DNTP Strategic Portfolio

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Overview

The mission of the Division of the National Toxicology Program (DNTP) is to improve public health through the development of data and knowledge that are translatable, predictive, and timely. The DNTP strategic realignment was initiated in late 2018 with a goal of refining our strategic intent and bringing more focus and cohesion to our research portfolio, such that DNTP will continue to be impactful far into the future. The DNTP Strategic Planning Framework[1] guided this effort to 1) assess opportunities and challenges that DNTP is exceptionally well-positioned to address and lead, 2) identify research focus areas that align with our goals and strategic objectives, and 3) develop strategic research programs within those focus areas. This strategic planning is a continuous process, and engagement with the Board of Scientific Counselors (BSC) is a critical input to this process. Discussions with the BSC in public meetings are structured to provide valuable insight as DNTP staff define program-specific strategic objectives, develop a portfolio of projects to achieve those objectives, and plan key implementation actions to deliver impactful products over the next 3–5 years.

Portfolio Strategy

The DNTP research portfolio is structured into four strategic areas of focus comprising ten research programs; a brief description of each is included in this overview. These programs are aligned with DNTP goals and three overarching strategic objectives:

- Accelerate our progress toward becoming a more predictive, precise, and preventive science through the deliberate application of a translational toxicology pipeline of capabilities
- Provide an evidence-based approach to identifying and understanding potential environmental contributors to contemporary and common diseases
- Improve our ability to conduct and communicate substance-based hazard evaluations that are more translational, innovative and responsive

Over the past year, DNTP program management teams have engaged internally and externally to develop individual research program plans, including sharing and presenting program concepts with the BSC. During these discussions, many recurrent themes emerged that have been incorporated into program plans and used to define a set of strategic research priorities that will guide focused efforts in the near- and medium-term. These research priorities are aligned with DNTP strategic objectives and, in many cases, cut across individual research programs, allowing for both operational efficiency and leveraging critical capabilities. DNTP research priorities are organized by strategic objective (Program Research Priorities) and an additional set of priorities emphasize cross-cutting and contemporary research foci (Thematic Research Priorities).

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[1] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/index.cfm

Program Research Priorities

1. Accelerate our progress toward becoming a more predictive, precise, and preventive science through the deliberate application of a translational toxicology pipeline of capabilities

1.1. Define and apply an innovative approach to identifying and characterizing hazards of complex and/or combined exposures for existing project areas (botanical dietary supplements, natural mineral fibers, HIV therapeutics)
1.2. Develop and apply defined approaches to infer hazard across specific structural (organohalogen flame retardants) and functional (personal care products) substance classes
1.3. Develop and qualify effective tools and approaches to support timely research responses to emerging public health issues and the assessment of safer alternatives

2. Provide an evidence-based approach to identifying and understanding potential environmental contributors to contemporary and common diseases

2.1. Define and apply a suite of screening approaches to evaluate bioactivities critical to understanding carcinogenicity, cardiovascular toxicity and altered neurodevelopment
2.2. Characterize the likelihood that specific environmental exposures represent human-relevant carcinogenic, cardiovascular, and developmental neurotoxic hazards by defining, developing, and adapting a pipeline of internal and external laboratory and computational assessment capabilities
2.3. Develop and apply an approach to identify and characterize the contributions of environmental exposures to a specific cardiovascular disease (gestational hypertension) and cancer (early onset colorectal carcinoma)

3. Improve our ability to conduct and communicate substance-based hazard evaluations that are more translational, innovative and responsive

3.1. Develop and evaluate a suite of complex in vitro 3D cellular systems (spheroids, organoids) to model human-relevant, organ-specific toxicity to support current portfolio priorities
3.2. Develop and evaluate a suite of multiscale computational models to support current portfolio priorities
3.3. Assemble and support a robust scientific cyberinfrastructure and advanced informatics toolset to enhance and expand the delivery of DNTP knowledge products

Thematic Research Priorities

4. Identify high-value opportunities to strategically implement contemporary and/or cross-cutting topics across all research programs

4.1. Refine current toxicology study and assessment approaches to better understand and account for social determinants of health
4.2. Selectively adapt current projects to address the disproportionate impacts of climate change on individuals and populations
4.3. Define creative approaches to effectively engage scientific, policy, and community stakeholders to increase the impact of DNTP research products

Strategic Areas of Focus and Research Programs

Exposure-based Research Programs[2]

The DNTP Exposure-based Research Programs aim to solve contemporary public health problems related to environmental exposures. The intent is to develop and apply novel tools and approaches to better predict potential harm to human health from environmental exposures we encounter at home, at work, and at play.

Combined Exposures and Mixtures[3] (CEM)

Humans are continuously exposed to mixtures of chemicals. Challenges continue in characterizing exposure to mixtures, evaluating their toxicity and hazard, and assessing associated risk. Limitations in understanding have led to the inconsistent use of available methods to assess mixtures and led to uncertainties in their application. The lack of harmonized terminology or methodological comparisons complicate the synthesis of information across disciplines and impede the use of mixtures data in decision-making.

Consumer Products and Therapeutics[4] (CPT)

People are exposed to numerous chemicals through the use of consumer products. This presents challenges for determining potential adverse human health outcomes, which cannot be assessed using traditional, single chemical toxicology testing. Therefore, this program aims to define optimal approaches to test the large number of chemicals and chemical mixtures in consumer products. For therapeutics, unforeseen health effects may necessitate additional toxicity testing to address potential concerns, such as those that may present with individuals exposed to HIV therapies across the lifespan or during different life stages.

Occupational and Inhalation Exposures[5] (OIE)

Inhalation exposure to potentially harmful substances in both the workplace and our everyday environments can cause adverse health effects to the respiratory tract and other organ systems. Evaluating the toxicity and carcinogenicity of inhaled agents is challenging, largely due to the complexities of the exposure models and systems required for testing. Nonetheless, hazard characterization is critical for creating safe living and working environments and reducing disease burden after inhalation exposure. In addition to inhalation exposure, other exposure routes exist in the workplace, such as through skin contact with substances. Additionally, workers and the general public are concerned about exposures to non-chemical stressors, such as radiation.

[2] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/exposure/index.cfm
[3] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/exposure/combined/index.cfm
[4] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/exposure/consumer/index.cfm
[5] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/exposure/occupational/index.cfm

Health Effects Innovation Programs[6]

The DNTP Health Effects Innovation Programs aim to develop disease-focused environmental toxicology. The intent is to apply novel tools in an integrated fashion and to provide an evidence-based approach that allows us to identify and understand potential environmental contributors to contemporary and common diseases.

Carcinogenicity Health Effects Innovation[7] (Carci)

Cancer continues to be a leading cause of death, and eliminating preventable cancers related to environmental exposures would have significant benefits to public health. Existing approaches for cancer hazard assessment rely extensively on data from whole animal tests that take years to complete and cost millions of dollars. To better protect public health, a scientifically robust framework is needed to characterize the carcinogenic risk posed by environmental exposures in a more human-relevant, predictive, and efficient manner.

Cardiovascular Health Effects Innovation[8] (CV)

Chronic progressive cardiovascular disease is a primary cause of both disease and death in the United States and globally. Current approaches to environmental hazard assessment do not include specific tests of cardiovascular bioactivity and hazards, despite growing evidence that environmental exposures contribute to the onset, risk, and progression of chronic cardiovascular disease. A defined approach is needed to investigate how environmental substances may be contributing to contemporary and common cardiovascular diseases.

Developmental Neurotoxicity Health Effects Innovation[9] (DNT)

Global concern exists that neurodevelopmental disorders, such as autism, attention-deficit hyperactivity disorder, and other learning disabilities are rising in populations worldwide, and that environmental exposures could be contributing factors. Current methods to evaluate environmental compounds with unknown developmental neurotoxicity potential are ineffective due to the complexity of neurodevelopment. An integrated testing strategy for developmental neurotoxicity that incorporates novel and innovative methods could better inform public health decisions on developmental neurotoxicity hazards.

[6] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/health/index.cfm
[7] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/health/carcinogenicity/index.cfm
[8] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/health/cardiovascular/index.cfm
[9] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/health/developmental/index.cfm

Responsive Research Programs[10]

The DNTP Responsive Research Programs aim to position the Division to readily address public health concerns related to novel environmental exposures. This can include rapid responses to identify potential impacts to human health from environmental emergencies, such as oil spills, or proactive evaluation of proposed safer alternative chemicals.

Emerging Contaminants and Issues of Concern[11] (ECIC)

Emergencies and developing issues arise unexpectedly yet regularly, and stakeholders often need high-quality, actionable data quickly in these situations to protect public health. However, rapid mobilization of scientific resources in response to such situations can be challenging. DNTP aims to have strategies in place to identify when rapid responses are required, to assist in prioritizing responses for emerging public health issues, and to meet these challenges successfully without significantly affecting the progress of other DNTP activities.

Safe and Sustainable Alternatives[12] (SSA)

Substances identified as hazardous are often replaced by new or existing substances, typically due to voluntary reasons, such as public pressure or economic consequences, or for mandatory reasons, such as a ban or updated regulation. When a substance is replaced, information about the replacement's potentially harmful impacts on human health is often limited or inaccessible. DNTP is uniquely positioned to empower proactive assessments and strategies, assess the relative safety of alternatives, and minimize the potential for harmful substitutions, which addresses a critical need for the toxicology research community.

[10] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/responsive/index.cfm
[11] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/responsive/emerging/index.cfm
[12] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/responsive/sustainable/index.cfm

Strengthening Capabilities Programs[13]

The DNTP Strengthening Capabilities Programs aim to advance the field of toxicology through the development and application of new and innovative approaches to solve traditional toxicology problems and position the Division at the cutting edge of scientific research. These advancements should enhance progress in toxicology becoming a more predictive science, thereby improving understanding of the effects of environmental exposures and improving their translation to human health and disease.

Novel Tools and Approaches[14] (NTA)

Advances in scientific technology are evolving at a rapid pace, providing a toolbox of exciting new methods. This program aims to identify, evaluate, and advance tools suitable for translatable, predictive, and timely toxicology in areas of direct importance to the field of toxicology. These new approaches, which encompass both non-animal and refined animal approaches, will define the core feature of creative and bold projects designed to address previously intractable and important toxicological questions.

Scientific Cyberinfrastructure[15] (SCI)

Work in toxicology relies heavily on the use of scientific cyberinfrastructure resources in support of research activities. This includes computer and storage systems, networking, systems-level software and database systems, data processing and analysis pipelines, and custom analytical and visualization tools. This usage requires significant costs to operate existing resources and to develop and acquire new resources in response to changing needs. Without coordinating efforts there is a significant risk that resources will not be strategically planned or efficiently deployed for a changing research landscape.

[13] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/strength/index.cfm
[14] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/strength/novel/index.cfm
[15] https://www.niehs.nih.gov/research/atniehs/dntp/strategic-plan/strength/cyberinfrastructure/index.cfm