NTP
National Toxicology Program

Consumer Products and Therapeutics Program

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NTP Board of Scientific Counselors Meeting
June 8, 2021

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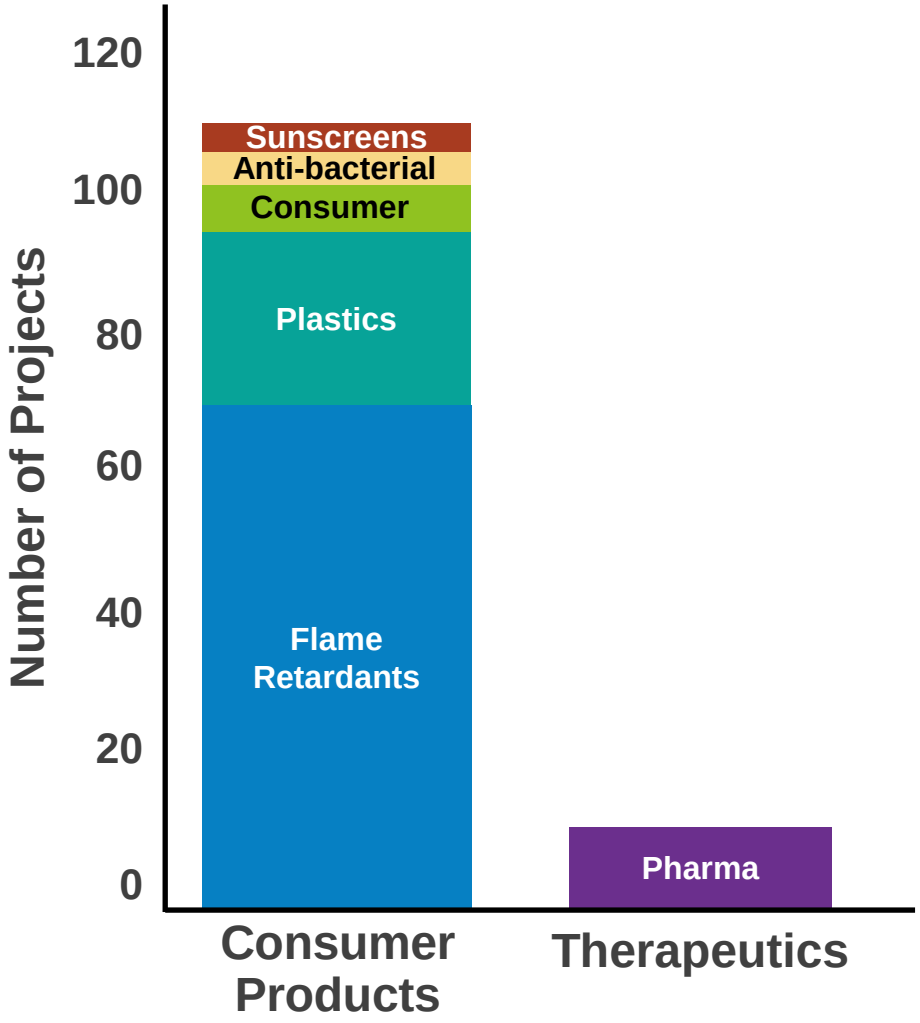
This Program was Asked to Address Two Exposure Categories

Consumer Products

Therapeutics

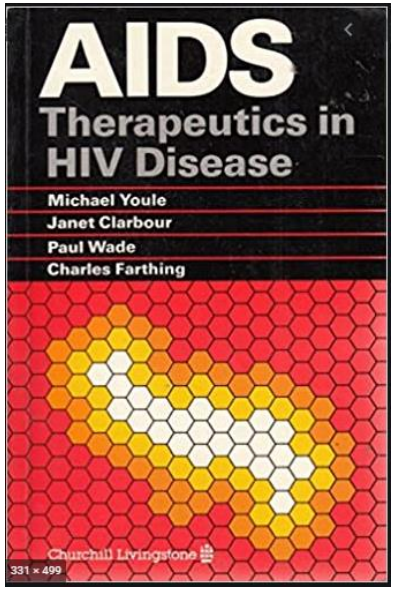
DNTP Research History

Exposure-Based Research Theme Portfolio Organization



Consumer Products

- DNTP extensive history of chemical testing involving consumer products
- Multiple chemicals
  - DNTP leads testing efforts in some of these compounds
- Multiple program areas



Therapeutics

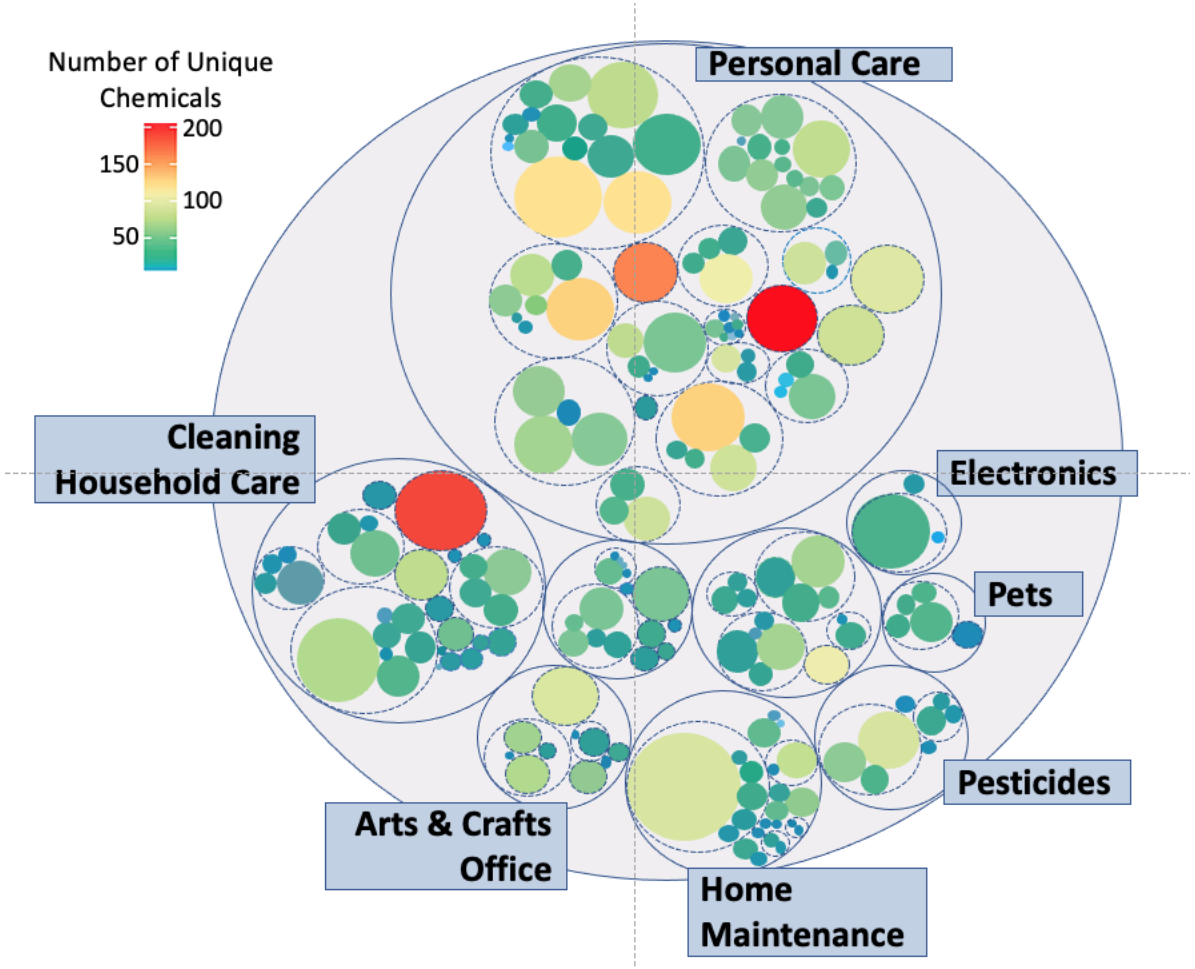
- Majority of work has been on AIDS therapeutics
- Working continues under Office of AIDS Research (OARD) to address long term concerns with combination therapies

Consumer Products

Objective 1

Consumer Products: The Problem

CPDat: EPA Chemical and Products Database



- Massive number of chemicals in consumer products (CPs)
- Chemicals migrate from CPs to the environment
  - daily exposure
  - bioaccumulate
  - adverse health effects due to long-term, chronic exposure
- Traditional chemical-by-chemical testing paradigm
- **Clear need to explore and apply a new strategy for toxicology testing**

Isaacs et al. Journal of Exposure Science & Environmental Epidemiology (2020) 30:171–183

Objective 1: Consumer Products – Focused Testing Approach

Within the next five years, evaluate whether class-based methodologies are an effective framework for assessing potential human health effects of chemicals in consumer products by considering in silico and empirical toxicity data.

Exemplar

Organohalogen Flame Retardants (OFRs)

1.1 **Engage appropriate stakeholders** for selection and planning of class-based OFR assessment.

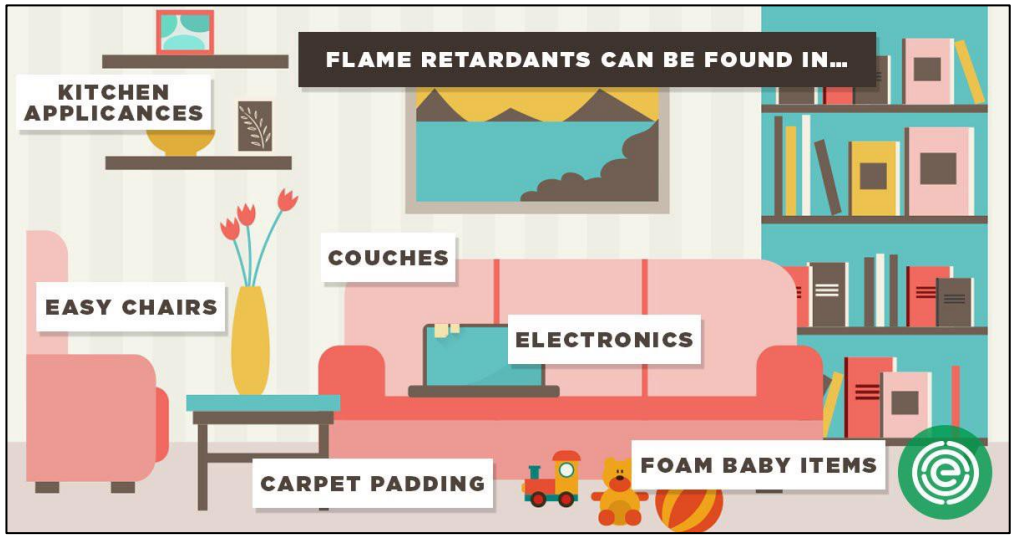
1.2 **Identify key concerns** associated with a chemical class.

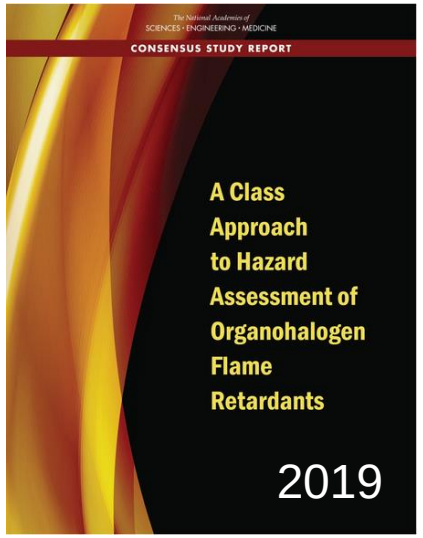
1.3 **Devise and implement a scoping plan** to categorize available research for directing the class-based synthesis and identification of data poor areas that limit evaluations.

1.4 **Evaluate available data** generated by traditional and high throughput new approach methodologies (NAMs) to predict, prioritize and assess toxicity potential.

1.5 **Assess the method's effectiveness** across a chemical class at providing translatable health effects information.

Exemplar: Organohalogen Flame Retardants (OFRs)





National Academies of Sciences, Engineering, and Medicine. 2019. *A Class Approach to Hazard Assessment of Organohalogen Flame Retardants*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25412.

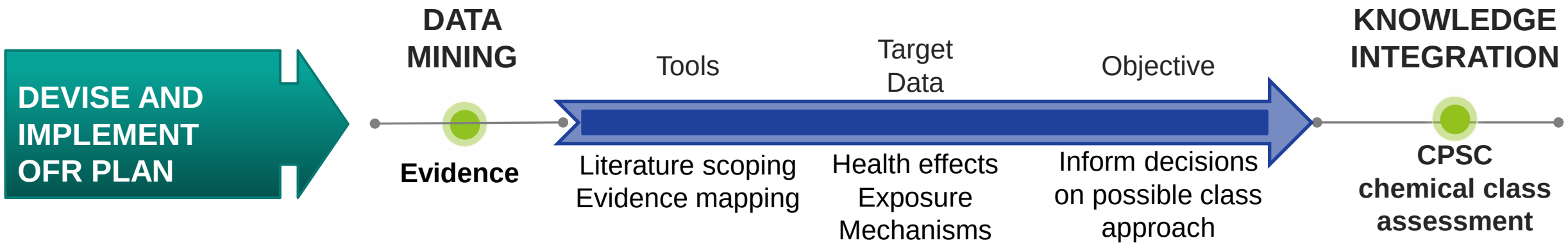
Key Concerns

- Present in numerous CPs (100+)
- Problematic
  - Bioaccumulate
  - Exposures – daily or long-term, chronic
  - High risk groups – pediatric
- **Resolve problem – advanced toxicity testing**

Proposed Solution

- Consumer Product Safety Commission (CPSC)
- National Academy of Science, Engineering and Medicine Panel
- **Class-based approach**

Class-based Approach – Data Strengths



- Evidence-Based Data Strengths for Class Approach
- Structurally related chemicals
  - Health effects and mechanistic data – assess health endpoint
    - (OFRs – endocrine, reproductive, neurological or cancer endpoints)
- Data rich to data poor chemicals
  - Start with a well-studied chemical - established health effects/mechanisms
    - Read across approaches
- Strong knowledge – integration – chemical class – hazard/risk assessment (CPSC)

Class-based Approach – Data Limitations

Evaluate Available Data
(Fit for purpose products)

Assess Effectiveness Class-Based Approach

Objective 1: Milestones

01 Consumer Products

Short Term (1 year)

- Establish class approach – OFRs
- Begin literature search, screening, and mapping of health effects and exposure evidence on 2-3 classes.

Mid Term (2-3 years)

- Collaborate stakeholders – combine inputs – potential class approach projects – assess other CP chemicals
- Publish OFR evidence maps - use for decision making

Long Term (4-5 years)

- Use targeted data generation – HTP methods – expand class approach application
- Assess class approach effectiveness for OFRs

02 Therapeutics

Short Term (1 year)

- Continue ongoing evaluations
- Engage with FDA

Mid Term (2-3 years)

- Complete & report out deliverables
- Cardio & neuro evaluations
- NIH-OAR input for future work
- Studies of mutual interest

Long Term (4-5 years)

- Address concerns of future HIV therapies with clinicians and FDA

03 Partnerships

Short Term (1 year)

- Outreach initial stakeholders
- Seek ideas – common interest that align with objectives
- Seek input BSC – program plan

Mid Term (2-3 years)

- Expand engagement
- Explore partnerships
- Plan workshops – share program objectives

Long Term (4-5 years)

- Devise approved plan for outreach – future projects
- Explore partnerships
- Plan event – engaged stakeholders to share Program advancements

Objective 1: Milestones

01 Consumer Products

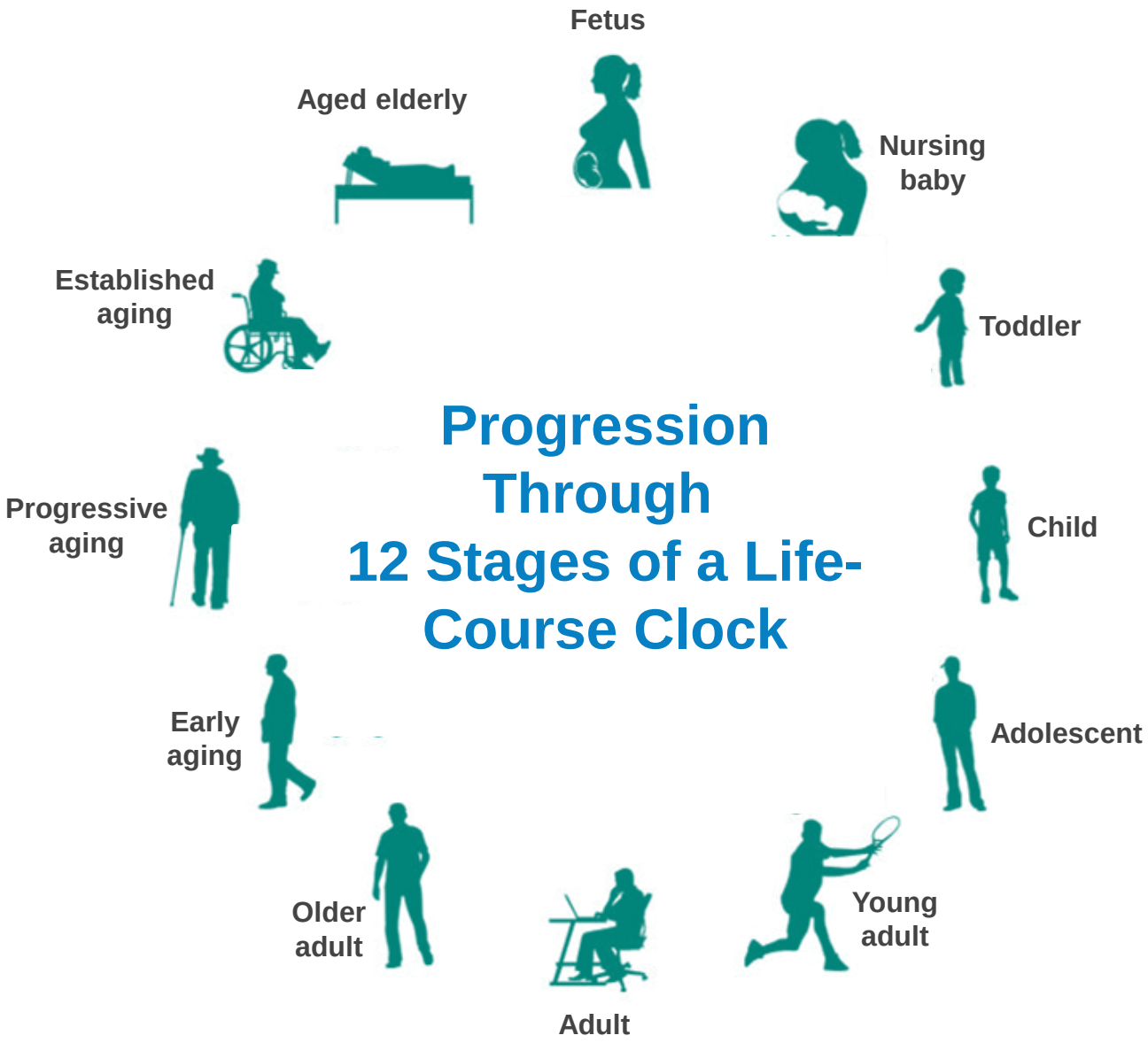
Short Term (1 year)	Mid Term (2-3 years)	Long Term (4-5 years)
• Establish class approach – OFRs • Begin literature search, screening, and mapping of health effects and exposure evidence on 2-3 classes.	• Collaborate stakeholders – combine inputs – potential class approach projects – assess other CP chemicals • Publish OFR evidence maps - use for decision making	• Use targeted data generation – HTP methods – expand class approach application • Assess class approach effectiveness for OFRs

- Milestone Priorities
  - Establish first exemplar class approach – OFRs
  - Build partnerships
  - Fully engage DNTP capabilities on class-based approach (OFRs)
  - Assess effectiveness of first exemplar class approach – provide translatable health effects information
  - Expand the class-based strategic approach as an advanced toxicity testing methodology for other chemical classes in consumer products (*e.g.*, personal care products)

Therapeutics

Objective 2

Therapeutics: The Problem

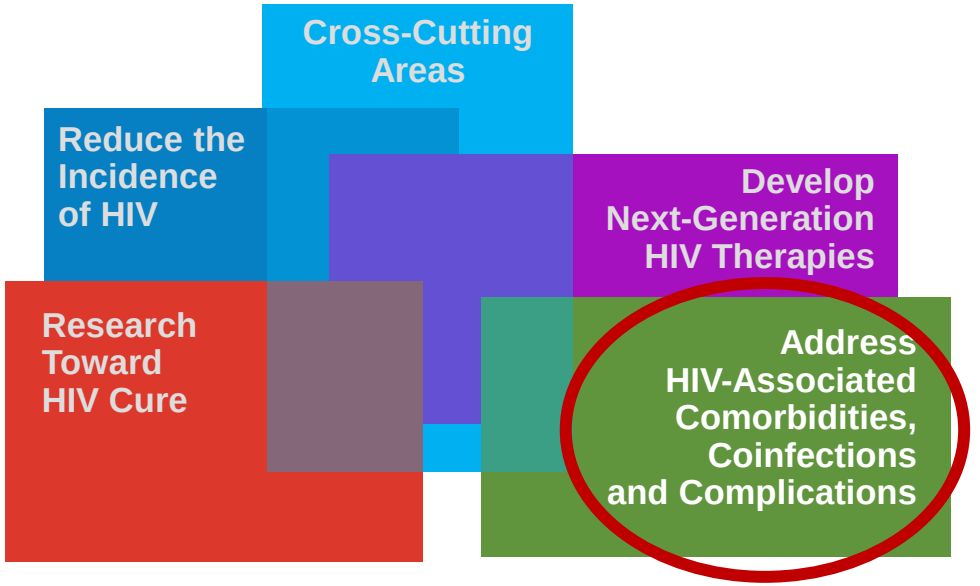


- Concerns associated with HIV combination therapies and long-term impacts due to exposure
- Are there are cross-cutting issues of mutual interest where we can provide information

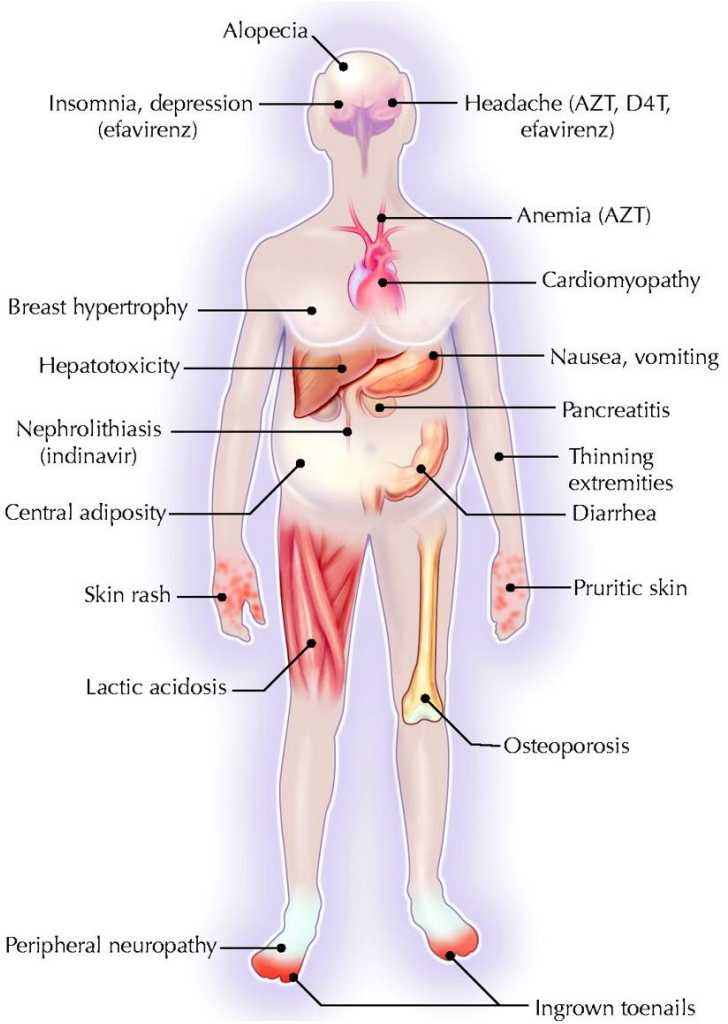
DNTP/NIEHS Receives Annual Funding from the NIH Office of Aids Research

- Current DNTP testing portfolio includes assessments of combined anti-retroviral therapies (cART) for use by HIV-positive individuals during pregnancy or as a prophylactic to prevent transmission
- The clinical perspective (PHACS/NIH)
  - cART therapy has many benefits including preventing transmission from mother to baby
  - Drug makers have evaluated the preclinical reproductive and developmental toxicity of *individual* ART but not in combination

Data gap = Some concern from clinicians for offspring exposed to the combination therapies for potential immediate and/or longer-term effects (fetal, post-natal development)



Combination Anti-Retroviral Therapy



- In utero exposure and effects on dam and offspring
- Long-term adverse health effects
- Cross-Divisional engagement

Therapeutics

Partner early with appropriate stakeholders to provide impactful gained scientific knowledge on therapeutics.

Objective 2.1

Support the NIH-OAR initiative to assess potential toxicities of combination antiretroviral therapies used for the treatment of HIV

Objective 2.2

Engage with stakeholders to share capabilities in toxicity evaluations unique to DNTP

Discuss cross-cutting issues of mutual interests where DNTP can provide impactful information

Objective 2: Milestones

02 Therapeutics

Short Term (1 year)

- Continue ongoing evaluations
- Engage with FDA

Mid Term (2-3 years)

- Complete & report out deliverables
- Cardio & neuro evaluations
- NIH-OAR input for future work
- Studies of mutual interest

Long Term (4-5 years)

- Address concerns of future HIV therapies with clinicians and FDA

- **Milestone Priorities**
  - Continue work with clinicians from the NIH Office of AIDS Research Maternal Exposures Working Group
    - Fully engage DNTP capabilities to address current and future concerns
  - Establish partnerships with FDA
    - Address issues of mutual interest

Partnerships

Objective 3

Objective 3: Partnerships

Strengthen and build new partnerships across federal and other non-governmental organizations to contribute value added research for Consumer Product and Therapeutics and facilitate a broader dissemination of information to guide public health decisions.

- Identify impactful questions of interest
- Encourage discussions, workshops, collaborations
  - Federal, non-federal – public organizations
- Disseminate research, gain awareness of other organizational efforts
- Build on opportunities in health disparity testing

Objective 3: Milestones

03 Partnerships

Short Term (1 year)	Mid Term (2-3 years)	Long Term (4-5 years)
• Outreach initial stakeholders • Seek ideas – common interest that align with objectives • Seek input BSC – program plan	• Expand engagement • Explore partnerships • Plan workshops – share program objectives	• Devise approved plan for outreach – future projects • Explore partnerships • Plan event – engaged stakeholders to share Program advancements

- Milestone Priorities
  - Build, strengthen and expand partnerships
  - Include government and non-government organization input
  - Workshops/Symposiums/Meetings – share, listen and gather feedback information
  - Ensure consumer products and therapeutics are part of DNTP's communication strategy outreach development

Building and Expanding Stakeholder Interest and Engagement

DNTP

- Health Effects Innovation
- Responsive Research
- Exposure-Based Research Themes
- Strengthening Capabilities

International Organizations

Non-government Organizations

- Environmental Working Group
- Silent Spring Institute

Federal Organizations

- Consumer Product and Safety Commission
- Environmental Protection Agency
- Food and Drug Administration
- Center for Food Safety and Applied Nutrition
- National Center for Toxicological Research
- National Institutes of Health
- Office of AIDs Research

State Organizations

- California Environmental Protection Agency

DNTP Program Connectivity

Health Effects Innovation

- Cardiovascular Health Effects Assessment
- Developmental Neurotoxicity Modeling
- Carcinogenesis Health Effect Innovation Program

Responsive Research

- Emerging Contaminants and Issues of Concern
- Safe and Sustainable Alternatives

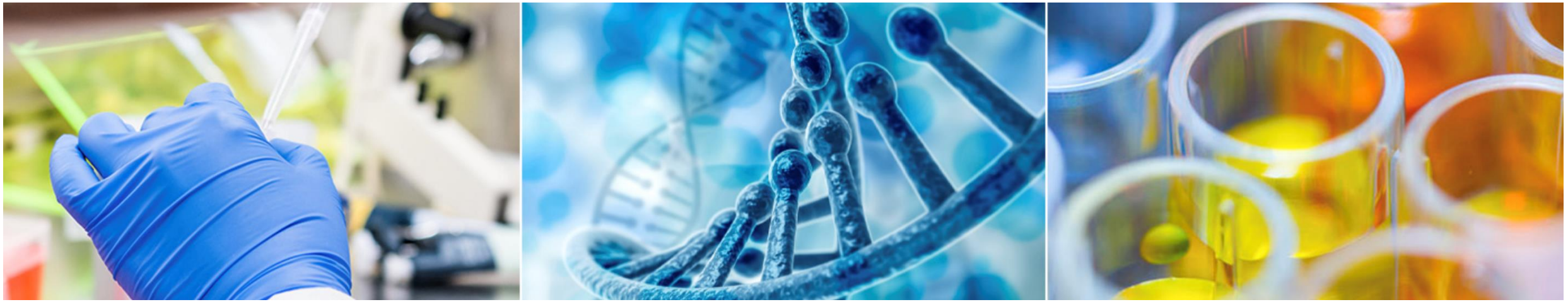
Exposure-Based Research Themes

- Combined Exposures and Mixtures
- Occupational and Inhalation Exposures

Strengthening Capabilities

- Novel Tools and Approaches
- Scientific Cyber-Infrastructure

Why Now?



- **DNTP is at a pivotal point in toxicity testing**
  - DNTP maintains a defining leadership role in advancing toxicology testing
  - Consumer Products: opportunity to redefine individualized examination of single chemicals
  - Therapeutics: address unforeseen research needs on health effects of HIV therapeutics secondary to lifetime and different life stage exposures identified by NIH/OAR and clinicians.
  - Partnerships: build rewarding partnerships will multiple organizations
    - Direct attention at critical consumer product and therapeutic research areas
    - Facilitate broader dissemination of information to guide public health decisions

Challenge

- How do we address translation of animal and novel approach methods research for human exposure to consumer products given that:
  - Human exposures are product mixtures that are poorly characterized
  - Experimental studies are routinely designed to test single chemicals

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Thank You!

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Open for Clarifying Questions