



NTP

National Toxicology Program

DNTP Strategic Planning Framework

Scott Masten, PhD, DABT

Division of the NTP

National Institute of Environmental Health Sciences

NTP Board of Scientific Counselors Meeting

December 3, 2020





Overview

- Planning framework and activities
- Purpose and strategy
 - Mission and goals
 - Research principles
 - Translational toxicology pipeline
- Implementation
 - Portfolio strategic areas of focus
 - Strategic research program development
- Engagement





Our approach

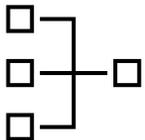
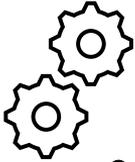
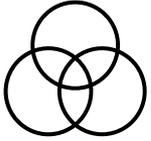
- Assess opportunities and needs that DNT is exceptionally well positioned to address and lead
 - Principles to guide decisions regarding what problems we take on
- Build upon existing organizational strengths
- Identify research focus areas that align to our goals and strategic intent



❖ *Strategic planning is a continuous process*



Activities in context of strategic realignment



- Portfolio – evaluation, structure, composition, focus
- Processes – program development, management, governance
- People – collaborative, team-based approach
- Products – program and project plans, milestones, deliverables
- Structure – organizational units, functional teams, operational model



- Expand our value and impact by emphasizing innovative translational approaches to human relevance that increases confidence in decision-making



What?

Work on topics important to organization, mission, stakeholders

Why?

Rationale and value for specific programs, projects, activities

How?

Pipeline of integrated capabilities that generate translational, knowledge-generating, decision-enabling outputs





National Toxicology Program (NTP) Division

To improve public health through the development of data and knowledge that are translatable, predictive and timely

<https://www.niehs.nih.gov/research/atniehs/dntp/index.cfm>



National Institute of Environmental Health Sciences

Your Environment. Your Health.

Our mission is to discover how the environment affects people in order to promote healthier lives.

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



- Collaborate with public stakeholders and global partners to identify and address public health issues



- Generate and communicate trusted scientific information to support decision-making on environmental hazards of public interest

- Lead the transformation of toxicology through the development and application of innovative tools and strategies

- Educate and train the next generation of translational scientists to be innovative leaders in the field





Key considerations guiding portfolio decisions

- Complex public health concerns with recognized stakeholders that leverage our full spectrum of animal and non-animal capabilities
- Responsive to discrete knowledge gaps where actionable outcomes can be achieved
- Integrate and leverage existing knowledge in clearly defined and systematic ways
- Facilitate the adoption of novel tools and approaches to generate information that is more human-relevant and predictive
- Translational and mechanistic investigation supporting practical application in decision-making contexts





Portfolio Aligned to Research Principles – Examples

(1) Complex public health concerns with recognized stakeholders that leverage our full spectrum of animal and non-animal capabilities



- Radiofrequency radiation exposures requiring specialized infrastructure
- Perinatal exposure studies evaluating chronic toxicity and carcinogenicity of PFOA
- Maternal health effects of GenX
- Chronic inhalation toxicology studies of carbon nanotubes
- CLARITY BPA integrated toxicity assessment





Portfolio Aligned to Research Principles – Examples

(2) Responsive to discrete knowledge gaps where actionable outcomes can be achieved

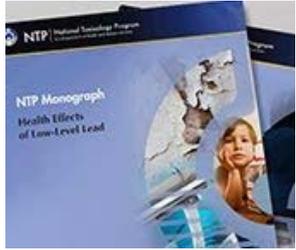
- Aqueous film-forming firefighting foams (AFFFs)
 - DoD request for comparative evaluation of current products
- Boron
 - Minnesota drinking water concern
- HIV combination therapies and in utero exposure
 - Increasing prophylactic use in HIV+ pregnant women





Portfolio Aligned to Research Principles – Examples

(3) Integrate and leverage existing knowledge in clearly defined and systematic ways



- Traffic-Related Air Pollution and Hypertensive Disorders of Pregnancy
- Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects
- Report on Carcinogens Monograph on Haloacetic Acids Found as Water Disinfection By-Products
- Report on Carcinogens Monograph on *Helicobacter pylori* (Chronic infection)





Portfolio Aligned to Research Principles – Examples

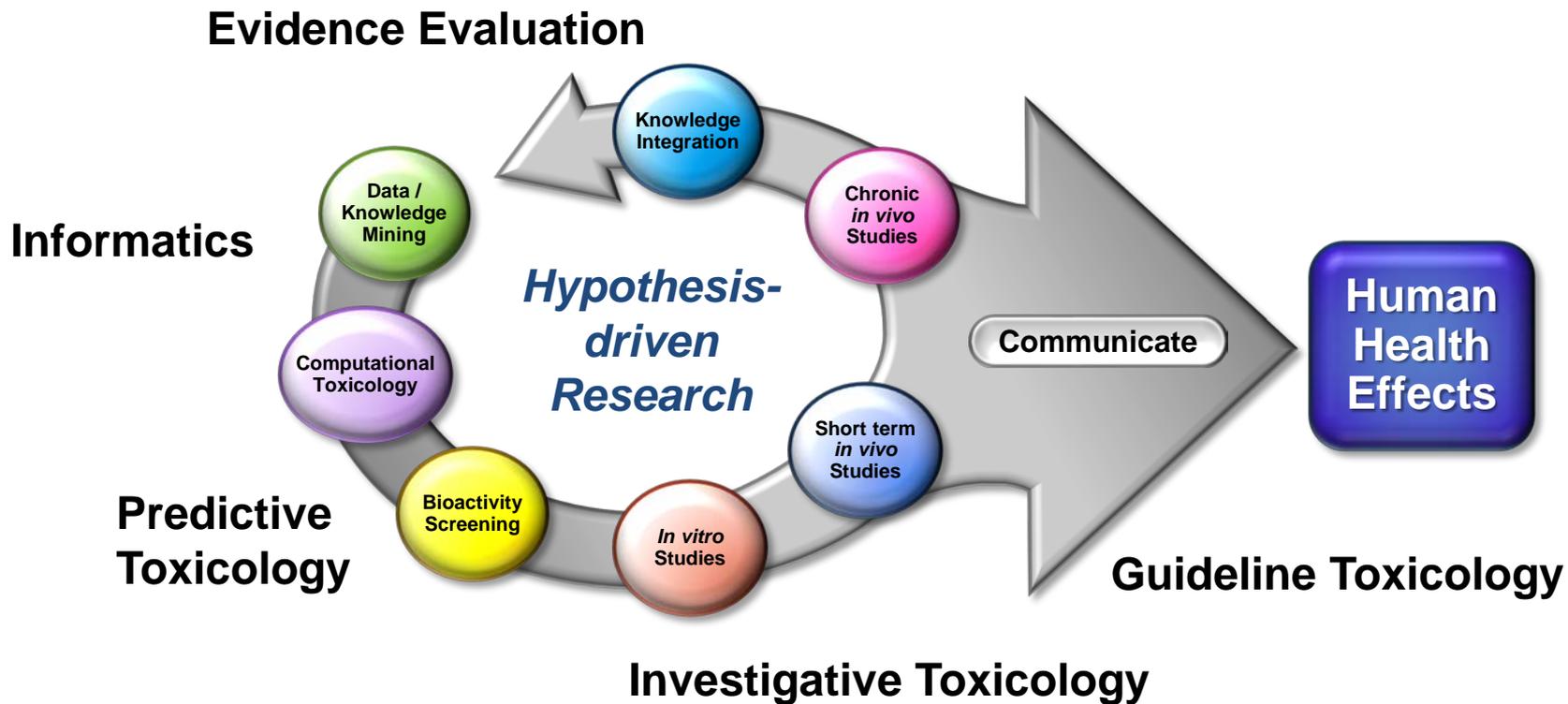
(4) Facilitate the adoption of novel tools and approaches to generate information that is more human-relevant and predictive

- Systematic Evaluation of the Application of Zebrafish in Toxicology (SEAZIT)
 - Developing standards for zebrafish modeling
- Skin sensitization new approach methodology
 - Recent adoption by EPA as more predictive of human outcomes
- 5-day in vivo transcriptomics
 - PFAS collaboration with EPA





Translational Toxicology Pipeline - Our strategic intent and tactical advantage





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Strategic Areas of Focus

Exposure-based Research Programs



Collaboratively address public health challenges

Health Effects Innovation Programs



Generate trusted scientific information to support decision-making

Responsive Research Programs



Develop and apply innovative tools and strategies

Strengthening Capabilities Programs





Strategic Areas of Focus (EBR, RR)

Exposure-based Research Programs



- Address contemporary public health problems related to environmental exposures
- Improve our ability to carry out substance-based hazard evaluations that are more translational, innovative and responsive

- Combined Exposures and Mixtures (CEM)
- Consumer Products and Therapeutics (CPT)
- Occupational and Inhalation Exposures (OIE)
- Emerging Contaminants and Issues of Concern (ECIC)
- Safe and Sustainable Alternatives (SSA)

Responsive Research Programs





Strategic Areas of Focus (HEI)

- Develop disease-focused environmental toxicology
- Provide an evidence-based approach to identify and understand potential environmental contributors to contemporary and common diseases
 - Carcinogenesis (Carci)
 - Cardiovascular (CV)
 - Developmental Neurotoxicity (DNT)

Health Effects Innovation Programs





Strategic Areas of Focus (SC)

- Enhance our progress in becoming a more predictive science through the deliberate application of a translational toxicology pipeline of capabilities
- Leverage and improve upon existing strengths
- Selectively develop and apply novel capabilities that directly enable multiple scientific initiatives
 - Novel Tools and Approaches (NTA)
 - Scientific Cyberinfrastructure (SCI)

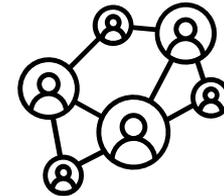
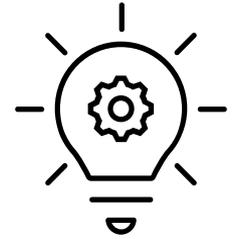
Strengthening Capabilities Programs





Program planning by DNTP staff teams

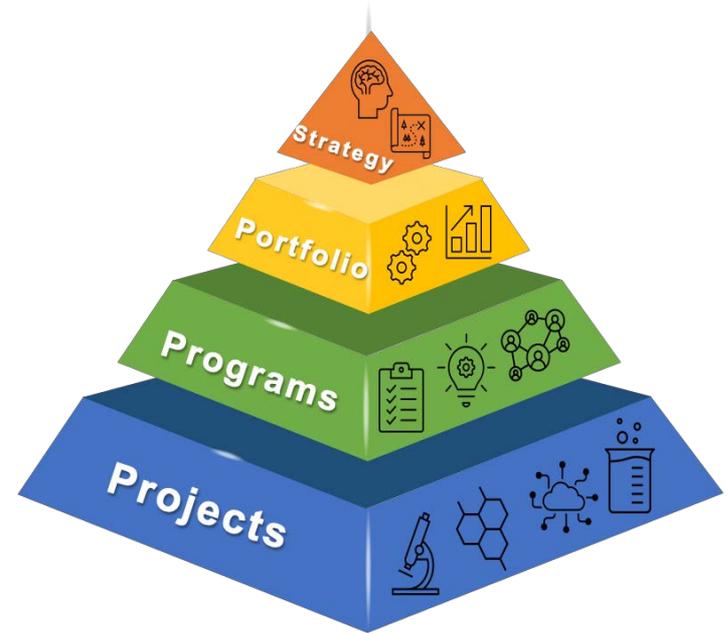
- Develop program-specific strategies and aligned projects
- Explore partnership opportunities within and outside of NIEHS
- Communicate program purpose and progress to internal and external stakeholders
- Manage portfolio of projects within program





Planning outputs

- Progressive document series
 - Program Introduction
 - Program Concept
 - Program Plan
- Continually revised and expanded – increasing detail, additional elements
- Used for internal decision-making and to facilitate external engagement





Research Program Introductions

Problem Statement

What is the opportunity?

Objectives

How will we approach the problem?

Rationale

Why is this problem/topic important for us to address?

Value Proposition

Why should we do this now?



- Public Health Context
- Alignment with Mission, Goals, Strategic Pipeline



Problem Statement

Objectives

Rationale

Value Proposition

Why should we do this now?

- *Why us, and not someone else?*
- *Why do this, and not something else?*
- *Why now, and not later, e.g., when more is known, and our knowledge, capabilities, capacity expand/improve?*





Research Program Concepts

Problem Statement

Objectives

Rationale

Stakeholder Interest and Engagement

Who is interested and in what capacity?

How will/have they been engaged?

Milestones and Metrics

When will key decisions be made, and (interim) products be delivered? How is progress and success measured?

Value Proposition

Developmental Neurotoxicity Health Effects Innovation Program

Presenter: Dr. Mamta Behl, Toxicology Branch, NIEHS/DNTP

Program Management Team: Mamta Behl, Laura Hall, Christopher McPherson, Nisha Sipes (prior member, now at EPA), and Robert Sills

Problem Statement

There is global concern that neurodevelopmental disorders (e.g., autism, attention-deficit hyperactivity disorder (ADHD), and other learning disabilities) are rising in populations worldwide, and that environmental exposures may be one of the contributing factors. The complexity of neurodevelopmental disorders is compounded by unknown developmental pathways and the complexity of neurodevelopmental processes. Innovative methods could better contribute to the etiology of neurodevelopmental disorders.

Objectives

The Developmental Neurotoxicity Health Effects Innovation Program has the following three objectives:

1. Implement a DNT screening battery that provides timely data on potential for DNT for further short-term animal models.
 - a. Identify key neurodevelopmental endpoints to be incorporated as part of the Screening Battery. Selected endpoints include: neurogenesis, neuroprogenitor cells (hNPC), midline crossing, human induced pluripotent stem cell formation/maturation in zebrafish behavior during embryonic and 3D neurosphere assay differentiation) to allow for evidence evaluation of DNT short-term in vivo behavior
 - b. Screen a set of approximately 100 environmental agents for evidence evaluation of DNT short-term in vivo behavior
 - c. Compare in vitro assay pairs (i.e., rodent models and/or (IVIVE) methods.

¹ Bal-Price et al. (2018) Recommendation on developmental neurotoxicity. ALTEX 35: 306-311

Cardiovascular Health Effects Innovation Program

Presenter: Dr. Brandiese Beverly, Office of Health Assessment and Translation, NIEHS/DNTP

Program Management Team: Brian Berridge, Brandiese Beverly, Nicole Kleinstreuer, Scott Auerbach, Michelle Cora, Sreenivasa Ramaiahgari, Shagun Krishna, Arif Rahman, Kevin Dreher (EPA), David Gerhold (NCATS)

Problem Statement

Chronic progressive cardiovascular (CV) disease is a primary cause of morbidity and mortality in the United States and globally. Current approaches to environmental hazard assessment do not include specific assessments of CV bioactivity and hazards despite growing evidence that environmental exposures contribute to the onset, risk, or progression of chronic CV disease. Additionally, current hazard assessment paradigms are better designed to identify overt injury or dysfunction in normal biology than exacerbation of a comorbidity. There is no defined approach to identify agents that might be contributing to contemporary and common CV diseases.

Objectives

The Cardiovascular Health Effects Innovation (CV HEI) Program is structured around the following three objectives:

1. Leverage existing knowledge to define key CV "failure modes" as a framework for modeling, link those modes to mediators of mechanistic bioactivity and screen existing databases to identify putative CV hazards.
2. Develop a suite of assay/testing/modeling/knowledge management capabilities that aligns to the current Division of the National Toxicology Program (DNTP) Translational Toxicology Pipeline and apply it, in an integrated fashion, to provide an evidence-based approach to assessing CV bioactivity of environmental substances.
3. Develop and implement an innovative capability for identifying potential environmental contributors to specific and contemporary clinical CV diseases.

Rationale

Public Health Context

CV disease in all its clinical manifestations is the most significant cause of morbidity and mortality in many developed countries and, increasingly, in those that are experiencing significant economic growth and prosperity. Lifestyle choices and genetics have clearly been demonstrated to be significant contributors but cannot alone or even in combination account for all the risk of developing CV disease and the individual variability in which people experience that disease. Environmental exposures are presumed to contribute to the risk of developing CV disease and, in some cases like air pollution, there is compelling evidence to support that likelihood. A broader recognition of potential contributors is limited because current approaches to environmental hazard assessment do not specifically interrogate CV

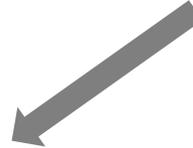


- Problem Statement
- Objectives
- Rationale
- Stakeholder Interest and Engagement
- **Portfolio – project alignment, evaluation, connectivity**
- **Project Duration, Resource Needs, Optionality**
- Milestones and Metrics
- **Programmatic Risk**
- Value Proposition



Planning outputs

- Program Plans (10)
- Objectives (30)
- Milestones (50-100)
- Projects (~250)





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Engagement with the BSC

- Focus on Strategies, Approaches and *Products* (SAPs)
- Understand our mission, goals, intent, value
- Gain perspective of entire portfolio, how it is structured, areas of focus
- Prospective advice during strategic program development
- Feedback on problems tackled, realistic objectives, tactical approaches, likelihood of success
- Assessing progress against milestones, contemplate strategic shifts in program direction or continuation





Cross-Cutting Strategic Themes

Output and outcome metrics

How to best measure success and ensure DNTP science will be impactful?

Diversity, inequality and racism

How to effectively address sociocultural factors that lead to environmental health disparities?

Optimizing stakeholder engagement

How to communicate during research planning, conduct, reporting phases?

Capability building

What enables a culture of innovative, forward-thinking?

Expanding our portfolio of products

What types of novel outputs will allow for broader and earlier knowledge dissemination?



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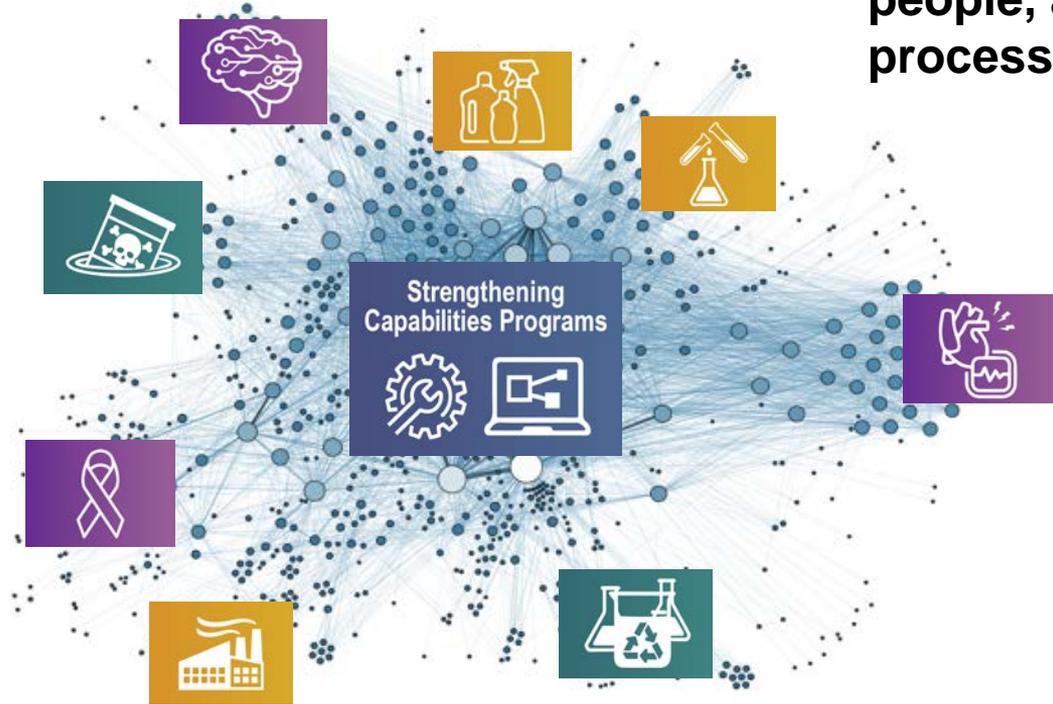
Our Portfolio Composition

Connectivity and interdependence is a strength

**Intersections
of projects,
people, and
processes**



**Not 10
independent
programs**



**For illustration purpose only, not real data*

Acknowledgements



'Culture eats strategy for breakfast'

Thank You!





Question 1

We continue to refine our strategic intent, ensure that our research creates value for multiple stakeholders, and improve how we articulate that value. What elements of opportunity, merit, and value expressed in the Program Introductions are most compelling and match your expectations regarding DNTP's mission and strengths? What obstacles, risks, or blind spots are most important to consider?



Question 2

Given there are many important things to work on that fall within the DNTP mission, what are factors to consider in maintaining a balanced, impactful portfolio?

We are interested in your perspective along a continuum with respect to the dimensions of risk, timeframe, stakeholder responsiveness, etc.