NTP
National Toxicology Program

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

Outline

- 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

Abee Boyles, PhD
Office of Health Assessment and Translation

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

Natasha Caitlin, PhD
Toxicology Branch

DNTP Response to NIEHS Strategic Plan 2012-2017

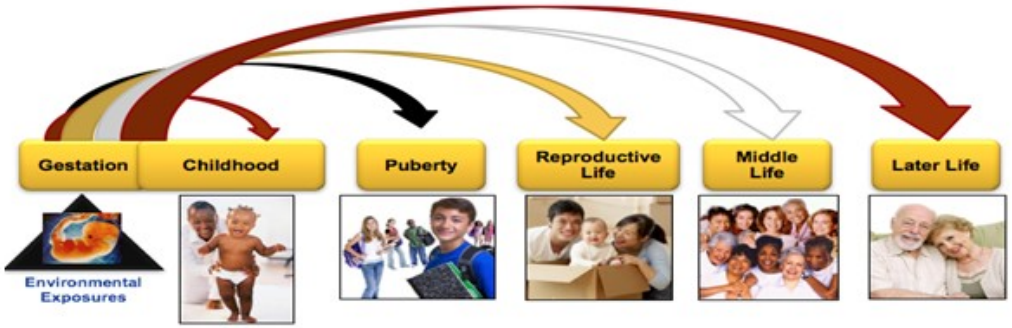
Fundamental (& applied) research

- Toxicology and Carcinogenesis TRs
  - 24 2-Yr Bioassay reports- Antimony, TBBPA, BDCAA, Cobalt, Aloe Vera, Acrylamide, Glycidamide, Ginko Extract, Indole-3-carbinol, Vinylidene Cl, 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*

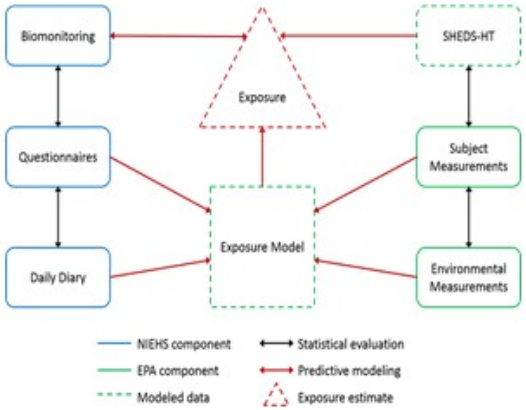
Individual susceptibility across lifespan

- 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



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

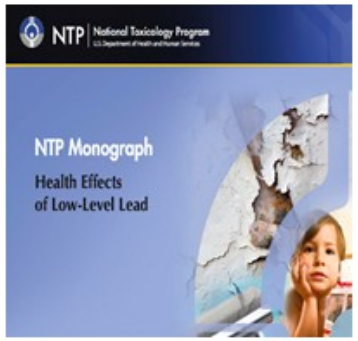
- Comparing between component-based and whole mixtures approaches
  - PAC-MAP: Testing whole mixtures of cookstove emissions and Superfund mixtures
- Informing decisions on which chemicals to include in a cumulative risk assessment
  - Hypolipidemics and phthalates: Assessing potential additivity of 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

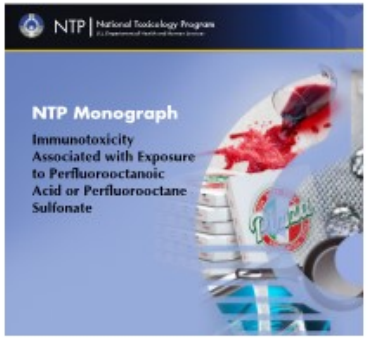
Whole Mixtures

- 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

Emerging (or re-emerging) environmental threats

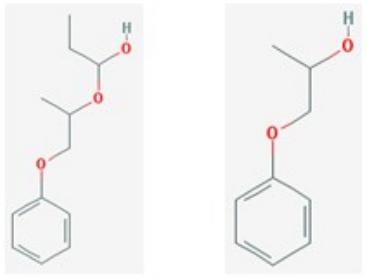
- Gulf Oil Spill
- Perfluorinated chemicals class studies
- Elk River spill
- Tire crumb rubber fields
- Lead



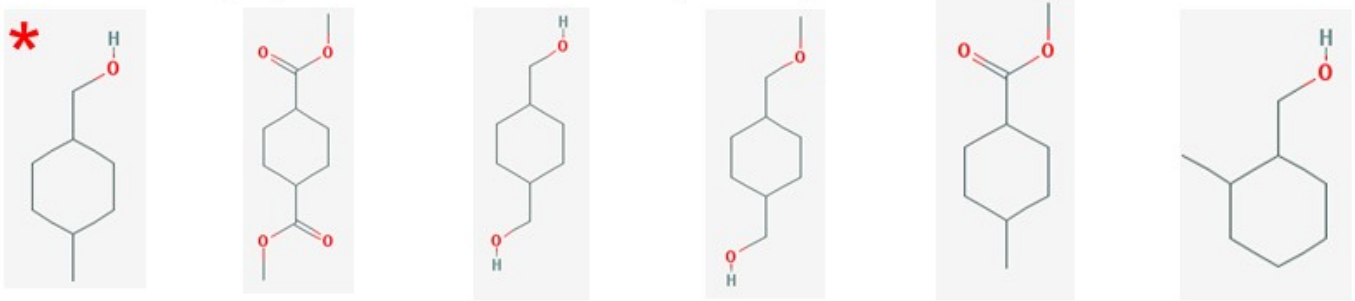


Elk River, West Virginia - January 9, 2014

Phenyl Ethers (PPH)



Crude Methylcyclohexanemethanol (MCHM)



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

Test Article [Abbreviation, CAS Number]	Studies							
	Rat Prenatal Toxicity	Mouse Dermal Irritation and Hypersensitivity	5-Day Rat Toxicogenomic	Bacterial Mutagenicity	Zebrafish Developmental	Nematode Toxicity	High Throughput Screening	Structure Activity Relationship (SAR) Analysis
4-Methylcyclohexanemethanol [MCHM, 34885-03-5]	X	X	X	X	X	X	X	X
Dipropylene glycol phenyl ether [DiPPH, 51730-94-0]			X	X	X	X		X
Propylene glycol phenyl ether [PPH, 770-35-4]			X	X	X	X	X	X
1,4-Cyclohexanedimethanol (CHDM; 105-08-8)				X	X	X	X	X
2-Methylcyclohexanemethanol [2MCHM, 2105-40-0]				X	X	X		X
4-(Methoxymethyl)cyclohexanemethanol [MMCHM, 98955-27-2]				X	X	X		X
Dimethyl 1,4-cyclohexanedicarboxylate [DMCHDC, 94-60-0]				X	X	X	X	X
Methyl 4-methylcyclohexanecarboxylate [MMCHC, 51181-40-9]				X	X	X		X
Technical product ["crude MCHM"]		X	X	X	X	X		

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

Building the EHS research workforce 2012-2017

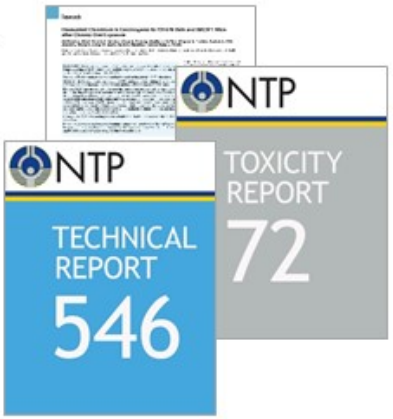
- Applied toxicology and carcinogenesis
  - 8 fellows
- Biomolecular screening and computational toxicology
  - 2 fellows
- Health assessment and translation
  - 1 fellow
- Lab animal medicine
  - 1 fellow
- Systems and mechanistic toxicology
  - 8 fellows
- Toxicologic pathology
  - 9 fellows

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

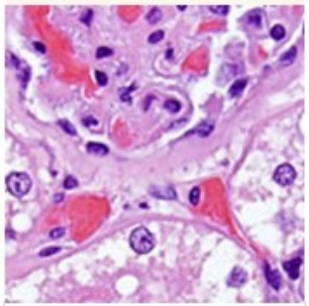
- Developed an approach for a comprehensive and objective assessment of NTP's effectiveness in multiple sectors
  - Xie Y, Holmgren S, Andrews DMK, Wolfe MS. 2017. Evaluating the impact of the U.S. National Toxicology Program: a case study on hexavalent chromium. *Environ Health Perspect* 125:181-188
- 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



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

Current framework

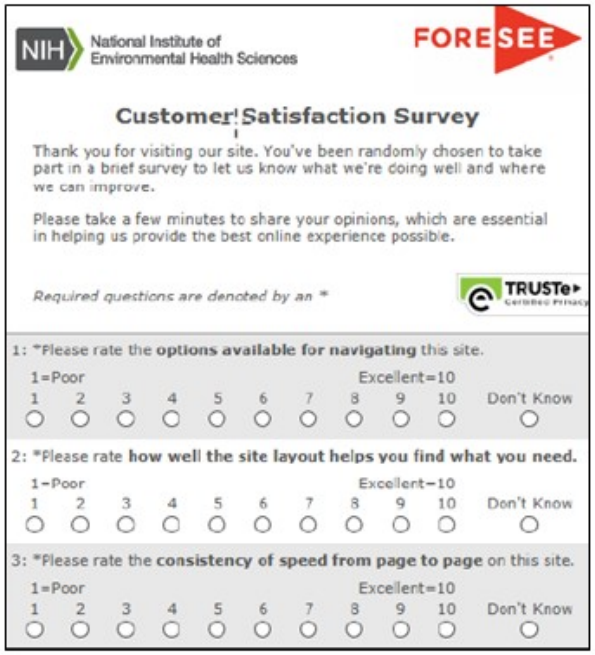
NTP
National Toxicology Program

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


NIH National Institute of Environmental Health Sciences

FORESEE

Customer Satisfaction Survey

Thank you for visiting our site. You've been randomly chosen to take part in a brief survey to let us know what we're doing well and where we can improve.

Please take a few minutes to share your opinions, which are essential in helping us provide the best online experience possible.

*Required questions are denoted by an **

TRUSTe

1: *Please rate the **options available for navigating** this site.

1=Poor Excellent=10

1 2 3 4 5 6 7 8 9 10 Don't Know

2: *Please rate **how well the site layout helps you find what you need.**

1=Poor Excellent=10

1 2 3 4 5 6 7 8 9 10 Don't Know

3: *Please rate the **consistency of speed from page to page** on this site.

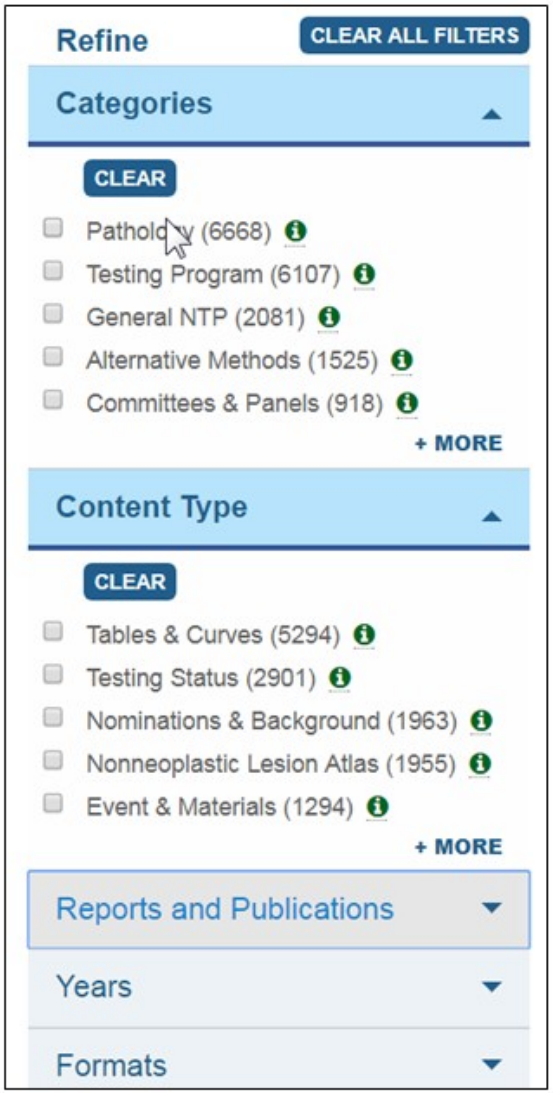
1=Poor Excellent=10

1 2 3 4 5 6 7 8 9 10 Don't Know

NTP Website Redesign

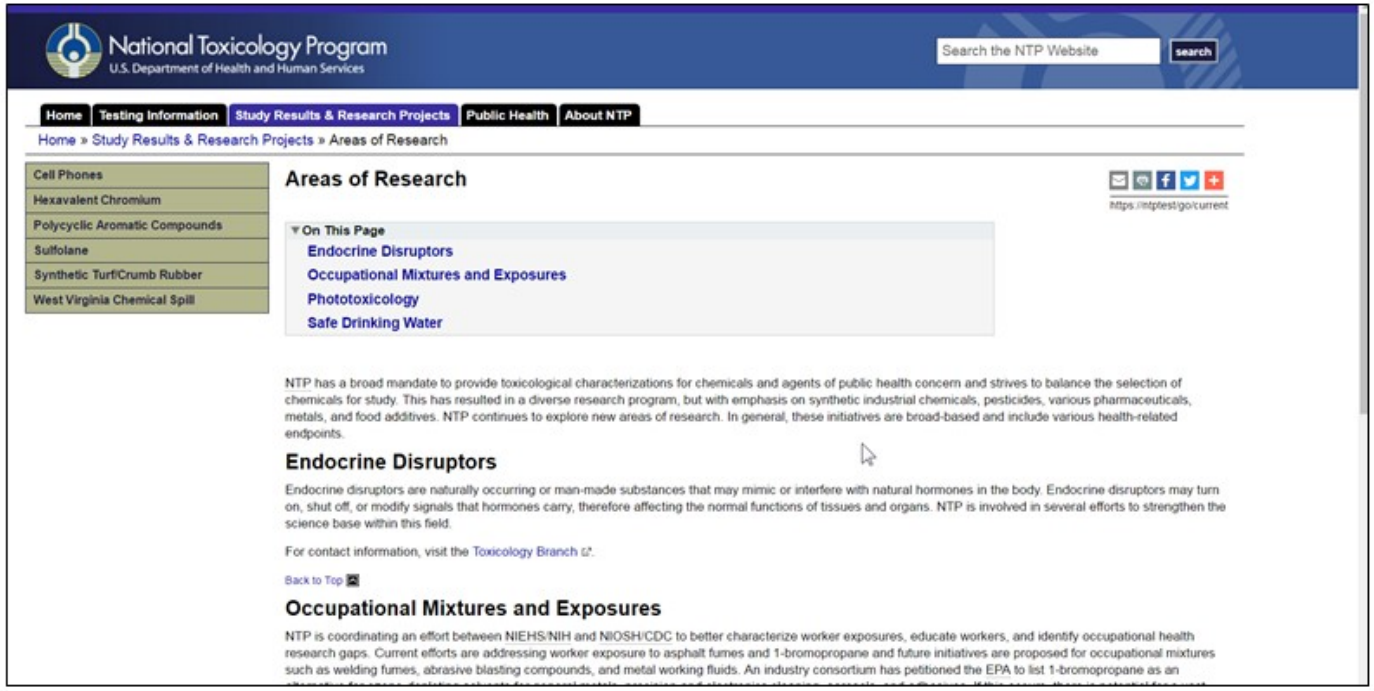
Incremental approach

- 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



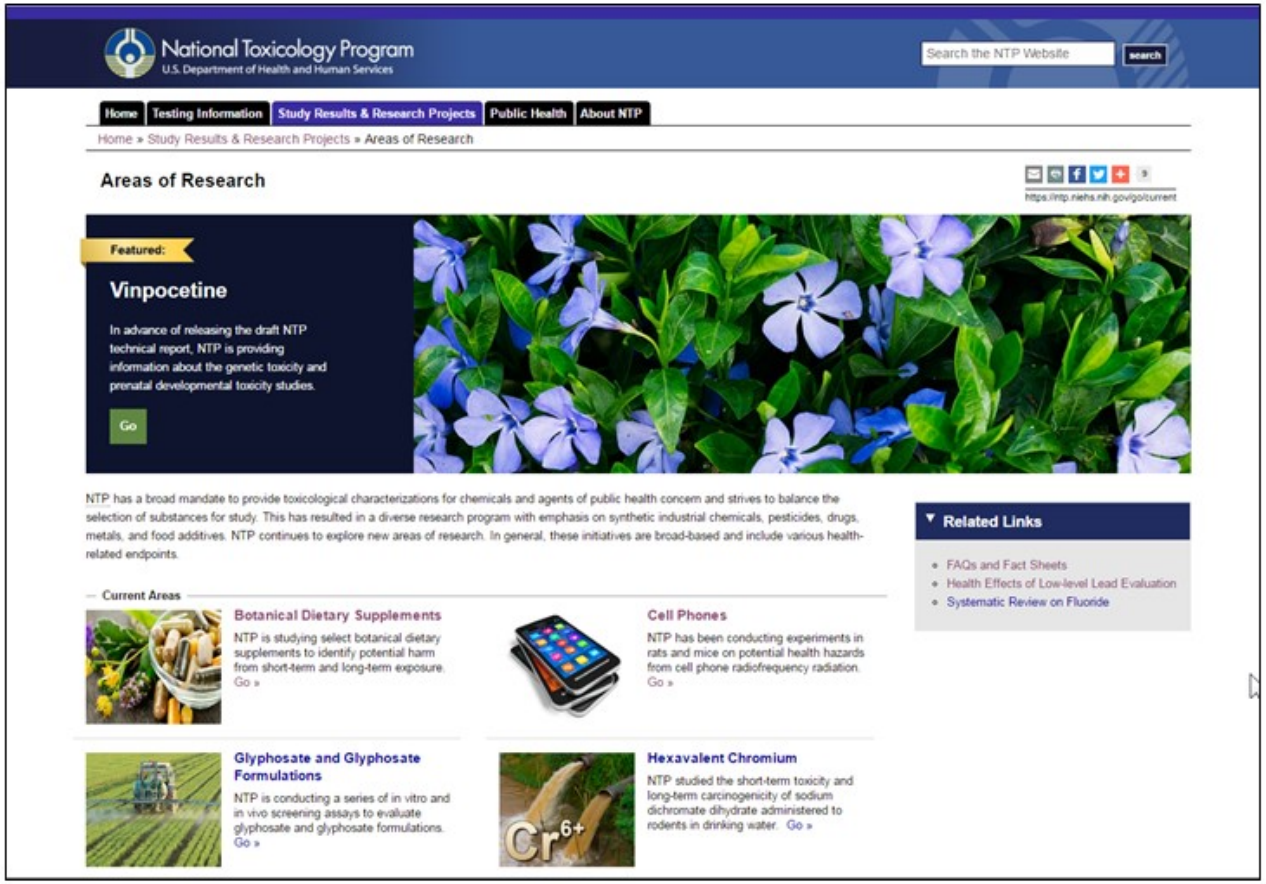
NTP Website Redesign

Old: “Areas of Research” landing page



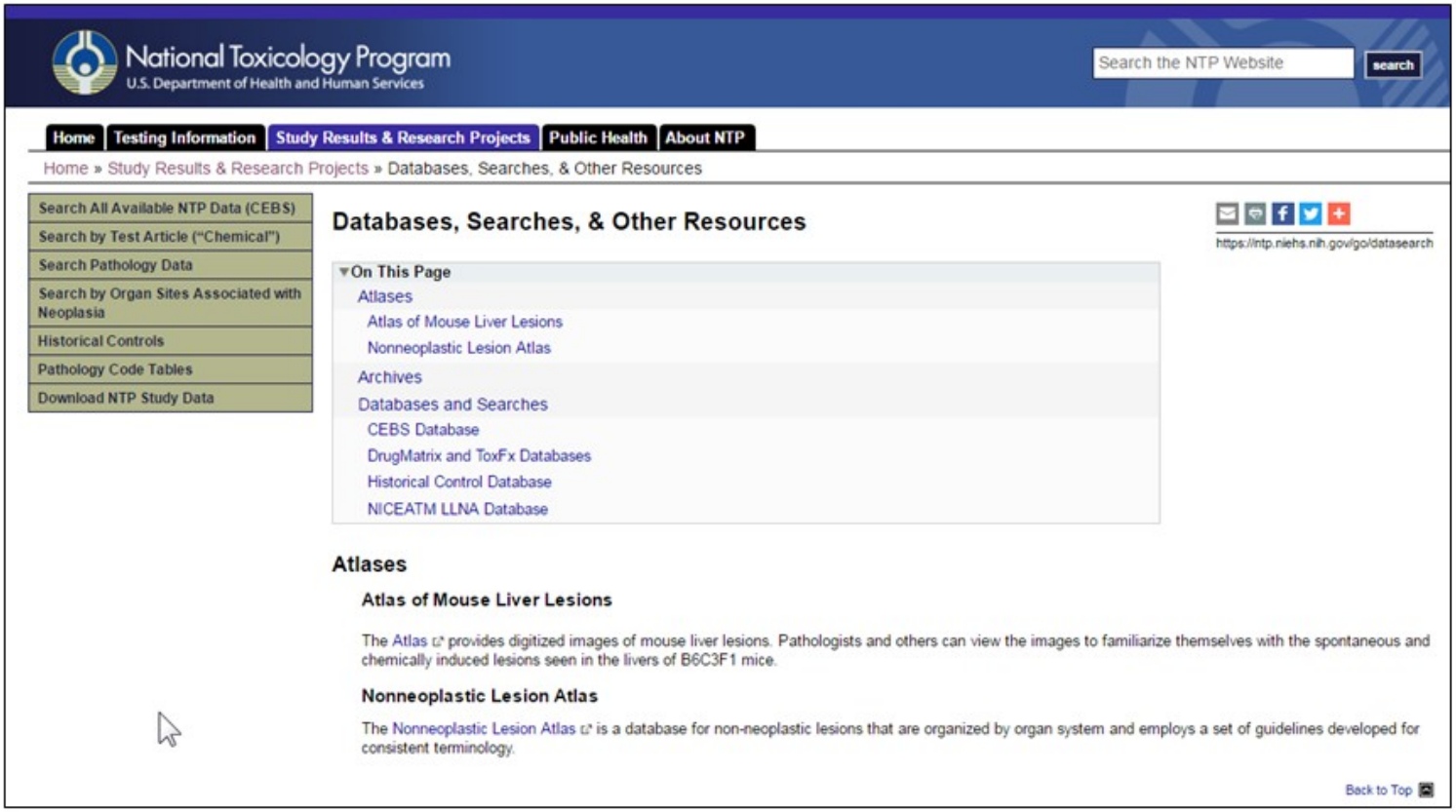
NTP Website Redesign

New: "Areas of Research" landing page – Now live

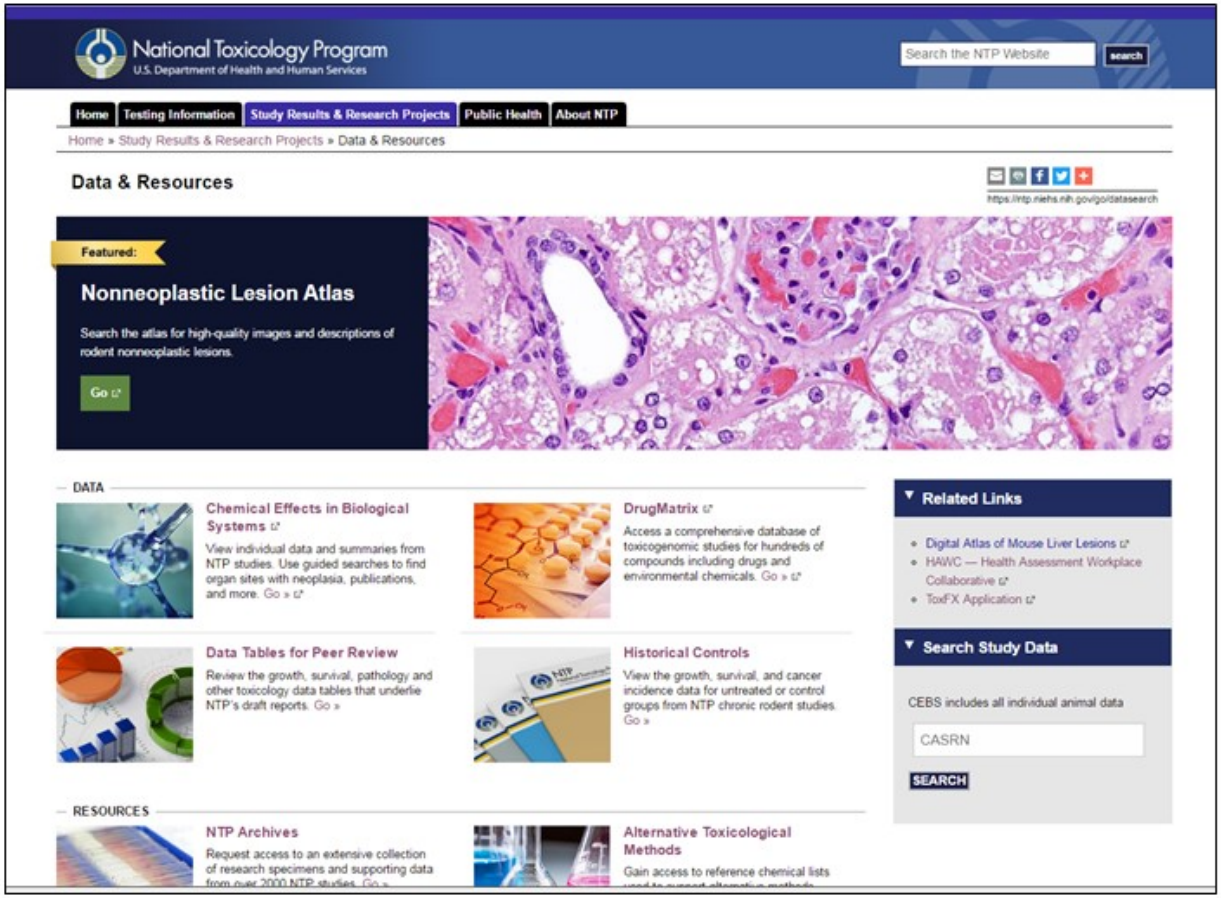


NTP Website Redesign

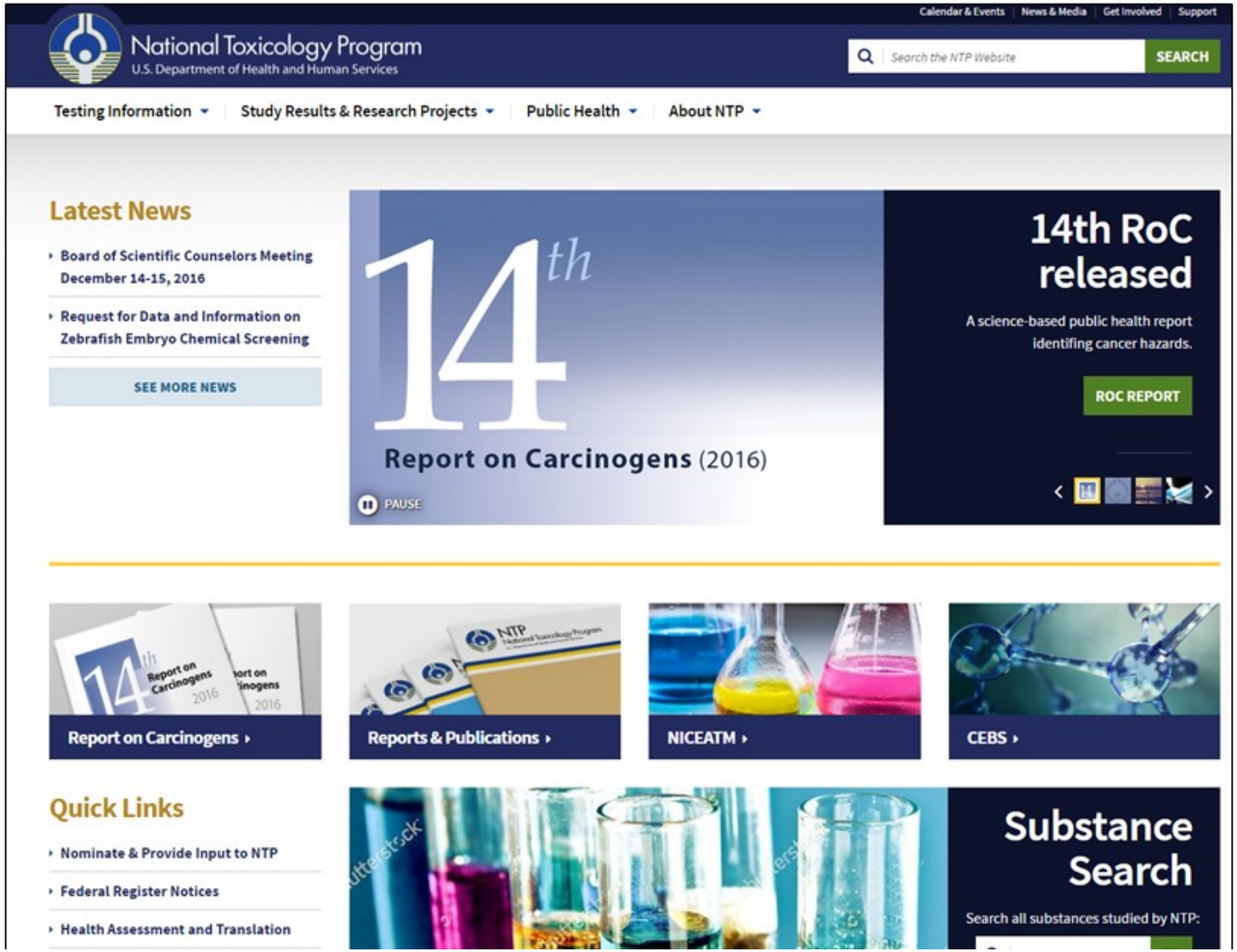
Old: “Database, Searches, & Other Resources” landing page



New: “Data & Resources” landing page – Now live

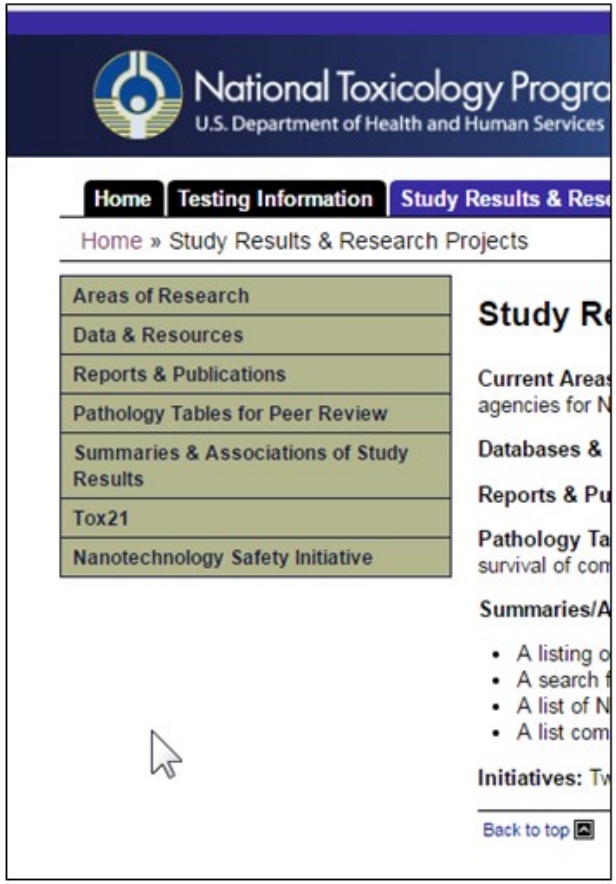


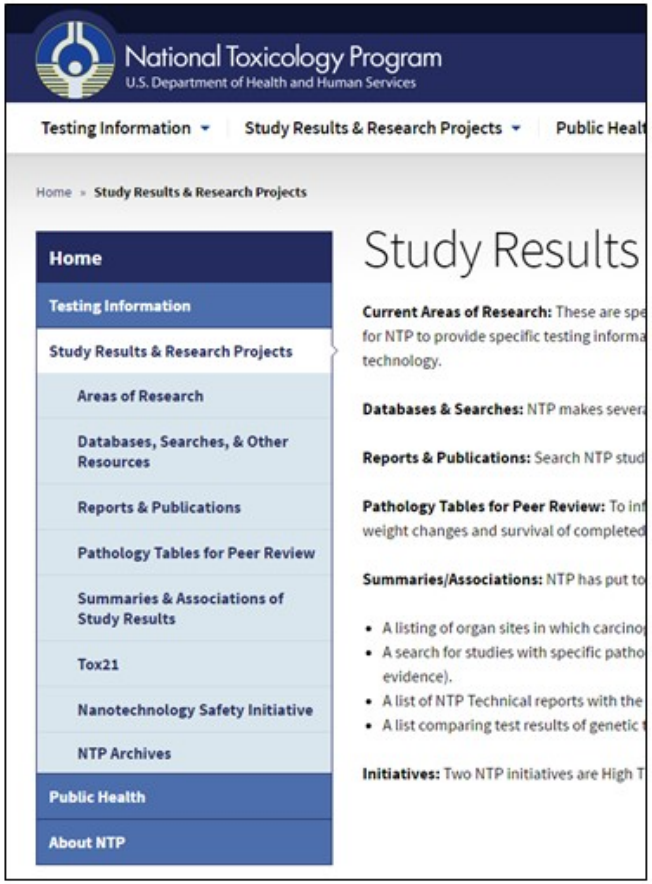
NTP Website Redesign: Draft Home Page



NTP Website Redesign: Organization

Draft: Navigation





Thank you!

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

NIH National Institute of Environmental Health Sciences

National Toxicology Program
U.S. Department of Health and Human Services