Report to the NTP Board of Scientific Counselors

John R. Bucher, Ph.D., DABT
NTP Associate Director
National Institute of Environmental Health Sciences

June 29, 2017
• Staff changes

• NIEHS Strategic Plan: 2012-2017
  – Selected accomplishments by the Division of NTP

• NTP website redesign
New DNTP Staff and Trainees

Brandy Beverly, PhD
Office of Health Assessment and Translation

Suril Mehta, MPH
Office of Report on Carcinogens

Amy Wang, PhD
Office of Report on Carcinogens

New Trainees in NTP Laboratory:
- Anthony Luz, PhD, Postdoc
- David Crizer, PhD, Postdoc
- Kevin Mauge-Lewis, Predoc

- Angeliz Concepcion, NIEHS Scholars Connect Program
- Shitij Kumar, NSCP
Said Good-Bye

Kris Thayer, PhD
Office of Health Assessment and Translation

Yun Xie, PhD
Office of Liaison, Policy, and Review

Abbe Boyles, PhD
Office of Health Assessment and Translation

Natasha Caitlin, PhD
Toxicology Branch
Fundamental (& applied) research

- **Toxicology and Carcinogenesis TRs**
  - 24 2-Yr Bioassay reports- Antimony, TBBPA, BDCAA, Cobalt, Aloe Vera, Acrylamide, Glycidamide, Ginko Extract, Indole-3-carbinol, Vinylidene CI, Green Tea Extract, RFR partial findings
  - Toxicity Reports- Fullerenes, MW Carbon nanotubes, abrasive blasting agents

- **Tox21**
  - ER/AR, ERR, p53, hERG channels, HIF-alpha, HDAC inhibitors, CAR, FXR, TR, Nrf2, aromatase, mitochondrial function, retinol signaling
  - diabetes, obesity, cardio-, neuro- & genotoxicity
  - S1500+ gene set
  - BMD assessments, in vivo & in vitro (IVIVE)
  - Zebrafish, *C. elegans*
Individual susceptibility across lifespan

- Clarity BPA U01 research program
- Mouse strain resequencing project (old)
- Multi strain aging study
- Diversity Outbred studies in vivo & in vitro
- Mouse methylome studies
- Gonadectomy studies on hepatic methylation
- Transgenerational inheritance Systematic Review
- Transgenerational study designs
Strategic Goal #3

Exposure science & exposome

- BPA toxicokinetic studies
- Cashier’s study
- NIEHS-EPA study of exposure to personal care and consumer product chemicals
  - Collaboration with EPA to improve characterization of PCP, consumer product, and home exposures
  - Provide important information to epidemiological and toxicology mixtures research
  - Validation of Sister Study PCP questionnaire
  - Assess and improve EPA exposure prediction models
- Sister Study research
  - Prospective cohort study of women with a sister who had breast cancer
  - Personal care product questionnaire to assess frequency of use
Combined environmental exposures and disease

- Projects to inform risk assessment of mixtures
  - **Component-based risk assessment:** Estimating the toxicity of mixtures using individual chemical dose-response data and additivity models
    - Assessing the application and limitations of additivity models
    - Identifying interactions among chemicals present in mixtures
    - Informing decisions on which chemicals to include in cumulative risk assessments
  - **Whole mixtures risk assessment:** Using a tested “reference” mixture to estimate the toxicity of an untested mixture
    - Determining sufficient similarity among related, complex mixtures by comparing chemistry and biological effects
    - Developing high throughput tools to evaluate the toxicity of complex mixtures
Component-based

• Assessing models of additivity and identifying interactions
  - Dioxin/PCB toxic equivalence factor studies (old)
  - Polycyclic Aromatic Compound Mixtures Assessment Program (PAC-MAP) [https://ntp.niehs.nih.gov/results/areas/pacs/index.htm](https://ntp.niehs.nih.gov/results/areas/pacs/index.htm)

• Comparing between component-based and whole mixtures approaches
  - PAC-MAP: Testing whole mixtures of cookstove emissions and Superfund mixtures

• Informing decisions on which chemicals to include in a cumulative risk assessment
  - Hypolipidemics and phthalates: Assessing potential additivity of chemicals that disrupt different pathways involved in testosterone production
  - Low Dose Hallmarks of Cancer study: Assessing mixture effects of chemicals that target different pathways leading to cancer
Whole Mixtures

- Understanding the chemistry and health effects of whole mixtures and developing better testing methods
  - 2014 Symposium: Assessing Exposures and Health Effects Related to Indoor Biomass Fuel Burning
  - NIEHS 2015 Workshop: “Statistical Approaches for Assessing Health Effects of Environmental Chemical Mixtures in Epidemiology Studies”
- Determining sufficient similarity of whole mixtures
  - Botanical Dietary Supplement case studies with *Ginkgo biloba* extract, *Echinacea purpurea* extract, and black cohosh extract
  - 2016 Workshop: Addressing Challenges in the Assessment of Botanical Dietary Supplement Safety
    https://ntp.niehs.nih.gov/about/presscenter/events/2016/index.html
Strategic Goal #5

Emerging (or re-emerging) environmental threats

- Gulf Oil Spill
- Perfluorinated chemicals class studies
- Elk River spill
- Tire crumb rubber fields
- Lead
A liquid used to wash coal was spilled from a leaking tank into the Elk River approximately 1.5 miles upstream of the water intake facility serving 300,000 people. Do not use water order issued.
# NTP Studies on Elk River Chemicals

<table>
<thead>
<tr>
<th>Test Article [Abbreviation, CAS Number]</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rat Prenatal Toxicity</td>
</tr>
<tr>
<td>4-Methylcyclohexanemethanol [MCHM, 34885-03-5]</td>
<td>X</td>
</tr>
<tr>
<td>Dipropylene glycol phenyl ether [DiPPH, 51730-94-0]</td>
<td></td>
</tr>
<tr>
<td>Propylene glycol phenyl ether [PPH, 770-35-4]</td>
<td></td>
</tr>
<tr>
<td>1,4-Cyclohexanedimethanol (CHDM; 105-08-8)</td>
<td></td>
</tr>
<tr>
<td>2-Methylcyclohexanemethanol [2MCHM, 2105-40-0]</td>
<td></td>
</tr>
<tr>
<td>4-(Methoxymethyl)cyclohexanemethanol [MMCHM, 998955-27-2]</td>
<td></td>
</tr>
<tr>
<td>Dimethyl 1,4-cyclohexanedicarboxylate [DMCHDC, 94-60-0]</td>
<td></td>
</tr>
<tr>
<td>Methyl 4-methylcyclohexanecarboxylate [MMCHC, 51181-40-9]</td>
<td></td>
</tr>
<tr>
<td>Technical product [“crude MCHM”]</td>
<td></td>
</tr>
</tbody>
</table>

Proposed study plan underwent cross-agency review

Guideline studies

Non-guideline studies
Knowledge management

- Office of Data Science
  - Develop and implement data science training opportunities
  - Enhance researcher’s ability to find, access, interoperate, and reuse data
  - Develop and support policies and standards for data integration and harmonization
  - Facilitate transformation of data and information into user-friendly knowledge-based platforms
  - Represent NIEHS in trans-NIH and interagency data science and knowledge management activities
Strategic Goal #9

Building the EHS research workforce 2012-2017

- Applied toxicology and carcinogenesis
  - 8 fellows
- Biomolecular screening and computational toxicology
  - 2 fellows
- Health assessment and translation
  - 1 fellow
- Lab animal medicine
  - 1 fellow
- Systems and mechanistic toxicology
  - 8 fellows
- Toxicologic pathology
  - 9 fellows
Strategic Goal #10

Improve impact by addressing public health issues

- NTP monographs on noncancer hazards
  - Low level lead, folate supplementation, fluoride neurobehavioral assessment in animals, PFOS/PFOA immunotoxicity, cancer chemotherapy in pregnancy

- Report on Carcinogens
  - 11 listings: 5 viruses (HIV Type 1, Epstein-Bar virus, Kaposi sarcoma-associated herpesvirus, HTLV Type 1, Merkel cell polyomavirus), 1-bromopropane, cobalt and cobalt compounds that release cobalt in vivo, cumene, pentachlorophenol and by-products of its synthesis, trichloroethylene, o-toluidine
  - NAS agrees with formaldehyde and styrene listings
  - In process: haloacetic acids found in water as disinfection by-products; Helicobacter pylori (chronic infection); antimony trioxide; shiftwork, light at night, and circadian disruption
Assess impact of NTP’s work

- Developed an approach for a comprehensive and objective assessment of NTP’s effectiveness in multiple sectors
  

- Applied to case study on hexavalent chromium: NTP’s work strengthened the science base and informed public health decision-making
  
  NTP’s research was key to the nation’s first-ever drinking water standard for CrVI adopted by California in 2014

- Working on methods to automate processes for assessing impact
Strategic Goal #11

Improve communication; new approaches & tools

- Systematic review methods
  - Applying to environmental health to increase transparency of literature analysis and hazard decisions

- Nonneoplastic pathology atlas
  - Standardizing terminology in toxicologic pathology for rodents

- ICCVAM strategic roadmap
  - Fostering new approaches for evaluating the safety of chemicals and medical products
Strategic Goal #11

Improve communication through new approaches & tools

- Level of Concern” research study
  - Updating framework for communicating NTP’s opinion whether an environmental substance is of concern for causing adverse effects on human health given its toxicity and human exposure

- NTP website redesign

- New “report” types or forums
NTP Website Redesign

Beth Bowden, MS
Program Operations Branch
National Institute of Environmental Health Science
NTP Website Redesign

- Improve communications by improving all aspects of the NTP website
  - Look and feel
  - Organization
  - Content

- Process includes:
  - Consultant's audit of website
  - Focus groups, interviews of external and internal users
  - Foresee survey
  - ITRAC's mapping of information architecture
  - Identification of personas
  - Prototyping
Incremental approach

- New “search” tool is live
- Landing pages are being reworked and go live as complete
- Updates to look and feel will go live this summer
- Content will go live as updated
Old: “Areas of Research” landing page

Areas of Research

On This Page
- Endocrine Disruptors
- Occupational Mixtures and Exposures
- Phototoxicology
- Safe Drinking Water

NTP has a broad mandate to provide toxicological characterizations for chemicals and agents of public health concern and strives to balance the selection of chemicals for study. This has resulted in a diverse research program, but with emphasis on synthetic industrial chemicals, pesticides, various pharmaceuticals, metals, and food additives. NTP continues to explore new areas of research. In general, these initiatives are broad-based and include various health-related endpoints.

Endocrine Disruptors

Endocrine disruptors are naturally occurring or man-made substances that may mimic or interfere with natural hormones in the body. Endocrine disruptors may turn on, shut off, or modify signals that hormones carry, thereby affecting the normal functions of tissues and organs. NTP is involved in several efforts to strengthen the science base within this field.

For contact information, visit the Toxicology Branch site.

Back to Top

Occupational Mixtures and Exposures

NTP is coordinating an effort between NIEHS/NHL and NIOSH/NIH to better characterize worker exposures, educate workers, and identify occupational health research gaps. Current efforts are addressing worker exposure to asphalt fumes and 1,3-butadiene and future initiatives are proposed for occupational mixtures such as welding fumes, abrasive blasting compounds, and naval working fluids. An industry consortium has petitioned the OSHA to list 1,3-butadiene as an occupational carcinogen.
New: “Areas of Research” landing page – Now live

NTP has a broad mandate to provide toxicological characterizations for chemicals and agents of public health concern and strives to balance the selection of substances for study. This has resulted in a diverse research program with emphasis on synthetic industrial chemicals, pesticides, drugs, metals, and food additives. NTP continues to explore new areas of research. In general, these initiatives are broad-based and include various health-related endpoints.

- **Botanical Dietary Supplements**
  NTP is studying selected botanical dietary supplements to identify potential harm from short-term and long-term exposure.

- **Dichloroacetic Acid**
  NTP is conducting a series of in vitro and in vivo screening studies to evaluate dichloroacetic acid and dichloroacetic acid formulations.

- **Hexavalent Chromium**
  NTP studied the short-term toxicity and long-term carcinogenicity of sodium dichromate and dichromate administered in rodents in drinking water.

**Related Links**
- FAQs and Fact Sheets
- Health Effects of Low-level Lead Evaluation
- Systematic Review on Fluoride
NTP Website Redesign
Old: “Database, Searches, & Other Resources” landing page
New: “Data & Resources” landing page – Now live
NTP Website Redesign: Organization

Draft: Navigation
Thank you!

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