



NTP

National Toxicology Program

Current Directions & Evolving Strategies



Looking Deeper:

How Today's Research
Is Building a Safer Tomorrow



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Glossary of Acronyms

AZT	Azidothymidine
BSC	Board of Scientific Counselors
<i>C. elegans</i>	<i>Caenorhabditis elegans</i>
CEBS	Chemical Effects in Biological Systems
CDC	Centers for Disease Control and Prevention
CPSC	Consumer Product Safety Commission
DoD	Department of Defense
EFV	Efavirenz
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FTC	Emtricitabine
HHS	Department of Health and Human Services
HIV	Human Immunodeficiency Virus
ICCVAM	Interagency Coordinating Committee on the Validation of Alternative Methods
NCEH/ATSDR	National Center for Environmental Health/Agency for Toxic Substances and Disease Registry
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
NTP	National Toxicology Program
OHAT	Office of Health Assessment and Translation
OSHA	Occupational Safety and Health Administration
PACs	Polycyclic Aromatic Compounds
PBDEs	Polybrominated Diphenyl Ethers
PFOA	Perfluorooctanoic Acid
PFOS	Perfluorooctane Sulfonate
RoC	Report on Carcinogens
SACATM	Scientific Advisory Committee on Alternative Toxicological Methods
TDF	Tenofovir
Tox21	Toxicology in the 21 st Century



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What We Do

The NTP's mission is to evaluate environmental substances of public health concern by developing and applying tools of modern toxicology and molecular biology.

The NTP is taking a close look at the thousands of substances in our environment, including substances used in personal care products, foods, prescription drugs, household cleaners and lawn care products, to identify any potential harm they might cause to human health.

Our focus is on prevention. As the largest government program in toxicology, we're safeguarding the public health by identifying the potential toxic effects of these substances. We're also working to advance our field, developing new study methods that will allow more efficient and cost-effective toxicology studies, both at the NTP and around the globe.

Our work falls into four main categories:

- 1. Coordinate toxicology testing programs** throughout the Federal Government and provide a centralized and integrated evaluation of the effects of chemicals and other substances on human health.
- 2. Strengthen the science base in toxicology** through our research and testing program. The program conducts and supports studies that fill significant gaps in toxicology research, help build understanding of the mechanisms of toxicity, or enhance the predictive value of future studies.
- 3. Develop and validate improved testing methods**, making it possible to study substances more quickly and cost-effectively. We're working to develop mechanism-based testing methods that may require fewer test animals, test more substances faster and provide information that is more useful from a human health perspective.
- 4. Provide information about potentially toxic substances** to health regulatory and research agencies, scientific and medical communities, and the public so that they can make informed decisions and determine if interventions or reductions in exposure are needed to protect human health.

We're continually evolving to remain on the cutting edge of scientific research and to develop and apply new technologies. To learn more about our current studies, see the "What We're Studying" section. To learn more about how we're changing the science of toxicology research, see the "A Look Ahead" section.

What We're Studying

We are all affected by our environment—by the products and substances we come in contact with at home, at work and at play. We do not know the effects of many of these substances on our health, yet we may be exposed to them while manufacturing, distributing, using and disposing of them or when they become pollutants in our air, water or soil.

The NTP is charged with evaluating high-priority products and substances for possible effects on human health. In our 30-plus years, we've studied over 2,500 substances, including industrial chemicals, pharmaceuticals, contaminants of finished drinking water, photoactive chemicals, dietary supplements and endocrine-disrupting substances. We've studied them for a variety of health-related effects, such as general toxicity, carcinogenicity (ability to cause cancer), genotoxicity (ability to damage genes), and effects on reproduction, development and the immune, cardiovascular and nervous systems. Our data have been used by regulatory agencies around the world when considering the need to regulate specific environmental substances to protect human health and the environment.

Below are brief overviews of some of our current initiatives. In general, they are broad-based and investigate various health-related effects. For more detailed information, visit the NTP Web site at <http://ntp.niehs.nih.gov>.

Consumer Products

Radiofrequency radiation emissions from cellular phones

With over three billion in use worldwide, cellular phones are one of the most popular electronic devices ever introduced. Yet despite their staggering popularity, their possible effects on public health have not been fully explored.

In the United States, cellular phones must meet current Federal Communication Commission guidelines on the emission of microwave radiation. However, these guidelines are only intended to protect the user from immediate injury due to the heat produced from this radiation. There is little information on whether long-term exposure to this radiation poses other health risks.

The NTP is working to provide this information, conducting studies that use laboratory animals and special chambers that simulate the exposures of cellular phone users. These studies will help clarify any potential health hazards, including cancer risk, and pave the way to better protect public health.



Sunscreens

Every year, millions use sunscreen to prevent sunburn and resulting skin damage. Specific chemicals in sunscreens can absorb or “block” ultraviolet radiation from the sun. Though these products are applied to the skin, sunscreen ingredients have been found in urine, indicating that they make their way into the body. Some data in the literature suggest that sunscreen ingredients may interact with the estrogen receptor and therefore have the potential to affect reproductive organ development and function.

Using short-term studies, the NTP is currently assessing two of the most commonly used sunscreen ingredients, 2-hydroxy-4-methoxybenzophenone and 2-ethylhexyl-p-methoxycinnamate, to characterize their potential interaction with steroid receptors. The NTP is also studying the effects of early life exposures on the developing fetus to determine if sunscreen ingredients are harmful, and to determine if they affect the offspring’s ability to reproduce in adulthood.

These studies will provide useful information to both the Food and Drug Administration (FDA) and the public regarding potential hazards of sunscreen ingredients.

Perfluorinated compounds

Perfluorinated compounds such as perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) have been used since the 1950s to make a variety of consumer products. Their resistance to water, oil, heat and chemicals makes them very useful in a variety of products, including nonstick cookware, grease-resistant food packaging and fabrics that are resistant to stains, water and wrinkles.

Although the use of these chemicals is decreasing, the same properties that make them commercially useful also make them very persistent, both in human tissue and in the environment. The NTP is collaborating with the Environmental

Protection Agency (EPA) to study how these chemicals behave inside the body, including potential effects on reproduction and development.

While much is known about the toxicity of PFOS and PFOA, less is known about other members of this chemical class. The NTP is exploring the use of tests in cells and isolated molecular targets to predict adverse responses to chemicals within this class. This study may ultimately help us to better understand the environmental health effects of the entire class of perfluorinated compounds.

Nanoscale materials

Nanoscale materials are defined as a set of substances where at least one critical dimension is less than about 100 nanometers (a nanometer is one billionth of a meter). Because of their unique optical, magnetic, electrical and other properties, they hold great promise for use in electronics, medicine and other fields. Increasingly, nanoscale materials are appearing in cosmetics, foods, sunscreens, prescription drug products and commerce products. As a result, the potential exists for new and unanticipated exposures for which the impact on human health and the environment is not known.

The NTP is engaged in a broad-based research program to address the potential human health hazards associated with their manufacture and use. Researchers are working to evaluate the toxicological properties of a representative cross section of several different classes of nanoscale materials: (1) metal oxides, (2) fluorescent crystalline semiconductors (quantum dots), (3) fullerenes (buckyballs) and (4) carbon nanotubes. We are using these classes as models to investigate if and how nanoscale materials can interact with biological systems. Key parameters of greatest concern relative to their potential toxicity are size, shape, surface chemistry and composition. Researchers are using studies in laboratory animals and cells, and mathematical models to evaluate and predict whether these materials can penetrate the skin, where they go in the body and what potential health effects they may cause.

Flame retardants

Polybrominated diphenyl ethers (PBDEs) are widely used as flame retardants in fabrics, furniture and electronics. Over the past 25 years, they have been proven to be effective in reducing fire-related damage and injury. However, use of these chemicals has led to their accumulation in the environment, and evidence of significant concentrations in human and animal tissue has led to concern about possible toxicity, including carcinogenicity and reproductive toxicity. As a result, the NTP is currently evaluating several of the most commonly found PBDEs, as well as two other brominated flame retardants: tetrabromobisphenol A and tetrabromobisphenol A-bis(2,3-dibromopropyl ether).

The NTP is also studying other nonbrominated flame retardants, including antimony trioxide and tris(chloropropyl) phosphate, a proposed substitute for PBDEs in flame retardant applications.

These studies should provide information useful to the Consumer Product Safety Commission (CPSC) to ensure the safety of consumer products containing these chemicals.

Medicines and Therapeutics

Dietary supplements

Millions of Americans routinely take dietary supplements for health reasons, and their use is widespread and growing. The ingredients in dietary supplements vary and may include vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes and metabolites. Dietary supplements can also be extracts or concentrates and may be found in many forms, such as tablets, capsules, gels, liquids and powders.

The FDA regulates dietary supplements under a different set of regulations than those covering other foods and drug products. Under the Dietary Supplement Health and Education Act of 1994, dietary supplements do not need FDA approval



for safety or effectiveness before they are marketed. Once a product is marketed, the FDA has responsibility for monitoring safety and must show that a dietary supplement is not safe before it can take action to restrict its use or remove it from the marketplace.

The NTP is working closely with the FDA to address questions about the safety of a broad range of dietary supplements and has completed studies for the following multipurpose and miscellaneous use supplements: *Aloe vera*, androstenedione, bitter orange, ephedra, *Ginkgo biloba*, ginseng, goldenseal, kava kava, milk thistle and senna. The NTP has ongoing studies for black cohosh, dong quai, *Echinacea purpurea*, evening primrose oil, *Garcinia cambogia*, gum guggul, green tea, resveratrol, *Usnea* lichen and valerian.

Human immunodeficiency virus (HIV) therapies

An estimated 35 million people worldwide are living with HIV, including about one million pregnant women who need treatment to prevent mother-to-child transmission of the virus during pregnancy, labor and delivery. Azidothymidine (AZT), the first FDA-approved anti-HIV agent, is often combined with other HIV drugs that target different aspects of viral replication. Because HIV drugs are administered in combination, the NTP is studying commonly used combinations (AZT, nevirapine, zidovudine and/or lamivudine) to characterize any potential toxicity to the offspring.

The World Health Organization has recommended the triple combination of tenofovir (TDF), emtricitabine (FTC) and efavirenz (EFV) as standard therapy for all HIV-positive individuals. While there is great benefit from this therapy, potential toxicity for the offspring is not known. The NTP is conducting studies to determine the potential effects of the TDF, FTC and EFV triple-combination therapy on fetal and postnatal development. The results of these studies can inform regulatory agencies worldwide of the impact of these drugs during pregnancy.

Our Surroundings

Mold

New construction methods, better sealing and insulation in buildings, and natural disasters, such as hurricanes, have all led to an increase in indoor mold levels. In recent years, there have been reports associating mold exposures with a variety of symptoms, including allergies and respiratory and neurological problems.

The NTP is currently conducting studies to better understand how exposure to mold may cause disease. Specific areas under study include:

- Fungal organisms that may be causing human health effects
- Target organs for fungal toxicity
- Dose-dependent effects, with particular emphasis on respiratory, immune and neurological end points
- Identification of biomarkers of exposure and effects

These studies will help us to better understand the causes of these symptoms, with the ultimate goal of creating healthier buildings and reducing mold-related health issues.

Polycyclic aromatic compounds

Polycyclic aromatic compounds (PACs) are a large class of widespread environmental contaminants. PACs occur naturally in crude oil or are created and released into the environment through the burning of organic material such as fossil fuels. People can be exposed to PACs by eating certain foods (e.g., charbroiled meat, smoked fish), breathing contaminated air or handling tainted soil. People are exposed not to single PACs but to complex mixtures of PACs that differ depending on the source of the exposure and other factors (such as sunlight or weathering).

Some substances of the PAC class are known human carcinogens; animal studies have shown that certain PACs can cause toxicity to immune, reproductive and other systems. However, the vast majority of PACs have not been evaluated. More research is needed to understand the combined effects of multiple PACs.

The NTP is studying PACs to gain a better understanding of the toxicity of both individual PACs and PAC mixtures, and how environmental exposures to PACs may affect human health.



Food

The NTP is conducting studies of several food constituents and flavorings to help the FDA determine whether their presence in food is harmful. One such constituent is furan, a by-product of some chemical manufacturing processes, which is sometimes reported to be found in canned or jarred foods such as soups, sauces, beans, pasta meals and baby foods. It appears to form as a result of heat treatment techniques used to process and preserve foods. Furans are of concern because they are considered carcinogenic based on studies in laboratory animals at high doses.

Our Workplace

Occupational exposures

The NTP is studying a variety of occupational chemicals to help the National Institute for Occupational Safety and Health (NIOSH) better understand the risks they pose to workers, develop exposure limits for workers and help create safer working environments for millions of workers in the United States. The NTP is currently testing a variety of substances to which workers in certain occupations are exposed every day. These substances include:

- Abrasive blasting materials: Safer alternatives to silica sand are being tested, including coal slag, garnet, crushed glass and specular hematite.
- Artificial butter flavoring, diacetyl and acetoin: Increased incidences of the lung disease bronchiolitis obliterans and other forms of respiratory impairment have been reported among workers in the microwave popcorn industry. Several studies suggest that exposure to volatile constituents of artificial butter flavoring released during the production process is the greatest risk factor. Diacetyl and acetoin are two main volatile components of the flavoring.
- 1-Bromopropane: An industrial chemical that has replaced ozone-depleting chemicals such as hydrochlorofluorocarbons and chlorinated solvents for metal cleaning and degreasing.
- Metalworking fluids: Complex mixtures of chemicals that are used by millions of workers for cutting, milling, stamping, drilling and grinding metal. The NTP will evaluate several commercial products.
- Welding fumes: Fumes generated by the process of joining or cutting pieces of metal by heat, pressure or both. NIOSH has developed a robotic system to generate fumes similar to those found in the workplace.

Researchers at NIOSH are using artificial human lung fluids to study the persistence of tungsten oxide fibers formed during the processing of tungsten-containing ores and assessing exposure of workers to these fibers in tungsten refining and manufacturing operations. As part of the NTP's research on nanomaterials, NIOSH scientists are characterizing workplace exposure to selected engineered nanoparticles.



How We're Assessing Human Hazards

The NTP maintains a number of activities to evaluate the potential for adverse effects on human health from exposure to substances in our environment. The reports from these health hazard evaluations provide critical information needed by Federal, state and local health regulatory and research agencies to conduct formal risk assessments.

Health Assessment and Translation

The NTP is committed to studying non-cancer health effects of potentially harmful substances through the Office of Health Assessment and Translation (OHAT). OHAT conducts literature-based evaluations to assess evidence that substances in our environment cause adverse health effects. For example, OHAT has studied the potential developmental effects of cancer chemotherapy during pregnancy and health effects of low-level lead exposure in children and adults.

OHAT also organizes workshops and webinars to address emerging environmental health issues such as a workshop on the role of environmental chemicals in the development of diabetes and obesity.

OHAT is applying systematic review methodology to address questions in environmental health and has developed a framework for systematic review and integration of scientific evidence for carrying out literature-based evaluations on environmental health topics. Such a framework enhances the transparency and quality of how OHAT reaches and communicates conclusions from its evaluations.

For every project, OHAT welcomes opportunities for external scientific, public and interagency inputs. The results of OHAT's work are published in a variety of formats, including NTP monographs, state-of-the-science workshop reports and peer-reviewed journal publications. For more information about ongoing projects and the full list of reports, visit <http://ntp.niehs.nih.gov/go/ohat>.



The Report on Carcinogens

The Report on Carcinogens (RoC) is one of the world's leading compilations of data on agents, substances, mixtures and exposure circumstances that may pose a cancer risk to humans. First requested by Congress in 1978, it is published every two years.

The RoC lists substances that are "known" or "reasonably anticipated" to cause cancer in humans and to which a significant number of people living in the United States are exposed. It combines data from both Federal and nongovernmental sources into one document, including:

- The carcinogenicity, genotoxicity and biological mechanism (modes of action in the body) of the listed substance in humans and/or animals
- The potential for human exposure to these substances
- Federal regulations to limit exposures

Each edition of the report is cumulative and includes substances newly reviewed, in addition to those listed in previous editions. The most recent edition of the RoC is available on the RoC Web site at <http://ntp.niehs.nih.gov/go/roc>.

The NTP follows a formal, multistep process for review of candidate substances nominated for listing in or removal from the RoC. To find out what's under review, visit the RoC Web site.

A Look Ahead

In addition to its current portfolio of toxicological studies, the NTP is working to make the future of toxicology research more efficient, allowing for a much greater number of substances to be tested and providing results that are more useful for human risk assessment.

The NTP and other Federal agency partners are working to change toxicology from an observation-based science using disease-specific models to a predictive science that uses mechanism-based biological observations. The NTP Roadmap supports this goal through three key initiatives:

- 1. Refine** traditional toxicology assays
- 2. Develop** rapid, mechanism-based, predictive screens for environmentally induced diseases
- 3. Improve** the overall utility of NTP products for public health decisions

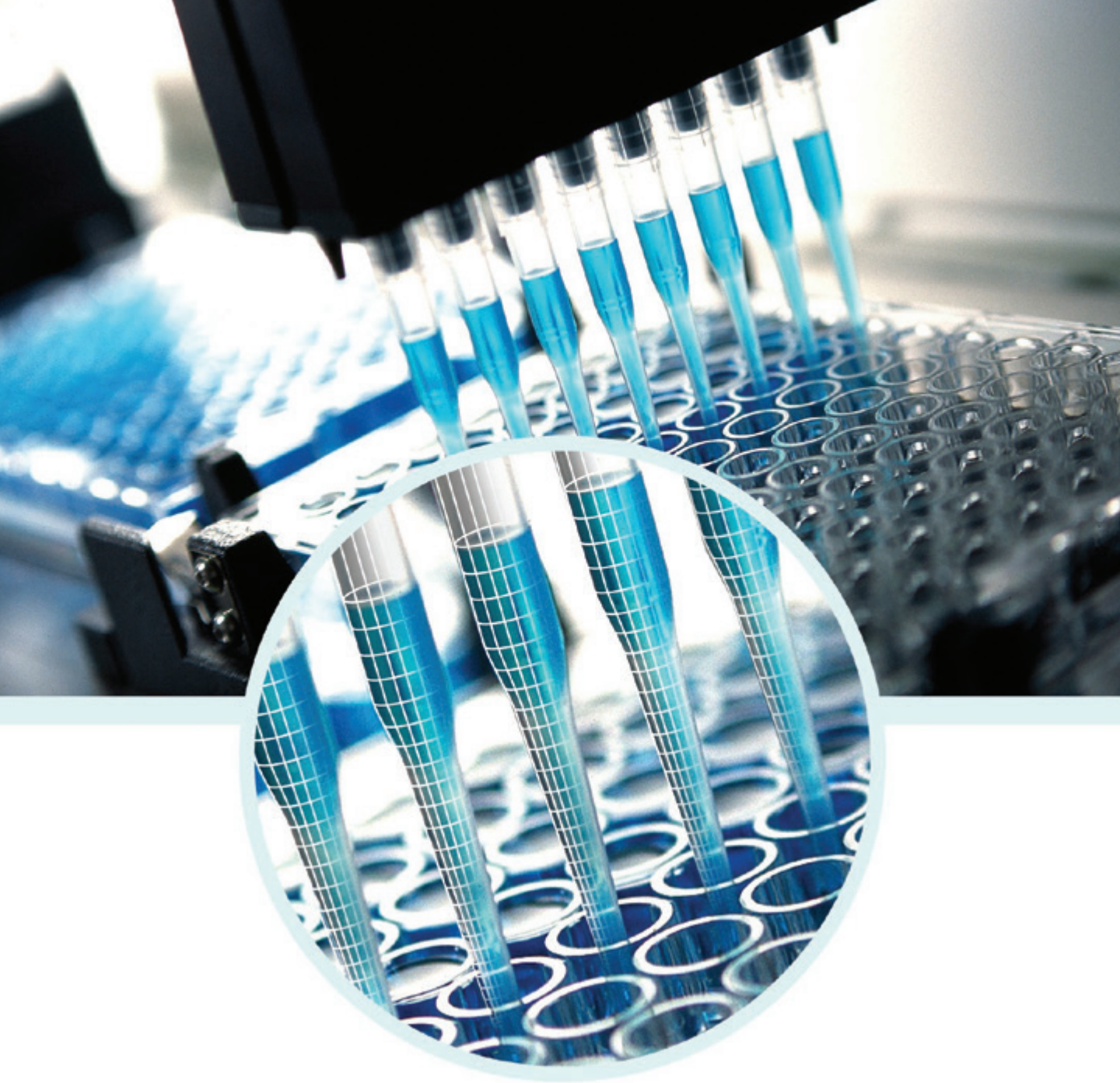
To that end, the NTP is developing a number of promising new testing approaches that are advancing the future of toxicology research, both at the NTP and elsewhere.

Alternative Toxicological Methods

A primary goal for the NTP is to advance the science of toxicology by developing toxicological testing methods that improve on current tests by:

- Predicting human health hazards more precisely
- Saving time and money
- Reducing, refining (by causing less pain and distress) or replacing animal use in testing, where feasible

To help reach these goals, two groups are specifically charged with addressing the development and use of alternative methods in regulatory safety testing.



The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) is a Federal committee charged with coordinating and promoting the development, validation, acceptance and national and international harmonization of new, revised and alternative test methods. ICCVAM consists of representatives from 15 regulatory and research agencies that generate or use toxicological testing data to safeguard the health of people, animals and the environment.

ICCVAM has evaluated many tests, some of which have been adopted or approved by U.S. regulatory agencies. For other tests, ICCVAM has recommended efforts to further characterize or improve their usefulness for regulatory safety testing. ICCVAM convenes workshops and expert panel meetings to assess research, development and validation efforts for alternative toxicological test methods. The results of ICCVAM evaluations are published in peer-reviewed reports or journals.

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) administers ICCVAM and provides scientific and operational support for ICCVAM-related activities. NICEATM also conducts validation studies to evaluate new or revised alternative methods for toxicity testing. In addition, it provides support in data analysis for the Toxicology in the 21st Century (Tox21) consortium, an ongoing collaboration among Federal agencies to characterize the potential toxicity of chemicals by using cells and isolated molecular targets instead of laboratory animals.

NICEATM is working with ICCVAM to develop alternative test methods for regulatory use. These include toxicity tests for short-term exposure to a substance by ingestion or skin contact, and safety tests for biologics, such as vaccines. ICCVAM and NICEATM communicate with partners and the public to foster acceptance and use of alternative toxicological methods by regulators and the regulated community. ICCVAM also works with other international organizations to promote cooperation, with the goal of more rapid acceptance of new safety testing alternatives to animal testing worldwide.

Non-Mammalian Model Systems

The NTP is continuing to explore the use of non-mammalian species as potential alternative models for toxicology testing. The NTP is currently evaluating two model organisms, *Caenorhabditis elegans* (*C. elegans*) and zebrafish, for assessing the potential toxic effects of chemicals on development and the immune and nervous systems of multicellular organisms. *C. elegans* is a roundworm about 1 mm in length that lives freely in soil and feeds on bacteria; zebrafish are vertebrate organisms that develop within a week most of the major organ systems present in mammals.

Both organisms hold promise as practical and efficient test models for several reasons:

- Both have short life cycles, are easy and inexpensive to maintain, and have genetic variants that are readily available
- A great deal of information is available on both organisms, including their complete genomic sequence, as well as detailed information on their cellular and developmental biology
- Their molecular and biochemical changes following chemical exposure appear to be similar to those seen in laboratory studies that use rodents

The use of these alternative animal models is consistent with NTP's strategy to reduce the number of mammals used in testing. Several toxicology tests that evaluate developmental toxicity, immunotoxicity and neurotoxicity have been developed. While both organisms are still under study, they hold a great deal of promise for faster, more cost-effective toxicology studies.

High-Throughput Screening and Tox21

The NTP is working to develop higher throughput toxicology testing methods that will allow researchers to evaluate a large number of substances faster. New automated processes can screen tens of thousands of substances for biological activity using cells and isolated molecular targets. The information from these studies will help the NTP do the following:

- Identify mechanisms of chemical toxicity for further study
- Develop models that predict how substances might react in biological systems
- Prioritize substances for further toxicological study

The Tox21 consortium uses a high-throughput screening approach that shows great promise for changing toxicology into a predictive science. This consortium is a collaboration of the NTP, the National Institutes of Health's National Center for Advancing Translational Sciences, the EPA's National Center for Computational Toxicology and the FDA. The Tox21 partners work together to develop, validate and translate innovative high-throughput screening methods to characterize the impact of chemicals on key steps in toxicity pathways. The goal of Tox21 is to use high-throughput screening methods to more accurately predict the effects of chemicals on human health and the environment. The Tox21 initiative also offers the potential for decreased use of animals in toxicity testing.

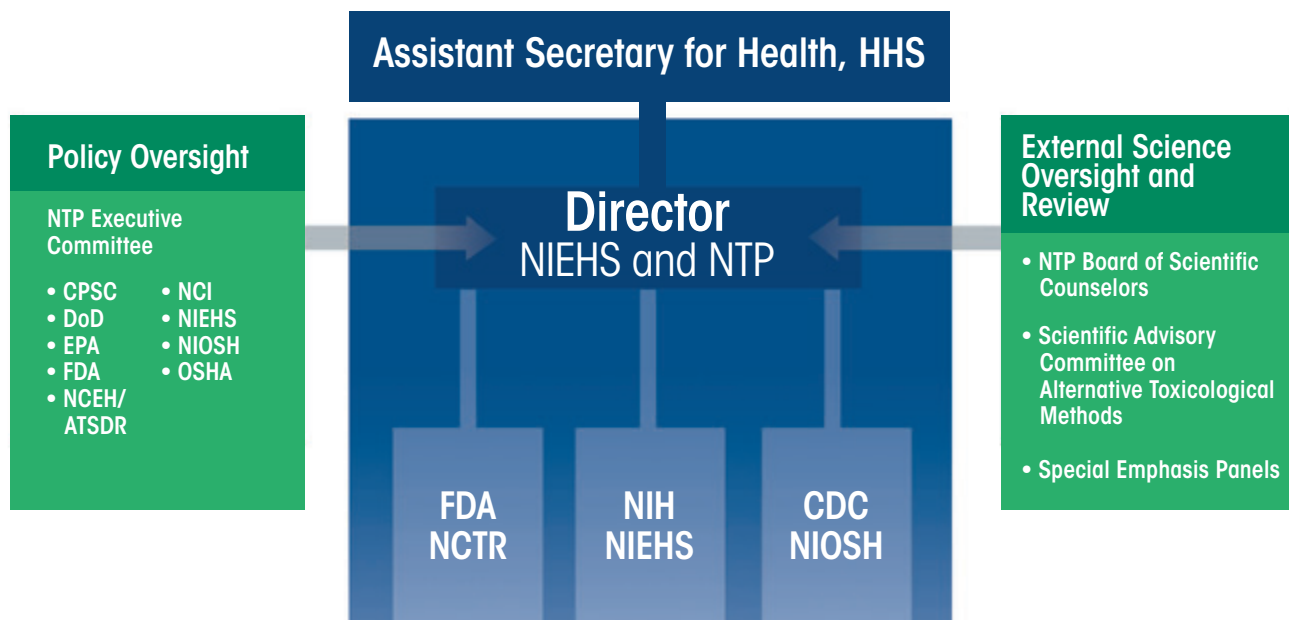
Population-Level Differences in Response to a Toxicant

Human populations have great genetic diversity and vary in responses to environmental factors. However, almost all toxicology studies utilize mouse models that are genetically homogenous. Using genetically diverse mouse populations for toxicology studies can provide better models for the variation in response to a given toxicant in the human population.

The NTP is working to identify the genetic reasons for differences in disease and disease incidence caused by toxic substances among different ages, sexes, ethnicities and other populations. The NTP is evaluating known toxicants in genetically diverse mouse populations to get an indication of the variation in response to each toxicant across the different mouse populations. This research will ultimately lead to greater insight into the genes and pathways involved in toxicity, and to better strategies for predicting the potential toxicity of substances we encounter in our daily lives.

National Toxicology Program

(Headquartered at the NIEHS)



How We Work

NTP Structure

The NTP is made up of three core agencies:

- 1. National Center for Toxicological Research (NCTR).** The NCTR is part of the FDA.
- 2. National Institute of Environmental Health Sciences (NIEHS).** The NIEHS is part of the National Institutes of Health (NIH).
- 3. National Institute for Occupational Safety and Health (NIOSH).** NIOSH is part of the Centers for Disease Control and Prevention (CDC).

These agencies work together to provide the resources that support the NTP. The NTP's operations are headquartered at the NIEHS, and the NIEHS Director also serves as Director of the NTP. The NTP Director reports to the Assistant Secretary for Health of the Department of Health and Human Services (HHS) on issues and activities related to the NTP.

There are also several groups that provide oversight and advice to the NTP. They include:

NTP Executive Committee: This committee provides policy oversight to the NTP. It is composed of the heads (or their designees) of Federal health research and regulatory agencies, including the CPSC, Department of Defense (DoD), EPA, FDA, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry (NCEH/ATSDR), National Cancer Institute (NCI), NIEHS, NIOSH and Occupational Safety and Health Administration (OSHA).

NTP Board of Scientific Counselors (BSC): This committee provides scientific oversight to the NTP. It is a federally chartered committee whose members are appointed by the Secretary of the HHS. The BSC meets once or twice each year, and meetings are open to the public.

Scientific Advisory Committee on Alternative Toxicological Methods (SACATM): This federally chartered committee provides advice to NICEATM and ICCVAM on priorities and directives related to the development, validation, scientific review, regulatory acceptance of new or revised alternative test methods, and on ways to foster partnerships and communication with interested parties. Its members are appointed by the NIEHS Director. SACATM meets once or twice each year, and meetings are open to the public.

Special emphasis panels are convened as needed to provide independent scientific peer review and advice to the NTP. These panels help ensure transparent, unbiased and scientifically rigorous input to the program. This input helps the NTP make credible decisions about human health hazards, set research and testing priorities and evaluate test methods for toxicity screening.

How NTP Studies and Evaluations Work

The NTP has a broad mandate to evaluate the toxicity of substances of public health concern, which it accomplishes through research and testing activities and evaluations of the scientific literature. The NTP selects substances to examine through a nomination process that is open to all interested individuals and groups, and strives to maintain a balanced

portfolio. Research and testing activities and literature-based evaluations are initiated as time and resources permit.

NTP studies follow approaches accepted by Federal regulatory authorities and evaluate substances for a variety of health-related effects, including general toxicity, reproductive and developmental toxicity, genotoxicity, immunotoxicity, neurotoxicity and carcinogenicity. In recent years, the NTP has expanded its capabilities to examine effects of chemicals on the developing fetus, as well as the offspring's ability to reproduce. The NTP studies both single chemicals and mixtures. Outcomes from the studies are assessed against established criteria for identification of potential human health hazards. Although these studies generally use rodent models, the NTP is exploring the use of non-mammalian species and cellular and molecular targets as alternative models.

NTP evaluations of the published literature focus on identification of both cancer and non-cancer hazards. Using structured approaches, the NTP evaluates the quality of the evidence for reported health effects to determine whether exposure to a substance affects human health. In parallel, the NTP is pursuing the use of free, web-based, publicly available data management resources that can be used to enhance our ability to analyze and evaluate results across studies.

The NTP hosts national and international workshops to discuss the state of the science and advance environmental health sciences. The NTP also communicates its findings and activities by attending conferences and hosting webinars and symposiums.

The results from NTP research and testing activities and literature-based evaluations are peer reviewed by external experts and published in various NTP reports or monographs, or peer-reviewed journals. Completed reports are available on the NTP Web site at <http://ntp.niehs.nih.gov/go/reports>.

NTP Resources

The NTP provides a variety of resources for public use, such as databases, atlases and the NTP Archives. The NTP maintains three databases: Chemical Effects in Biological Systems (CEBS) Database, which houses environmental health science study information and data; DrugMatrix[®], a toxicogenomics reference database with accompanying extensive frozen tissue archives and informatics system; and ToxFx, an automated toxicogenomics analysis application. These databases can be found at <http://ntp.niehs.nih.gov/go/datasearch>.

The NTP provides digitized images of a variety of lesions through the Digitized Atlas of Mouse Liver Lesions (<https://www.niehs.nih.gov/research/resources/liverpath/index.cfm>) and the NTP Nonneoplastic Lesion Atlas (<http://ntp.niehs.nih.gov/nnl>).

NTP Archives is a state-of-the-art facility that houses NTP's expansive collection of research specimens and supporting data from NTP studies. To gain access to the archives, submit a request to the NTP Archives (see "Contact Information" section).

NTP Training Programs

The NTP offers postdoctoral training fellowships in a wide range of research and testing activities and literature-based evaluations. The postdoctoral training program funds fellowships at the NTP for up to five years. Information about these programs is available on the NIEHS Web site at <http://www.niehs.nih.gov/careers/research/postdoc-training/index.cfm>.

How to Get Involved

The NTP welcomes feedback from the public and all interested parties. If you would like more detailed information about our work, would like to nominate a substance for evaluation, or have any other concerns, these are the best places to reach us:

The **NTP Office of Liaison, Policy and Review** constantly seeks input from the public and all interested parties. Inquiries and comments are always welcome. Contact this office for general inquiries and requests for information (see "Contact Information" section).

The **NTP Web site** offers searchable access to NTP activities and other information. Data from NTP studies are available with download and search capabilities. The NTP also offers a free online listserv that provides subscribers with email notification of new NTP publications and upcoming events, including advisory committee meetings, peer reviews, expert panel meetings and workshops. To subscribe to this listserv, visit the NTP Web site at <http://ntp.niehs.nih.gov/go/231>.

The NTP welcomes the nomination of substances for evaluation by NTP programs in research and testing, literature-based evaluations or alternative test methods. Nominations can be made through the NTP Web site at <http://ntp.niehs.nih.gov/go/27911>.

Public comments are welcome on all NTP activities. Public comments can be sent directly to the specific NTP program (see "Contact Information" section) or through the NTP Web site at <http://ntp.niehs.nih.gov/go/opensolicitations>.

Central Data Management is a resource for locating substance-specific study information and other NTP documents on request, including the NTP Annual Report, NTP study status reports, fact sheets, background documents for substances nominated to the NTP for study, and copies of draft NTP reports and monographs. Access these reports on the NTP Web site or contact Central Data Management (see "Contact Information" section).

Contact Information

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