

For the past 37 years, NTP has been a leader in toxicology testing, research, and analysis and provided important scientific information upon which public health decisions are based.

NTP has earned distinction as an honest broker through its continuing commitment to open debate, impartiality, and rigorous review.

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Headquartered at the

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

PO Box 12233

RESEARCH TRIANGLE PARK, NORTH CAROLINA 27709

PHONE 919-541-3419 | EMAIL cdm@niehs.nih.gov

ONLINE <http://ntp.niehs.nih.gov>

The National Toxicology Program

milestones

1978–2015
**Thirty-Seven Years
of Toxicology
for Public Health**

Since 1978, NTP has played a critical role in generating and interpreting toxicological information about potentially hazardous substances in our environment and communicating that knowledge to government agencies, medical and scientific communities, and the public. In the 21st century, NTP strives to remain at the cutting edge of scientific research and the development and application of new technologies to provide a strong science base for decisions that protect human health and the environment.

Research Information Communication

NTP's expertise in toxicology combined with the experience and needs of other agencies provides a consolidated approach to identifying and controlling hazardous substances in our environment and safeguarding public health. NTP has evaluated more than 2800 environmental substances for a variety of health-related effects, among them general toxicity, carcinogenicity, reproductive and developmental toxicity, genetic toxicity, immunotoxicity, and neurotoxicity, in appropriate experimental systems. Its disseminations, including technical reports, toxicity reports, reports on genetically modified models, the Report on Carcinogens, monographs on non-cancer health hazards, and other special reports, are used widely as authoritative resources.

NTP and its federal partners support the development and validation of alternative toxicological tests that meet regulatory needs and reduce, refine, or replace the use of animals. NTP leads the interagency Tox21 effort to characterize key steps in toxicity pathways through new and innovative methods and prioritize substances for in-depth toxicological evaluation through high throughput screening techniques.

Sponsorship of more than 75 conferences, over 130 public advisory committee meetings, and more than 30 special panels reflects NTP's commitment to openness, transparency, and careful examination of scientific issues important to public health.

NTP exists to develop the information and the tools that both agencies of government and industry need so that we can all live together safely in the same world

—DAVID P. RALL, MD, PhD
DIRECTOR, 1978–1990

milestones

Department of Health, Education, and Welfare established NTP
David P. Rall, MD, PhD, named 1st director
NCI/NTP published 100th technical report

HHS transferred NCI Carcinogenesis Testing Program to NIEHS

Technical Reports series on carcinogenesis bioassay broadened to include toxicology evaluations
Cellular and genetic toxicity integrated into cancer bioassays

NIEHS/NTP established an interagency agreement with CDC/NIOSH for immunotoxicity of workplace xenobiotics

NIEHS/NTP established interagency agreement with FDA/NCTR for conducting comprehensive toxicological evaluations for substances of concern to FDA

Scientific consensus toward mechanistic-based approaches for understanding toxicity reached
International workshop on validation and regulatory acceptance of alternative toxicological methods convened with ad hoc ICCVAM

ICCVAM established to support the development, validation, acceptance, and harmonization of alternative toxicological test methods
NIEHS/NTP established interagency agreement with CDC/NIOSH to characterize and evaluate adverse effects of complex occupational exposures

Regulatory acceptance of the Murine Local Lymph Node Assay and Corrositex[®] for dermal safety testing achieved through ICCVAM

10th RoC published
NICEATM initiated first international validation study with the European Centre for the Validation of Alternative Methods

Use of toxic equivalency factor approach for cancer risk assessment of dioxin mixtures supported by NTP studies
Roadmap completed and a course planned for the 21st century to include a greater use of high and medium throughput, mechanism-based assays

NIEHS/NTP funded dense single nucleotide polymorphisms mapping of 15 mouse strains to identify genetic variation as a tool for exploring genetic susceptibility to environmental diseases
Samuel H. Wilson, MD, designated as acting director
NRC report *Toxicity Testing in the 21st Century* echoed themes from NTP Roadmap (2004) in calling for new approaches to toxicity screening
Prenatal exposure as default paradigm in toxicity testing adopted

New criteria for evaluation of outcomes from studies on reproduction, development, or immune system announced
NIEHS/NTP established ICATM—formal agreement to cooperate on alternative test methods with Europe, Japan, and Canada

Scientific literature assessments expanded to include all non-cancer toxicities
Korea joined ICATM
Modified one generation reproduction study design adopted
12th RoC published

Nonneoplastic lesion atlas as guide for standardizing terminology in toxicologic pathology launched
Systematic review methodology adopted for literature-based scientific assessments
Research to evaluate WV Elk River spilled chemicals combining high throughput, computational, and traditional toxicology approaches initiated
13th RoC published

Key

- CDC—Centers for Disease Control and Prevention
- CERHR—Center for the Evaluation of Risks to Human Reproduction
- EPA—Environmental Protection Agency
- FDA—Food and Drug Administration
- HHS—Department of Health and Human Services
- ICATM—International Cooperation on Alternative Test Methods
- ICCVAM—Interagency Coordinating Committee on the Validation of Alternative Methods
- NCEH—National Center for Environmental Health
- NCI—National Cancer Institute
- NCTR—National Center for Toxicological Research
- NICEATM—NTP Interagency Center for the Evaluation of Alternative Toxicological Methods
- NIEHS—National Institute of Environmental Health Sciences
- NIH—National Institutes of Health
- NIOSH—National Institute for Occupational Safety and Health
- NRC—National Research Council
- NTP—National Toxicology Program
- OECD—Organisation for Economic Co-operation and Development
- RoC—Report on Carcinogens
- WV—West Virginia

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2015

1st RoC published; 26 listings
NCI/NTP published 200th technical report
Developmental toxicity testing initiated

Immunotoxicology incorporated into testing strategy and comprehensive testing battery defined to evaluate immune system alterations
Reproductive Assessment by Continuous Breeding studies initiated

Standards for quality assurance for pathology established
5 categories to define levels of evidence of carcinogenic activity set
1st systematic evaluation of the predictability of various genetic toxicity screens for cancer published
300th technical report published

Kenneth Olden, PhD, named director
Toxicity Report series initiated

400th technical report published

HHS approved revised listing criteria for RoC allowing consideration of all relevant information
Formal process for removing a listing from the RoC established
NIEHS/NTP initiated agreement with CDC/NCEH to provide funding for expanded biomonitoring of environmental toxicants in the National Health and Nutrition Examination Survey

NICEATM established to convene scientific panels to evaluate alternative toxicological methods
CERHR established to conduct scientific assessments of the reproductive and developmental toxicity literature on selected environmental agents
8th RoC published; 1st report to apply revised criteria

9th RoC published; 1st report to apply new criteria to remove listings: saccharin and ethyl acrylate and to upgrade listings based on consideration of mechanistic data: dioxin and ethylene oxide
ICCVAM became permanent under NICEATM with passage of ICCVAM Authorization Act of 2000
Center for Phototoxicology established
Collaborations with the European Ramazzini Foundation of Oncology and Environmental Sciences formalized through NIEHS/NTP
500th technical report published

NTP-CERHR monograph series initiated
Technical Report series for genetically modified models created
Regulatory acceptance of revised Up-and-Down Procedure achieved through ICCVAM
NICEATM and ICCVAM proposed and defined performance standards concept to allow for regulatory acceptance of proprietary test methods

11th RoC published; 1st report to list biological agents
Celebrated a quarter century of toxicology for public health and unveiled a new toxicology for the 21st century
Program to identify and evaluate high throughput screening assays for toxicity testing initiated
David A. Schwartz, MD, PhD, named director

Collins et al. *Perspectives* article in *Science* responded to 2007 NRC report *Toxicity Testing in the 21st Century* by laying out a comprehensive federal agency response
NIEHS/NTP established formal agreement with EPA and NIH Chemical Genomics Center for high throughput toxicity testing; Tox21
NTP-CERHR Monograph on Bisphenol A released
Linda S. Birnbaum, PhD, named director

Chemical Effects in Biological Systems—new database for housing, integrating, and managing data—published
FDA joined Tox21

Regulatory acceptance of BG1 luciferase estrogen receptor transactivation test method by EPA and 1st OECD performance-based test guideline for estrogen receptor agonists (PBTG 455) achieved through ICCVAM

Diversity outbred mouse as a tool for identifying inter-individual variation in toxicity response demonstrated
Collaboration with EPA enabled waivers of animal-based uterotrophic testing for EPA Endocrine Disruptor Screening Program, the first use of Tox21 approaches by a regulatory agency to replace animal testing
Funding to map gene expression during differentiation in mouse and human stem cells and to standardize zebrafish development protocols awarded