTP

National Toxicology Program

The National Toxicology Program: An Interagency Partnership With a Global Reach

Rick Woychik, Ph.D.

**Director, National Institute of Environmental Health Sciences
and National Toxicology Program (NTP)**

Joined by Panel of NTP Federal Agency Representatives

Tuesday, March 12, 2024

3:00 – 4:00 p.m.

**Salt Palace Convention Center
Room 155F**





- **Welcome and Director's Remarks (5')**
 - Richard Woychik, Ph.D., National Institute of Environmental Health Sciences (NIEHS) and National Toxicology Program (NTP)
- **NTP Scientific Operations and Coordination (10')**
 - Nigel Walker, Ph.D., D.A.B.T., NIEHS, Division of Translational Toxicology (DTT)
- **6PPD-Quinone Interagency Working Group (10')**
 - Annette Guiseppi-Elie, Ph.D., FAIMBE, US Environmental Protection Agency (EPA), Office of Research and Development (ORD)



- **Panel Discussion and Q&A (20')**

- Annette Guiseppi-Elie, Ph.D., EPA/ORD
- Christina Lawson, Ph.D., Centers for Disease Control and Prevention (CDC), National Institute for Occupational Safety and Health (NIOSH)
- Tucker Patterson, Ph.D., Food and Drug Administration (FDA), National Center for Toxicological Research (NCTR)
- Robert C. Sills, D.V.M., Ph.D., NIEHS/DTT
- Nigel Walker, Ph.D., NIEHS/DTT (Moderator)
- Richard Woychik, Ph.D., NIEHS and NTP

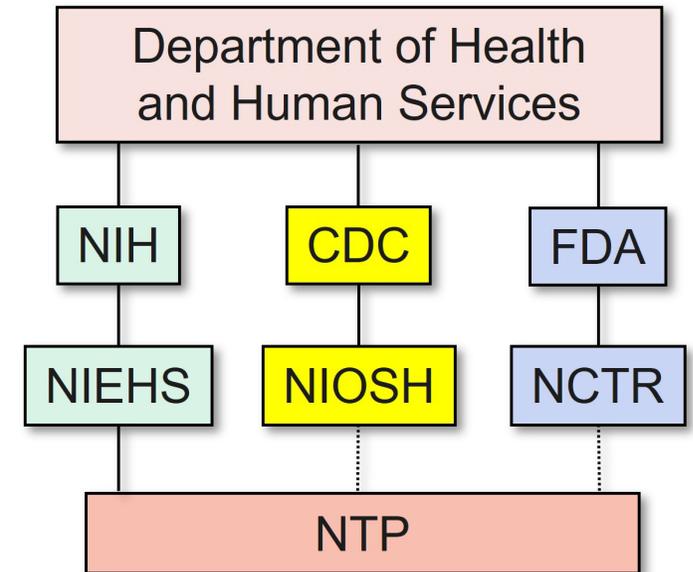
- **Meet & Greet Opportunity (10')**



US National Toxicology Program (NTP)

- An Interagency partnership of relevant toxicological research activities at NIEHS, NIOSH, and FDA
- Since 1978, the partnership has played a critical role in generating, interpreting, and sharing toxicological information about potentially hazardous substances in our environment
- Science is used for programs, activities, and policies that promote health or lead to the prevention of disease

“Science you can depend on for decisions that matter”



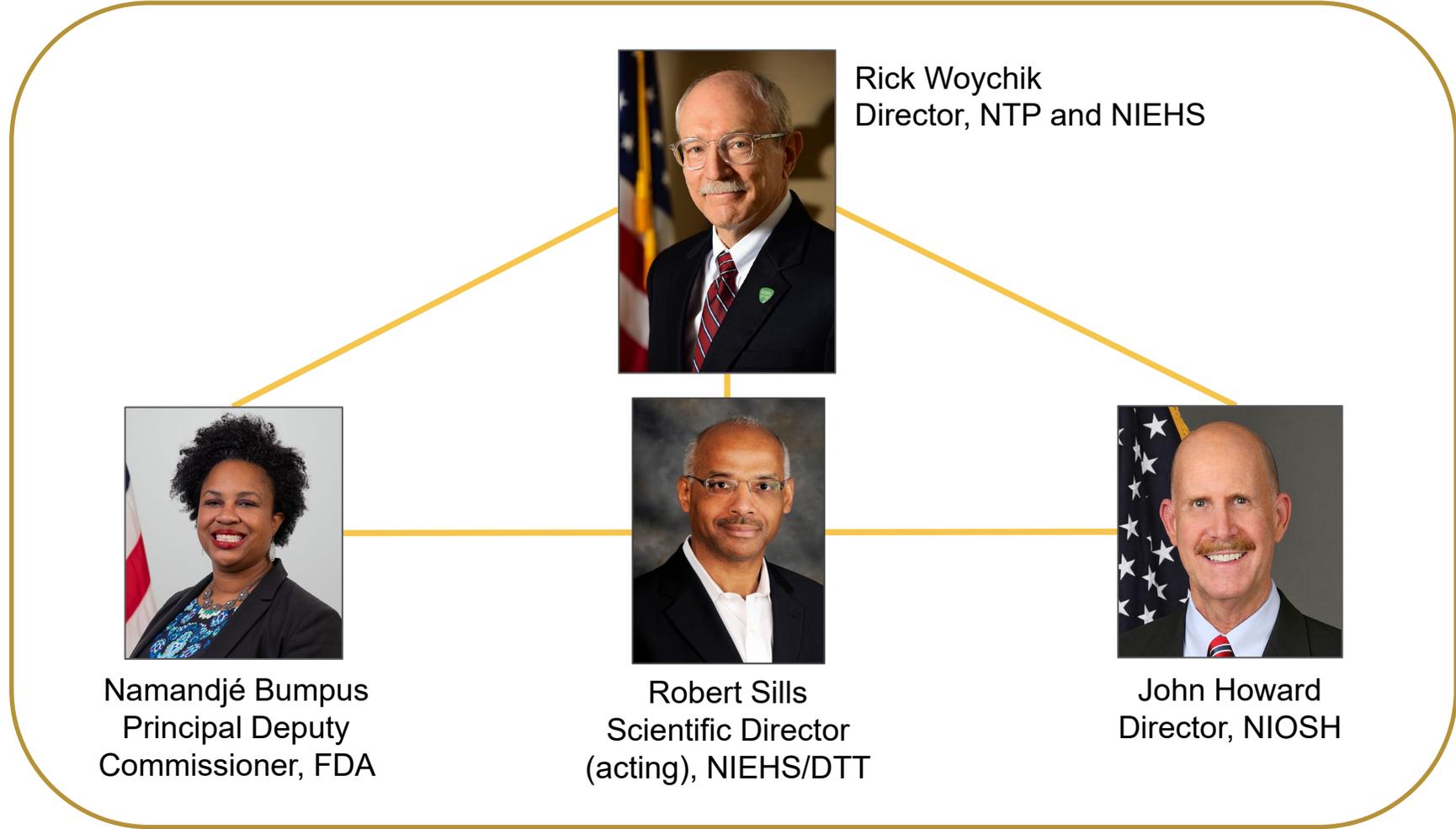
<https://ntp.niehs.nih.gov>



- **Researching substances or issues of concern**
 - Conducting short-term, long-term, and/or mechanistic studies to determine health-related effects, including cancer, and effects on reproduction, development, or immune system
- **Developing better ways to predict what effect chemicals will have on people**
 - Testing chemicals faster and more efficiently, through the implementation of New Approach Methodologies (NAMs)
- **Reducing reliance on the use of animals in toxicity testing**
 - Coordinating federal and international efforts to advance the acceptance of scientifically valid non-animal alternative tests
- **Informing public health decision-making**
 - Identifying substances that pose a cancer hazard to humans, through the Report on Carcinogens
- **Facilitating research by other scientists/public by providing freely available data and tools**
 - Sharing results and supporting information from more than 9,000 toxicology and toxicogenomic studies in NTP databases



NTP Leadership and Committees



NTP Steering Committee

- Focal point for broader federal coordination of NTP activities
- Decision-making group that provides oversight of NTP interagency activities

NTP Executive Committee (EC)

- Department of Defense
 - Environmental Protection Agency
 - National Cancer Institute
 - National Center for Environmental Health/Agency for Toxic Substances and Disease Registry
 - Consumer Product Safety Commission
 - Occupational Safety and Health Administration
- Provides programmatic and policy advice to the Director, NTP
 - Works with NTP core partners and other agencies, including those on the Executive Committee, to address contemporary public health challenges and emerging issues in toxicology

NTP Board of Scientific Counselors

- Advises NTP EC and Director on scientific program content
- Provides analysis and direction on NTP's scientific activities



- **NTP Vision and Mission**

- Vision: Innovative and trusted toxicological science protecting human health
- Mission: Partnering to build knowledge and advance toxicological sciences to protect and promote human health

- **Steering Committee**

- Composed of leadership from NIEHS, FDA, and NIOSH that meets regularly to discuss NTP business

- **Office of NTP Scientific Operations and Coordination (ONSOC)**

- Interagency implementation team with representatives from each NTP partner
- Supports interagency coordination and engagement on NTP activities

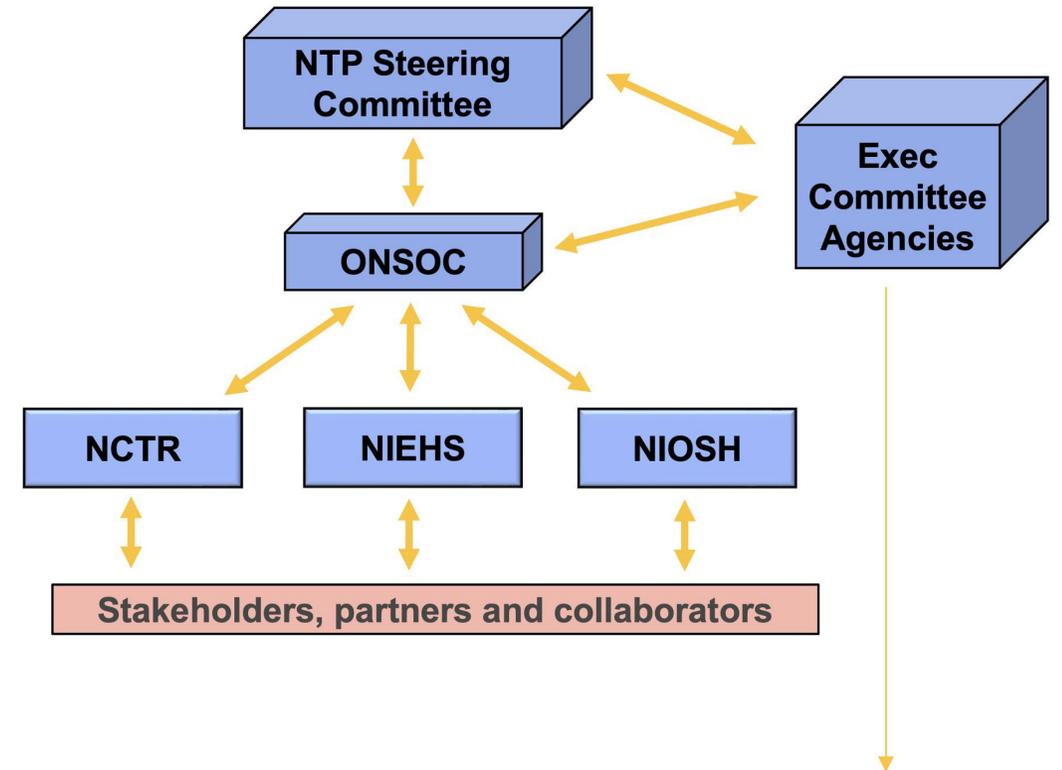
NTP Scientific Operations and Coordination

Nigel Walker, Ph.D., DABT
Acting Director, Office of NTP Scientific Operations and Coordination
Division of Translational Toxicology (DTT)
NIEHS



Federal Interagency NTP Coordination

- NTP Steering Committee
 - Decision-making group for NTP
 - Oversight and approval authority for the NTP portfolio
- NTP Executive Committee
 - High-level representatives of 7 other agencies
 - Additional federal agency input as needed
- Office of NTP Scientific Operations and Coordination (ONSOC)
 - Principal “organizational unit” for the operational implementation of interagency NTP activities
 - Representatives from each Steering Committee partner
 - FDA, NIEHS, NIOSH



- Department of Defense
- Environmental Protection Agency
- National Cancer Institute
- National Center for Environmental Health
- Agency for Toxic Substances and Disease Registry
- Consumer Product Safety Commission
- Occupational Safety and Health Administration

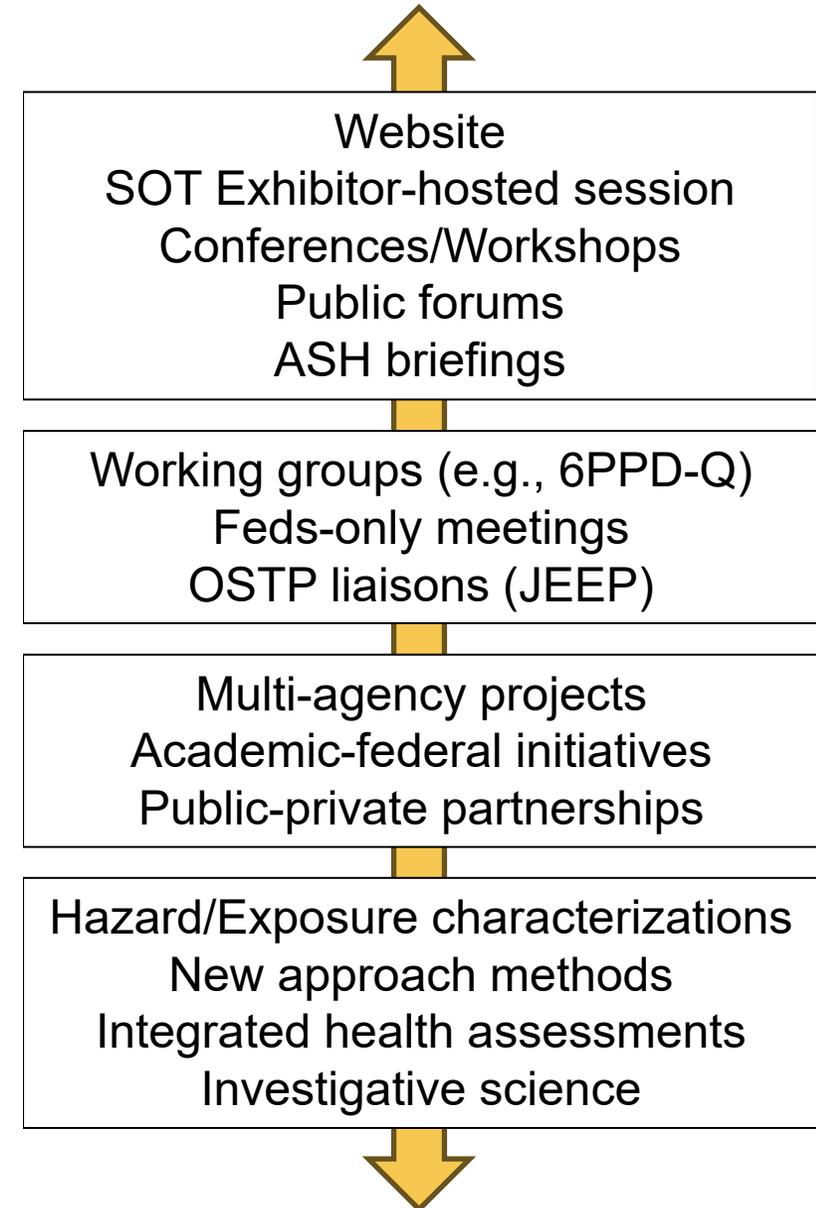
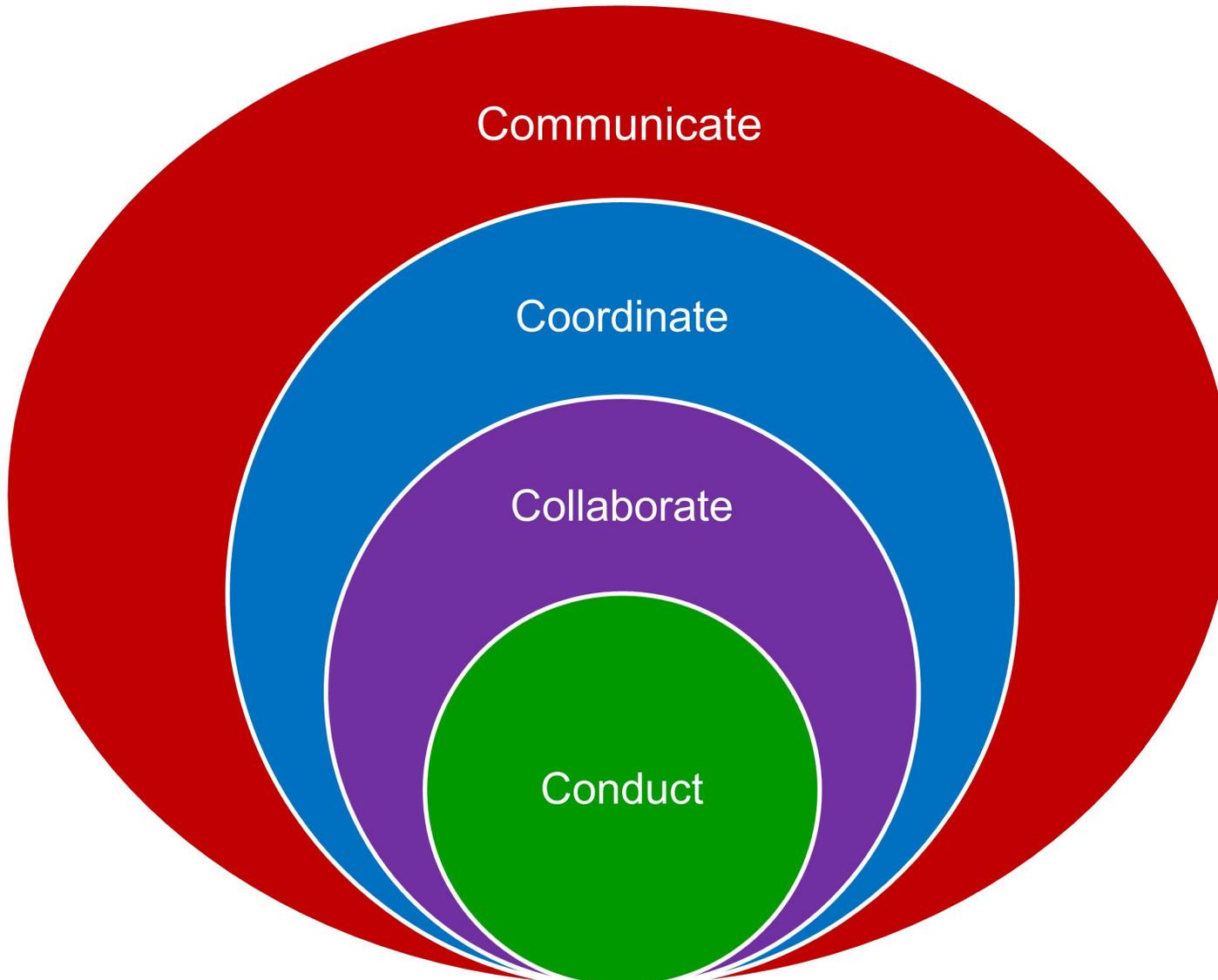


Key Things Carried Out Under the NTP Partnership

- Researching substances or issues of concern
 - Conducting short-term, long-term, and mechanistic studies to determine health-related effects including cancer, and reproductive and developmental disorders.
- Developing better ways to predict what effect chemicals will have on people
 - Testing chemicals faster and more efficiently, through the implementation of New Approach Methodologies (NAMs).
- Reducing reliance on the use of animals in toxicity testing
 - Coordination of federal and international efforts to advance the acceptance of scientifically valid non-animal alternative tests.
- Informing public health decision-making
 - Identifying substances that pose a cancer hazard to humans, through the Report on Carcinogens.
- Enabling other scientists/public by making data and tools freely available
 - NTP databases integrate more than 9,000 toxicology and toxicogenomics study results and supporting information.



NTP Modalities: The Four Cs





ONSOC Key Areas and High-level Goals

Research Strategies and Research Team Coordination

- Foster identification of new impactful NTP initiatives
- Implement an NTP working model of transparent and inclusive communication and coordination around research initiatives

Research Implementation, Resourcing, Conduct, and Progress

- Ensure establishment of interagency working groups and development of research strategies and implementation plans
- Conduct regular review of the projects in support of the NTP

Reporting, Review, Conclusions, Translation, and Impact

- Maintain interagency oversight of partner-agency “NTP portfolios”
- Ensure review of draft reports/conclusions by NTP partner agencies

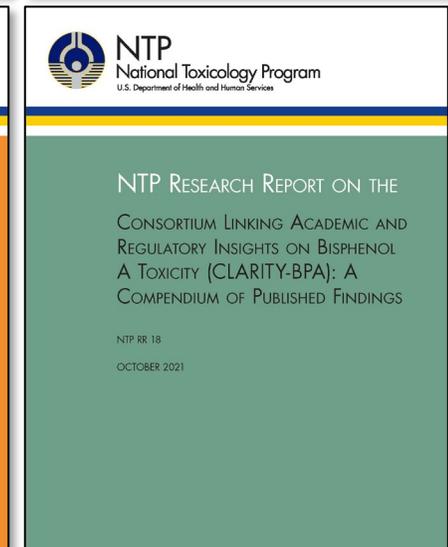
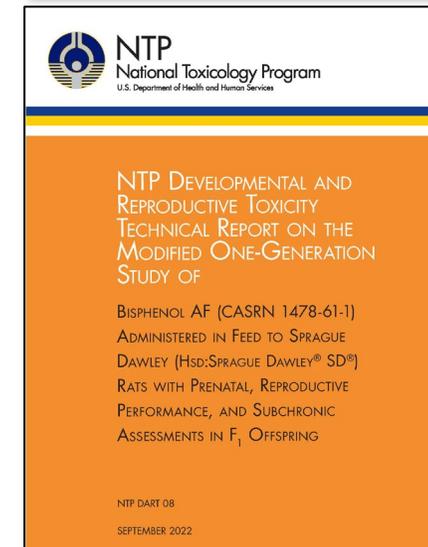
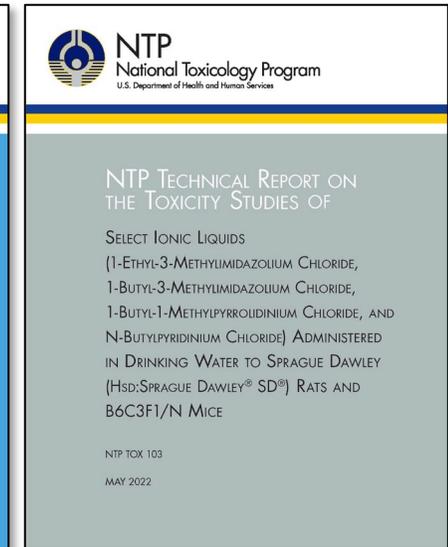
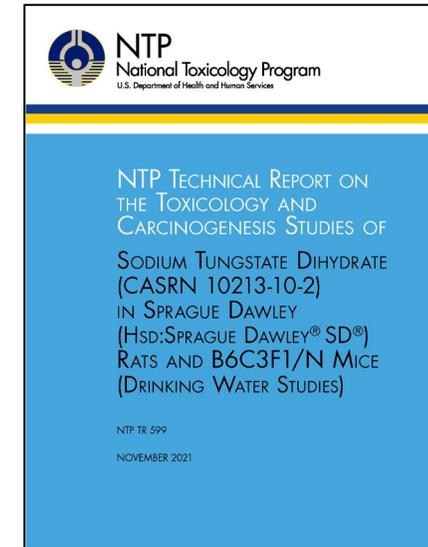
NTP Communication and Interagency Coordination

- Ensure there is contemporary and responsive public-facing communications about NTP
- Lead effective planning for NTP business meetings



NTP Reports: In Peer Review or Published

- NTP Toxicity Reports (short-term/specialty studies)
 - Sodium metavanadate/vanadyl sulfate (environmental substance)
 - Acetoin and 2,3-Pentanedione (butter flavorings)
 - *Stachybotrys chartarum* (fungal mold)
- NTP Technical Reports (chronic carcinogenicity studies)
 - TCP (flame retardant)
 - Black cohosh extract (dietary supplement ingredient)
 - Triclosan (antimicrobial substance in consumer products)
- NTP Research Report 19
 - Trend Test for Binary Data with Survivability and Clustering Adjustments





Assessing in Vivo Toxicity in Rodent Models

Crude oil fractions: C9
Alkylbenzenes

- 2-Ethyltoluene and 1,2,4-Trimethyl benzene

Organophosphate flame
retardants

- Triphenyl phosphate (TPHP) and Isopropylated phenyl phosphate (IPP)

Plasticizer for
polyamide compounds

- N-Butylbenzenesulfonamide

Ground water
contaminants

- Boron and Thallium sulfate

UV stabilizers

- Phenolic benzotriazoles class study



Assessing Chronic Carcinogenic Hazards in Vivo

Sulfolane

- Alaskan refinery groundwater contaminant

Alpha-pinene

- Occupational forestry exposures and in consumer products

Multiwalled carbon nanotubes

- Nanoscale material

Mixed xylenes

- Petroleum component



Report on Carcinogens Cancer Hazard Assessments

- Woodsmoke
 - Indoor heating and wildfires
- Polycyclic aromatic hydrocarbons (PAH) and Nitro-PAHs
 - Byproducts of combustion of organic substances and ingestion via grilled meats
- Halogenated flame retardants
 - Consumer products and environmental sources
- Para-chlorotrifluorotoluene (PCTF)
 - Cleaning solvent and component of used in paints and coatings in automotive body shops

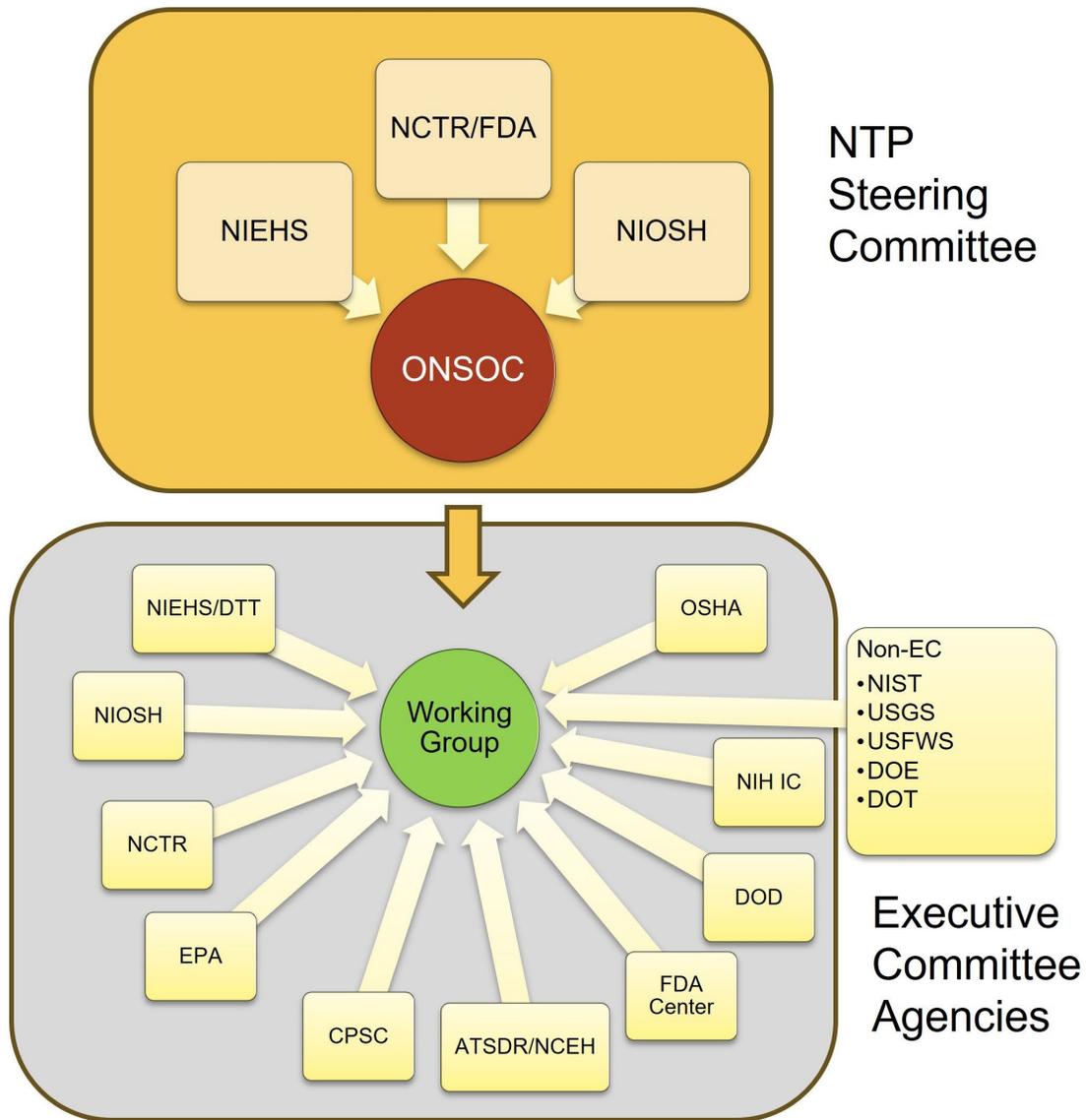




- Liaise with the Office of Science and Technology Policy (OSTP) Joint Subcommittee on Environment, Innovation, and Public Health (JEEP)
 - Contaminants of emerging concern
 - 6PPD-Quinone: Creation of interagency NTP Working Group
 - PFAS
 - ICCVAM PFAS New Approach Methodologies (NAMs) Working Group
- Briefings to the Assistant Secretary for Health, U.S. Department of Health and Human Services, on pertinent issues and activities
 - Cannabinoids
 - Combined Exposures and Mixtures



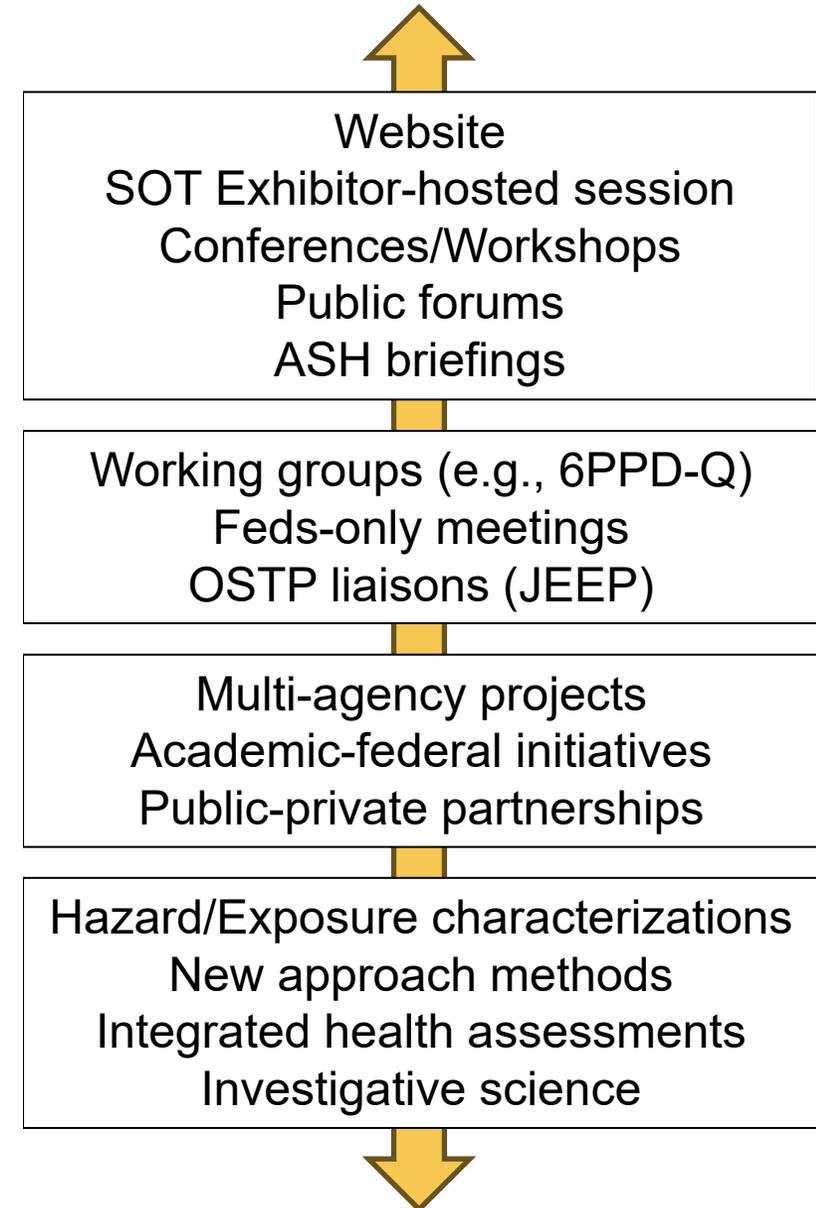
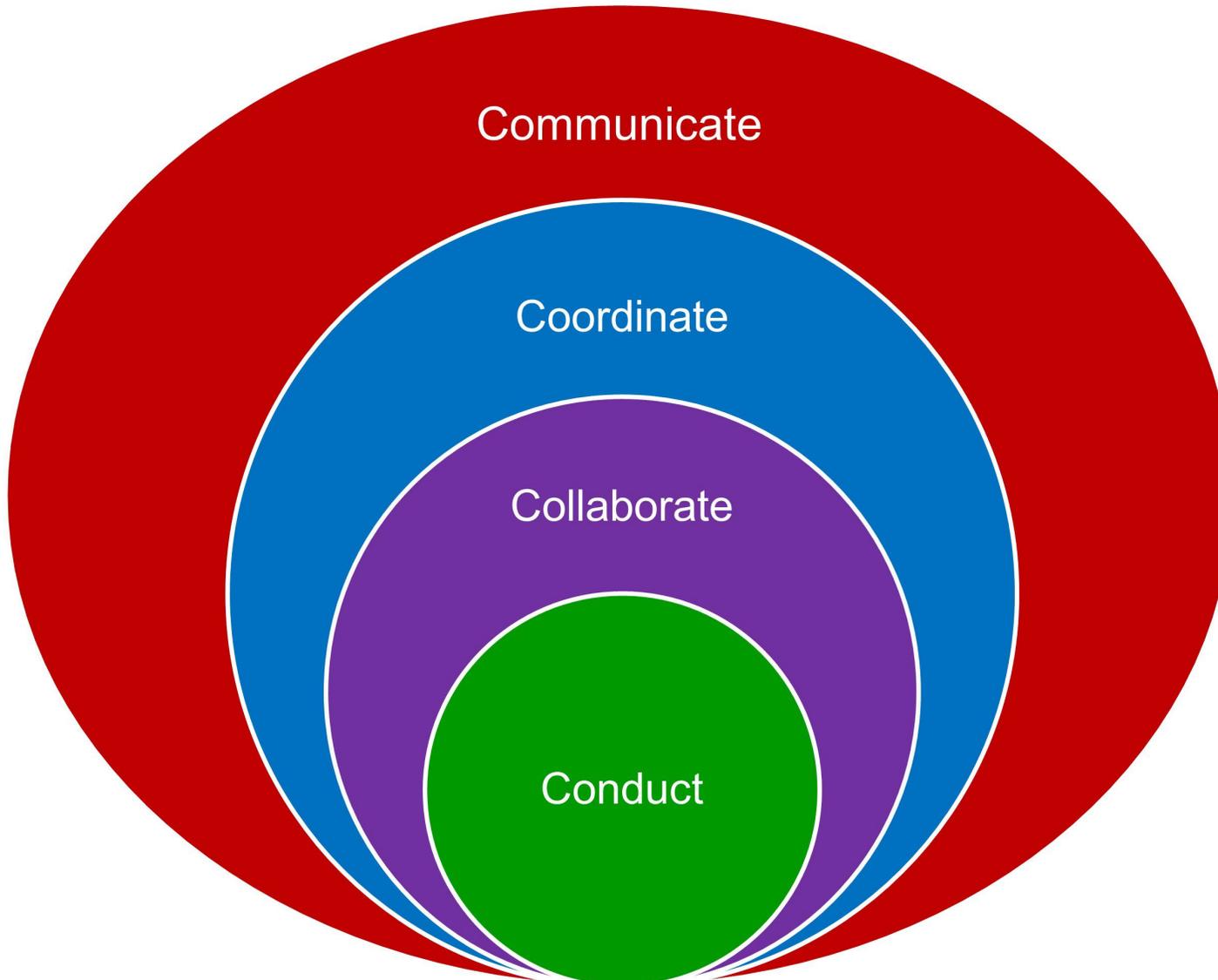
NTP Operational Working Group Model



- Current model for 6PPD-Quinone
- Model for future NTP initiatives
- Core partners (Steering Committee) as stewards of the brand and NTP portfolio
- Other agencies organized via a NTP Working group... per topic
 - EC agencies
 - Non-EC agencies as needed



NTP Modalities: The Four Cs



6PPD-Quinone Interagency Working Group

Annette Guiseppi-Elie, Ph.D., FAIMBE

National Program Director, Chemical Safety for Sustainability, Office of Research and Development, EPA and Co-Chair OSTP JEEP Contaminants of Emerging Concern Strategy Team

Society of Toxicology Annual Meeting, March 12, 2024

Disclaimer: The views expressed in this presentation are those of the author and do not necessarily reflect the views and policies of the U.S. EPA.

Conflict of interest: None



6PPD-Quinone – Cross-Governmental Coordination

6PPD-Quinone is a contaminant of emerging concern

Issue –

- The potential of 6PPD-quinone to have ecotoxic effects and impact salmon populations is a key issue.
- These fish species have cultural, commercial, and ecological importance, and some coho salmon populations are endangered and threatened.
- Many Tribes rely heavily on salmon and other aquatic resources for food and cultural practices.
- Limited information is available regarding release to the environment, fate and transport, and human health effects of 6PPD-quinone.
- Needed – Data to inform timely decisions on protection of human health and the environment.

Cross-governmental coordination can leverage existing activities, avoid duplication, and support timely development of needed information



6PPD-Quinone – Cross-Governmental Coordination

Contaminant of Emerging Concern

- Breakdown product of tire rubber antiozonant, 6PPD
- Present at toxic concentrations in stormwater-affected creeks
- Identified as highly toxic to coho salmon
(Tian et al. 2021, Science)*

Key information needs/research gaps

- Effects on other fish/aquatic species and people;
- Release, Fate and Transport, Mitigation

Considerations for cross-governmental coordination

- Inform research gaps in an agile manner
- Provide access to data and expertise to address areas of interests
- Explore appropriate assays to evaluate human and ecological endpoints
- Safer alternatives (what might be appropriate assays)
- Help procure chemicals

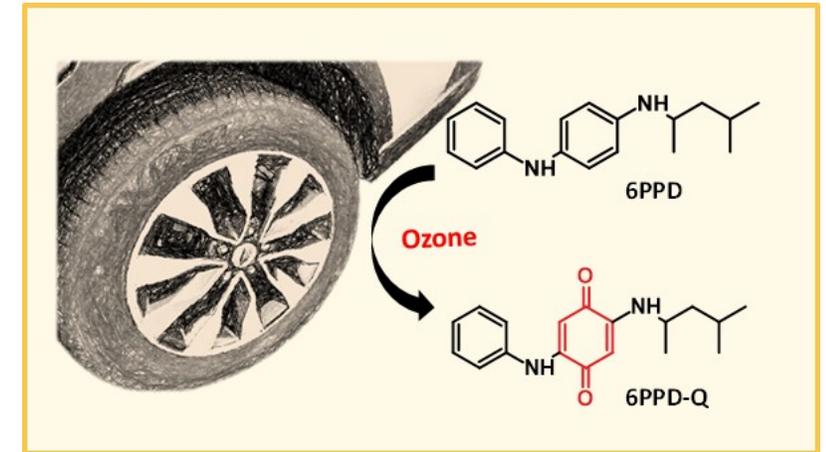


Image credit: G. Gamboa, FDA

*A ubiquitous tire rubber-derived chemical induces acute mortality in coho salmon; Coho Urban Runoff Mortality Syndrome -

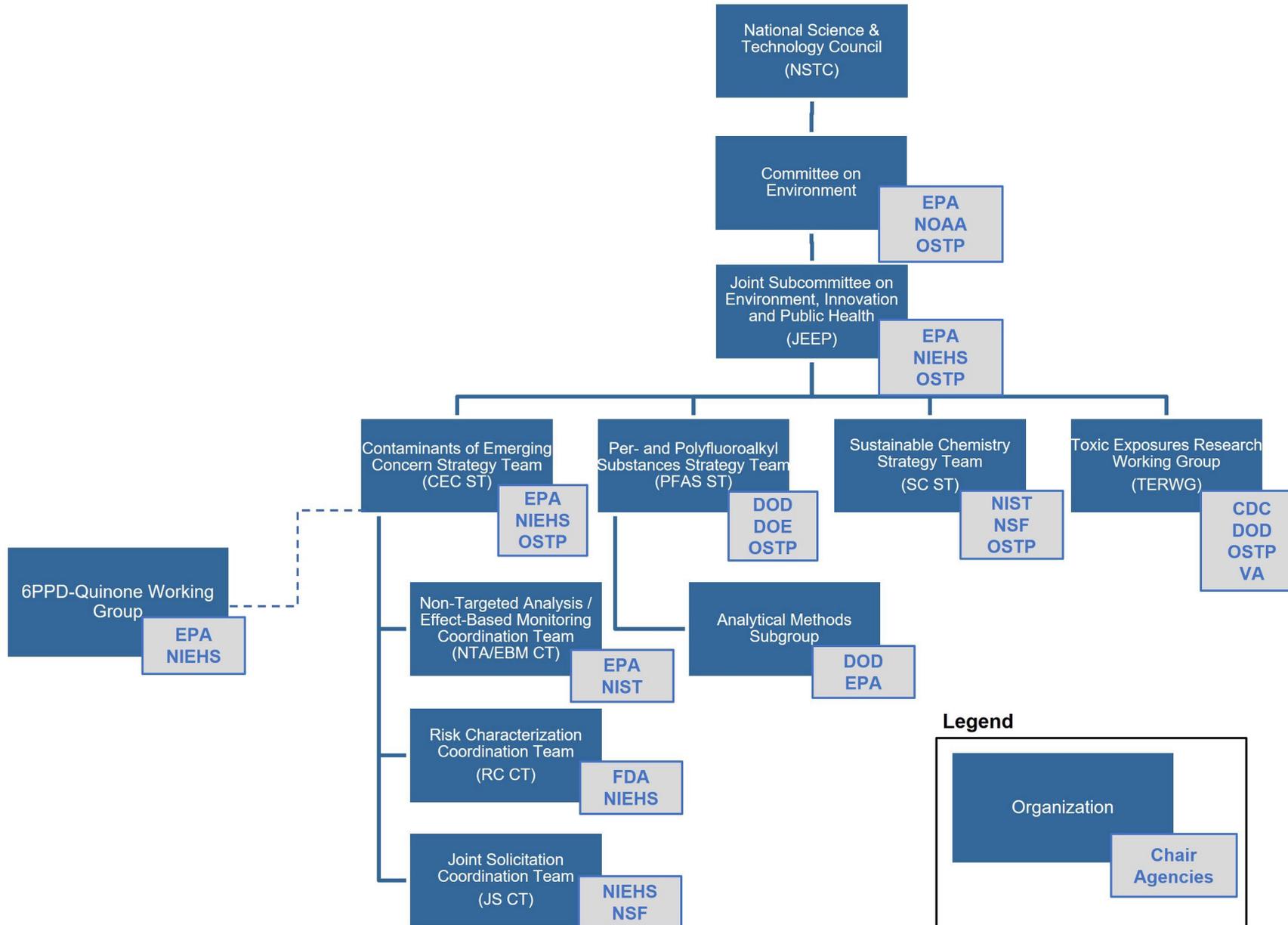


The “JEEP”

- **Purpose:** Promote Federal cross-disciplinary R&D activities
 - **Contaminants of Emerging Concern (CEC)**
 - Per- and Polyfluoroalkyl Substances (PFAS)
 - Sustainable Chemistry
 - Toxic Exposures Research
- **Scope**
 - Landscape and gap analysis
 - Strategic planning
 - Coordination of Federal research and development efforts
 - Recommending policy options
- **Cross-Agency Involvement**
- **National Emerging Contaminants Research Initiative (NECRI)**



The “JEEP” Structure



Agency Involvement

- Department of Homeland Security (DHS)
- Department of Commerce (DOC) - National Institute of Standards and Technology (NIST) and National Oceanic and Atmospheric Administration (NOAA)
- Department of Defense (DOD)
- Department of Energy (DOE)
- Department of Transportation (DOT)
- Environmental Protection Agency (EPA)
- Office of Management and Budget (OMB)
- Office of Science and Technology Policy (OSTP)
- Department of Health and Human Services (HHS) - Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), National Institute of Environmental Health Sciences (NIEHS)
- National Aeronautics and Space Administration (NASA)
- National Science Foundation (NSF)
- Small Business Administration (SBA)
- United States Department of Agriculture (USDA)
- United States Geological Survey (USGS)
- Veterans Affairs (VA)

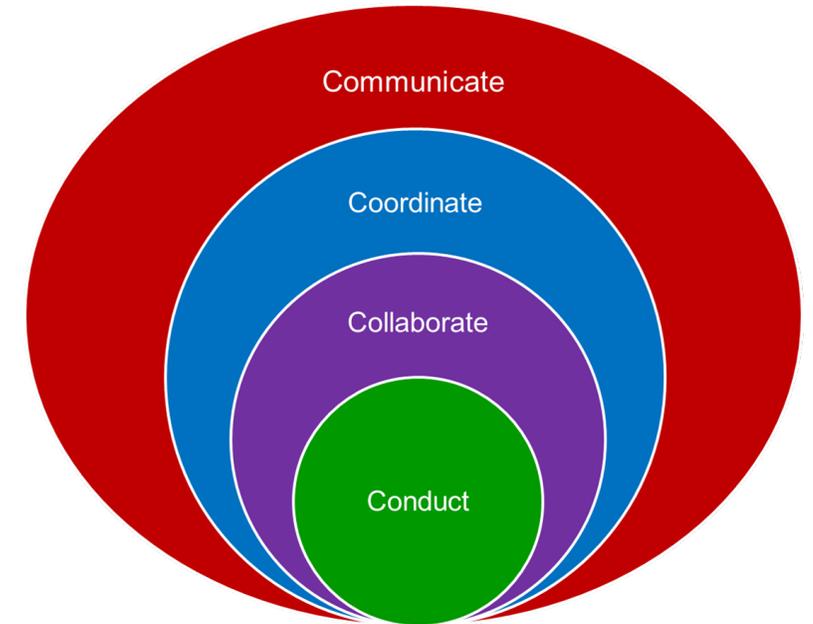
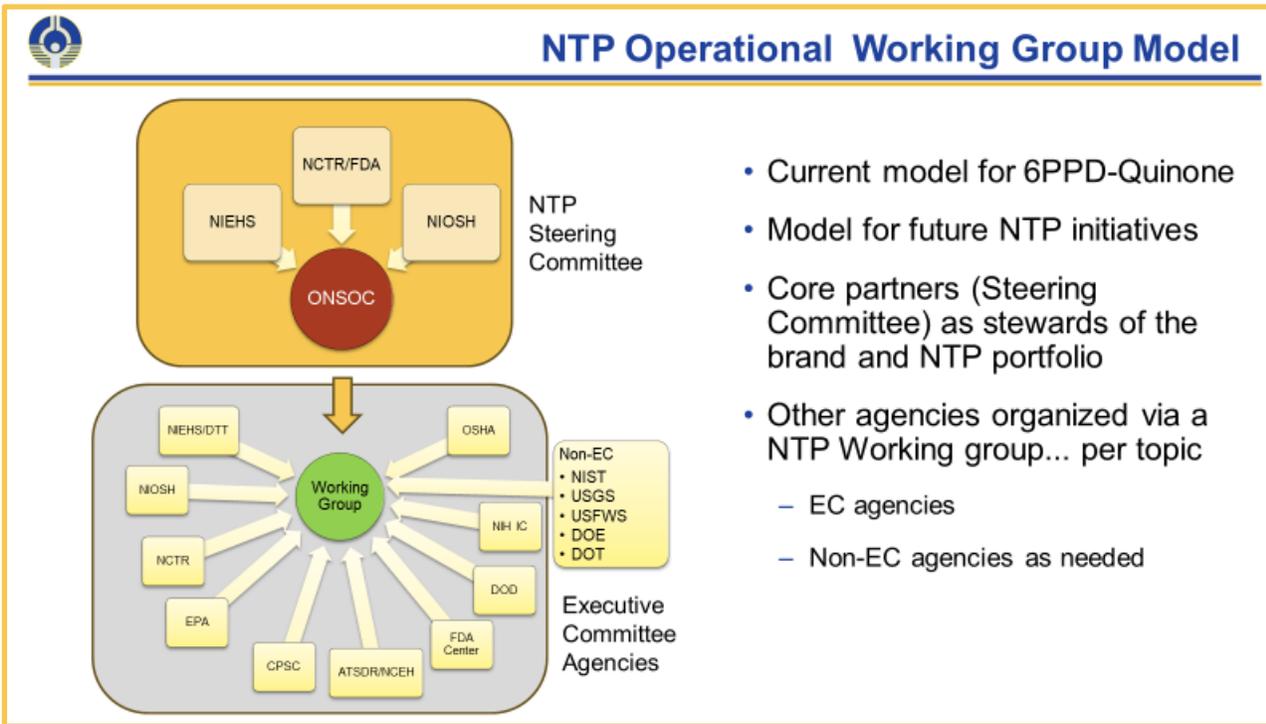
Legend





6PPD-Quinone (6PPD-Q) Interagency Working Group (WG)

- NSTC JEEP reached out to NTP for coordination (August 2023)
- NTP Executive Committee concurred (September 2023)
- An operational Working Group Model embracing the “4Cs” (kick off October 2023)





Key Goals for the WG

- To be focal point for **communication and coordination** on federal efforts related to 6PPD-Q
 - Understand extent of activities across the federal space
 - Identify areas that may be complementary and where we can reduce redundancy
 - Identify key activities to advance understanding of relevant human health effects of 6PPD-Q
 - Serve as an information hub/portal for sharing
- Facilitate participation on **conduct of coordinated and/or collaborative** effort(s) related to 6PPD-Q (broader than human health)

Overall – timely acquisition of critical data to inform decisions protective of humans and the environment



In Progress Coordination Activities

Sharing information, including contacts, challenges, knowledge gaps, interests

- Bimonthly meetings (established 01/24) and working discussions
- Compilation of current and planned activities
- Procurement issues
- Tribal and cultural issues (environmental justice)

Fostering coordinated communication

- Internal hub for document sharing
- External public-facing website (Expected launch 2Q 2024)
- Scientific conferences (SOT, March 2024)

Activities across federal space (for a coordinated nimble response) include

- Literature search strategy (e.g., leveraging searches across agencies)
- Human health effects studies (e.g., short-term NAMs studies for human health effects)
- Ecological effects studies (e.g., bioassays for rapid assessments)
- Alternatives assessment (e.g., evaluation of 6PPD alternatives using bioassays)



- **FDA:** Yeisley et al., *“Disruption of primary human hepatocyte functions by 6PPD-Quinone, the transformation product of a ubiquitous vehicle tire rubber additive”* (Poster Session - Abstract 5029)
 - **Thur., March 14th, 8:30-11:30 AM, Salt Palace Convention Center, Hall E, Poster 130**
- **EPA:** Guiseppi-Elie on *Coordinating to Fill Critical Knowledge Gaps on the Tire Anti-Degradant Contaminant of Emerging Concern 6PPD-Quinone*; part of Hot Topics Session *“Where the rubber meets the road: Impact of tire wear particles on the environment and human health”*
 - **Thur., March 14 from 10:20-10:45 AM, Grand Ballroom A**



Numerous members across the US Government

Department of Commerce (**DOC**)/National Institute of Standards and Technology (**NIST**) and DOC/National Oceanic and Atmospheric Administration (**NOAA**), Department of Defense (**DOD**), Department of Energy (**DOE**), Department of Transportation (**DOT**), Environmental Protection Agency (**EPA**), Food and Drug Administration (**FDA**), Centers for Disease Control and Prevention (**CDC**)/National Center for Environmental Health (**NCEH**)/Agency for Toxic Substances and Disease Registry (**ATSDR**) and CDC/National Institute for Occupational Safety and Health (**NIOSH**), National Institute of Environmental Health Sciences (**NIEHS**), Office of Science and Technology Policy (**OSTP**), United States Fish and Wildlife Service (**USFWS**), United States Geological Survey (**USGS**)



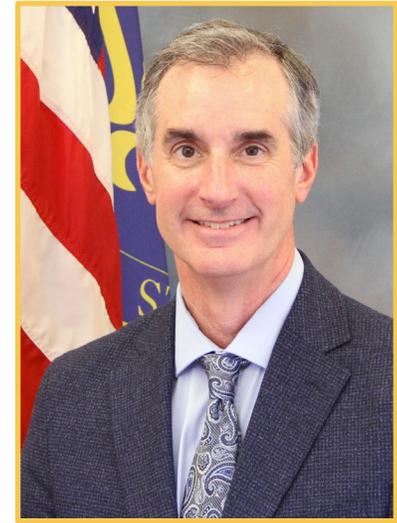
Panel Discussion



Annette Guiseppi-Elie, EPA/ORD



Christina Lawson, CDC/NIOSH



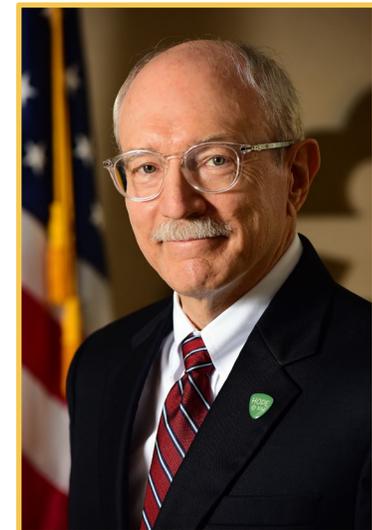
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