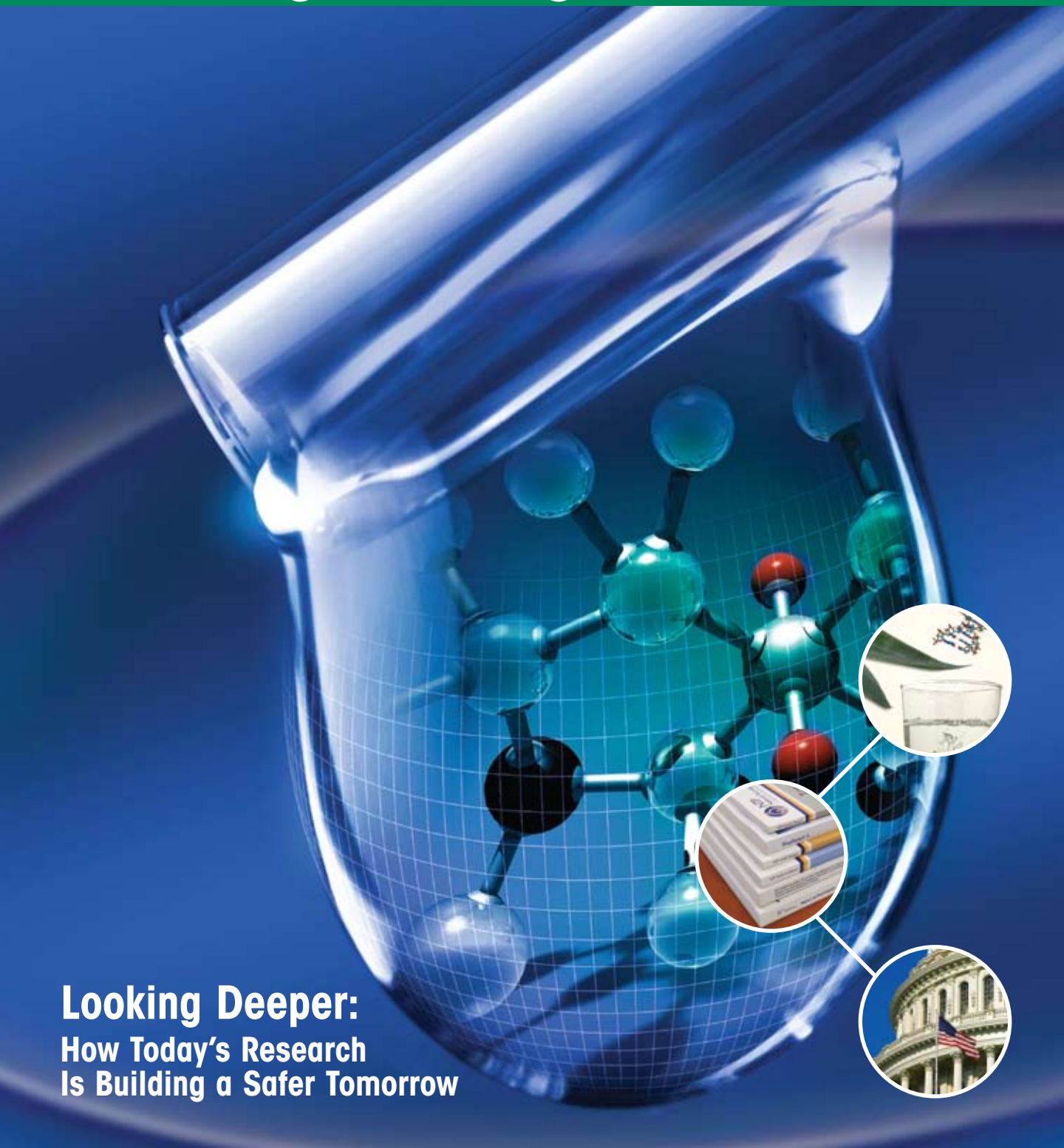
National Toxicology Program

NTP

Current Directions & Evolving Strategies



Looking Deeper:
How Today's Research Is Building a Safer Tomorrow

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Glossary of Acronyms

AIDS	Acquired immune deficiency syndrome
ATSDR/NCEH	Agency for Toxic Substances and Disease Registry/National Center for Environmental Health
AZT	Azidothymidine
BSC	Board of Scientific Counselors
CDC	Centers for Disease Control and Prevention
CERHR	Center for the Evaluation of Risks to Human Reproduction
CPSC	Consumer Product Safety Commission
DNA	Deoxyribonucleic acid
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
HIV	Human immunodeficiency virus
ICCVAM	Interagency Coordinating Committee on the Validation of Alternative Methods
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
NCGC	NIH Chemical Genomics Center
NIOSH	National Institute for Occupational Safety and Health
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PBDE	Polybrominated diphenyl ethers
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonate
RoC	Report on Carcinogens
SACATM	Scientific Advisory Committee on Alternative Toxicological Methods
UV	Ultraviolet

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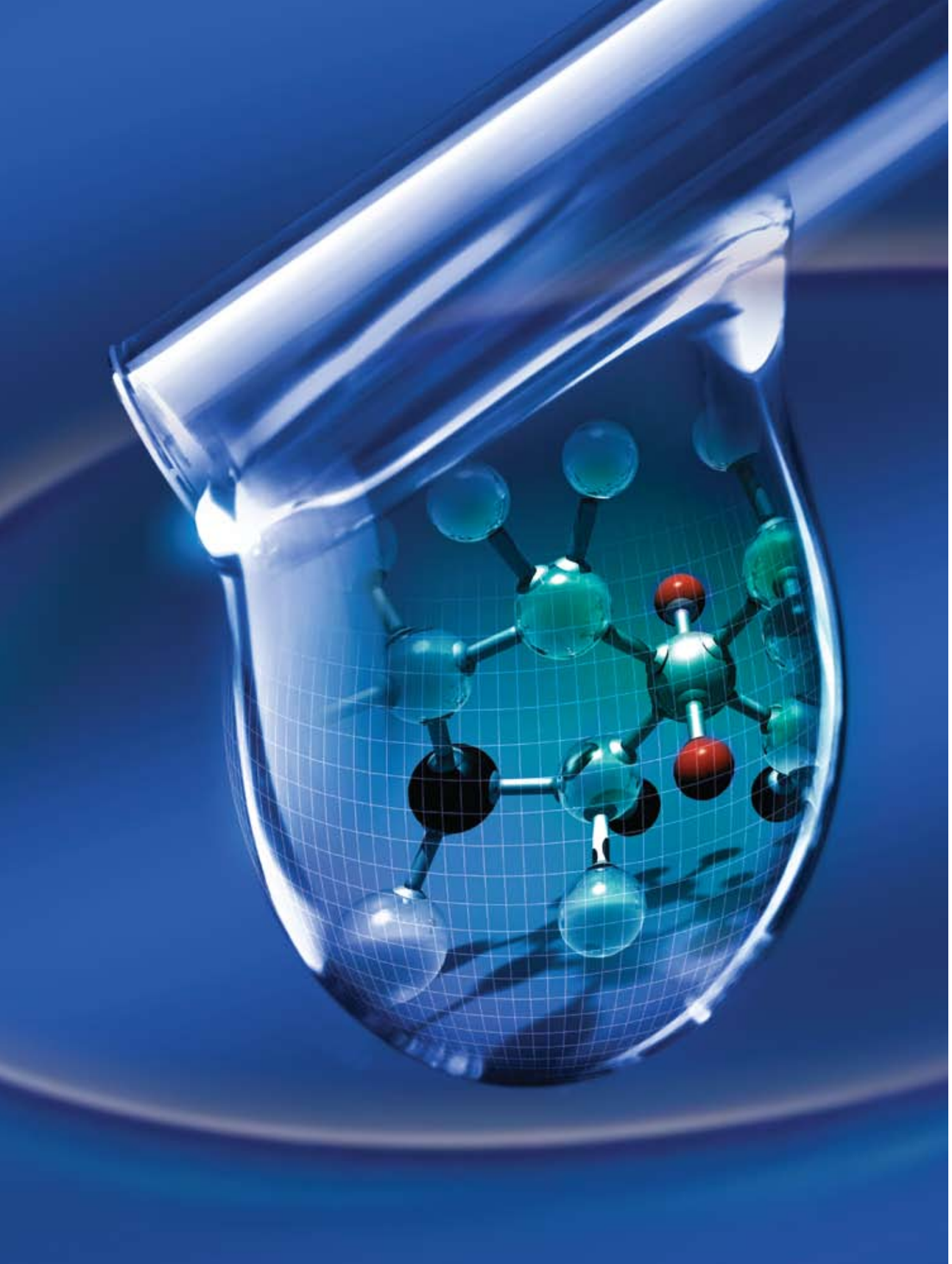


What We Do

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 protection for the public health.

Skin products

Little is known about how many common products applied to the skin react in the presence of UV radiation from sunlight or tanning booths. The study of how UV radiation or sunlight affects the toxicity of these products is called phototoxicology. Our increasing exposure to UV radiation parallels a rise in skin cancer and raises concern about how our lifestyle or the products we use might contribute to its development.

Through its Center for Phototoxicology at the National Center for Toxicological Research (NCTR), the NTP is studying the phototoxicology of ingredients that are commonly used in cosmetics, sunscreens, permanent makeup ink, and other products. Some of these substances are used in topically applied creams or lotions. These ingredients include:

Aloe vera gel found in dietary supplements and cosmetics

Retinyl palmitate used as an "anti-wrinkle" compound

Titanium dioxide and **zinc oxide** present as nanoscale particles in sunscreens

To learn more about the NTP Center for Phototoxicology, visit its Web site at http://www.fda.gov/nctr/science/centers/phototoxicology.

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 nonstick cookware, stain, wrinkle, and water-resistant fabrics, grease-resistant food packaging, and many other products.

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 *in vitro* assays to predict adverse response 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. 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 in the United States. 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 non-brominated 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 Food and Drug Administration (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 the 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 including:

- Multipurpose and miscellaneous use supplements (e.g., goldenseal and milk thistle)
- "Women's health" supplements (e.g., black cohosh)
- Cancer chemoprevention supplements (e.g., green tea and resveratrol)
- "Anti-aging" supplements (e.g., *Ginkgo biloba* and ginseng)
- Weight loss aids and sports supplements (e.g., bitter orange and androstenedione)

Gene therapies

It is now possible to correct defective genes responsible for certain inherited diseases. DNA-based delivery systems hold a great deal of promise for new therapies. The most common approach is to deliver the therapeutic gene to target cells using a vector (carrier molecule), such as a virus that's been altered to carry normal human DNA. But, with new treatment options come new concerns. By their nature, DNA-based therapies pose the risk of unintended gene interactions and the disruption of cell functions.

Currently, gene therapies are experimental. To help ensure the safety of these treatments, the NTP is collaborating with the FDA and sister NIH institutes. Areas currently under study include:

- Biodistribution of the vector in the body
- Potential for reproductive toxicity
- Potential for transmission of altered genetic material to future generations
- Potential for autoimmune disease or immune dysfunction

AIDS therapeutic drugs

Presently, about 40 million people are estimated to be infected with HIV, including approximately 1 million pregnant women who need treatment to prevent mother-to-child transmission of the virus during pregnancy, labor, and delivery. AZT (azidothymidine), the first FDA-approved anti-HIV agent, is known to be toxic, but can be combined with other drugs to permit lower doses that are still effective. The FDA cannot require drug companies to test combinations of AIDS therapeutics, so the NTP is studying commonly used combinations (AZT, neverapine, nelfinavir, and/or 3TC) to characterize any potential toxicity for the offspring. The goal is to better define and minimize the risk of any adverse effects in fetuses or infants exposed to these drugs.

Our Surroundings

Mold

Natural disasters such as hurricanes, new construction methods, and better sealing and insulation in buildings 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 neurologic end points
- Identification of biomarkers of exposure and effect

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

Drinking water

The introduction of chlorination as a way to disinfect drinking water was one of the great public health advances of the 20th century. The NTP has worked with the EPA to ensure safe drinking water by providing scientific data on a variety of chemical byproducts of the chlorination process. The NTP is also providing information from its studies on contaminants in drinking water, including toxins produced by cyanobacteria and algae, nanosilver, and tungsten. This information will help the EPA set limits on acceptable levels of these contaminants in public drinking water supplies.

Food

The NTP is conducting studies of several food constituents and flavorings to help the FDA determine whether their presence in food is harmful. In addition to being a widely used industrial chemical, **acrylamide** is a natural byproduct that forms when carbohydrate-rich foods are fried, baked or roasted at a high temperature. And recently it has been found in foods such as potato chips, French fries, and bread. The discovery of acrylamide in food is a concern because it can cause cancer in laboratory animals at high doses and is a known neurotoxicant, although it is not clear whether acrylamide is harmful at the much lower levels found in food.

The NTP is studying **furan**, a byproduct of some chemical manufacturing processes, but occasionally reported to be found in some 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 exposures.

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 studying the persistence of **tungsten oxide fibers** formed during the processing of tungsten-containing ores in artificial human lung fluids and assessing exposure of workers in tungsten refining and manufacturing operations to these fibers. 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.

The Center for the Evaluation of Risks to Human Reproduction

Evaluation of chemicals that may cause reproductive harm or affect the development of children is a special priority for the NTP. As a consequence in 1998, we established the Center for the Evaluation of Risks to Human Reproduction (CERHR).

CERHR provides scientifically based, uniform health hazard evaluations with three main goals in mind:

- Interpret scientific evidence for the public about the strength of the evidence that a given exposure or circumstance poses a hazard to reproduction, or to the normal development of children.
- Provide regulatory agencies with scientific assessments of data related to adverse reproductive/developmental health effects associated with environmental exposures.
- Identify knowledge gaps to help establish research and testing priorities.

CERHR follows a formal, open process for nomination, selection, and review of chemicals, and public input is encouraged. To date, CERHR has evaluated more than 20 substances, including industrial chemicals, drugs, and chemicals such as phthalates and bisphenol A found in some consumer products. For more information about CERHR, including a list of substances evaluated and CERHR reports, visit the CERHR Web site at http://cerhr.niehs.nih.gov or contact CERHR (for contact information, see page 22).

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 biologic mechanisms (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

The most recent 11th RoC is available on the RoC Web site at http://ntp.niehs.nih.gov/go/roc, or in printed form from the RoC Center (for contact information, see page 22).

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 for the 12th RoC, 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 a much greater number of substances to be tested and providing results useful for human risk assessment.

To make this possible, 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:

Refine traditional toxicology assays.

Develop rapid, mechanism-based, predictive screens for environmentally induced diseases.

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:

1. Predicting human health hazards more precisely
2. Saving time and money
3. Reducing, refining (by causing less pain and distress), or replacing animal use – the 3Rs of alternatives

To help reach those goals, two groups are specifically responsible for 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. Established by the National Institute of Environmental Health Sciences (NIEHS) in 1997 and U.S. law in 2000, 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.

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 that may impact the 3Rs.

In February 2008, NICEATM and ICCVAM unveiled a five-year plan as a blueprint for advancing the 3Rs. Prepared in response to a request from Congress, the plan identifies priority areas for research, development, translation, and validation activities needed to support the regulatory acceptance of alternative test methods. The four areas of highest priority are safety tests for ocular (eye) injuries, dermal (skin) damage, and acute poisoning and tests for biologics such as vaccines. A cornerstone of the plan is forming partnerships with industry and other national and international groups to foster regulatory acceptance and use of alternative methods.

In the past 10 years, ICCVAM has evaluated more than 185 test methods; many of these test methods have now been adopted and are in widespread use around the world, including 18 alternative methods adopted or approved by U.S. regulatory agencies. For the other test methods, ICCVAM has recommended development and validation efforts needed to further characterize or improve their usefulness for regulatory safety testing. For more detailed information about NICEATM and ICCVAM, including test methods that have been approved or are under consideration, visit the ICCVAM/NICEATM Web site at http://iccvam.niehs.nih.gov, or contact NICEATM (for contact information, see page 22).

Nonmammalian Model Systems

The NTP is continuing to explore the use of nonmammalian species as potential alternative models for toxicology testing. *Caenorhabditis elegans (C. elegans)* is a nematode or roundworm about 1mm in length that lives freely in soil and feeds on bacteria. The NTP is currently evaluating *C. elegans* as a study organism for assessing the effects of potential developmental and neurological toxicants on multicellular organisms.

C. elegans holds promise as a practical and efficient test model for several reasons:

- The organism has a very short life cycle (about 3-4 days), is easy and inexpensive to maintain, and genetic variants are easy to obtain.
- A great deal of information is available on *C. elegans*, including its complete genomic sequence, detailed information on its cellular and developmental biology, and maps of all its neuronal pathways.
- The molecular and biochemical changes in *C. elegans* following chemical exposure appear to be similar to those seen in laboratory studies that use rodents.

The use of *C. elegans* is consistent with the NTP's strategy to reduce the number of mammals used in testing. Several toxicology assays for feeding, growth, reproduction, and movement have been developed. While *C. elegans* is still under study, it holds a great deal of promise for faster, more cost-effective toxicology studies.

High Throughput Screening

The NTP is working on toxicology testing methods that will allow researchers to evaluate a far larger number of substances. New, automated processes will use *in vitro* systems to screen hundreds of thousands of substances for biological activity. The information from these studies will help the NTP:

- 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

In February 2008, the NIEHS and the NTP launched a new collaboration with the National Insitutes of Health (NIH) Chemical Genomics Center (NCGC) and the EPA. It leverages the strengths of each group to evaluate a new toxicity testing process that uses high-speed, automated screening robots to test substances using cells and molecular targets instead of laboratory animals. This activity builds upon the NTP's toxicology expertise and data resources, the EPA's computational capabilities, and the NCGC's high throughput technologies. It is anticipated that this collaboration will transform toxicity testing by generating data more relevant for humans, expanding the number of environmental substances that can be tested, and reducing animal use. If successful, this testing process will provide a path toward better protection of public health with regard to identifying harmful substances in our environment. For more information about this exciting new initiative, visit the High Throughput Screening Web site at http://ntp.niehs.nih.gov/go/28213.

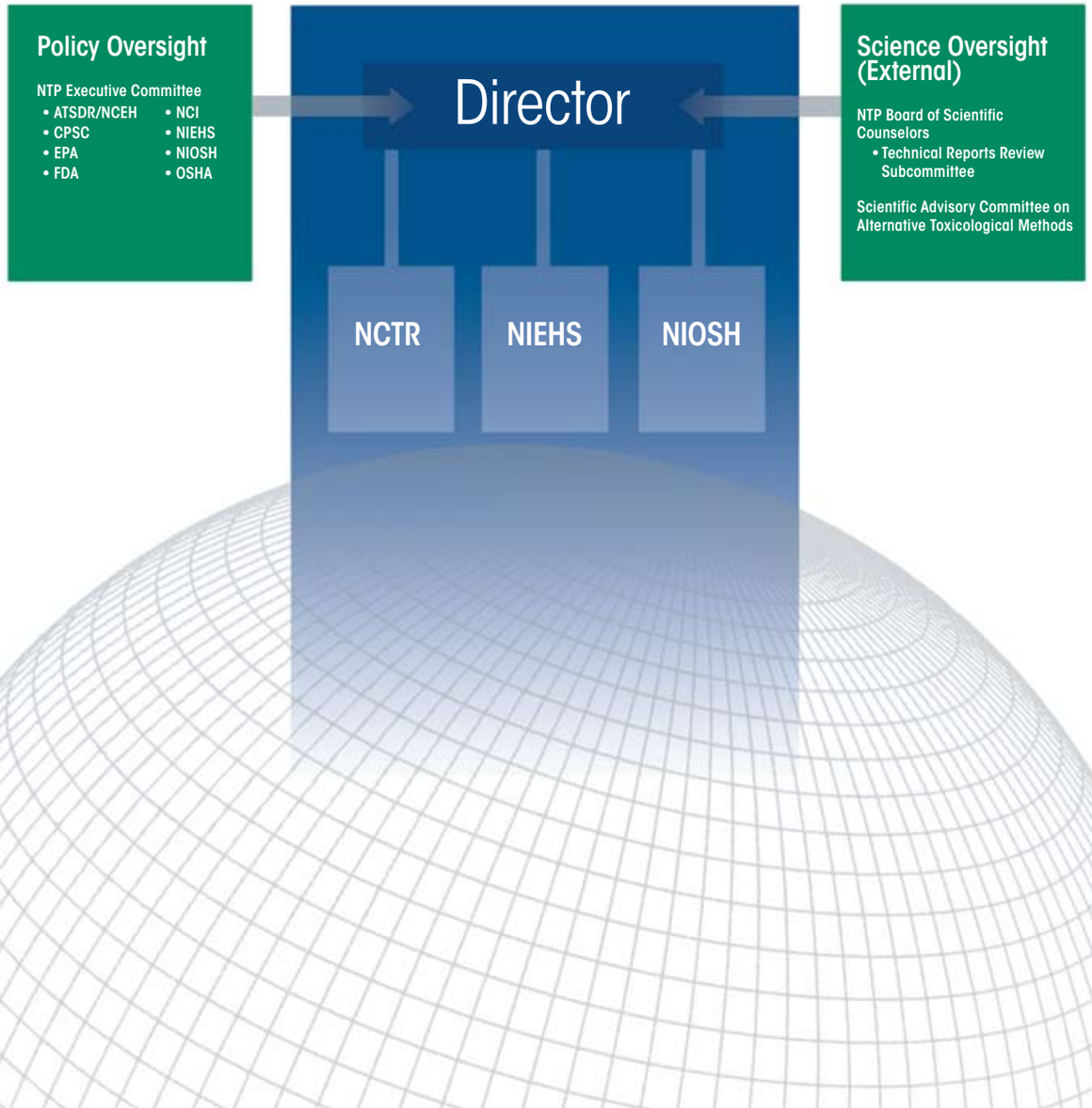
Host Susceptibility

The NTP's Host Susceptibility Program aims to find the genetic reasons why different ages, sexes, ethnicities, and other groups vary in their susceptibility to the effects of toxic substances resulting in disease and morbidity. The program will evaluate known toxicants in different strains of rodents that show broad genetic diversity to see which strains are more or less susceptible.

This research will ultimately lead to greater insight into the genes and pathways involved in toxicity. It also will provide better strategies for predicting the potential toxicity of substances we encounter in our daily lives and for preventing or mitigating their effects.

How We Work

National Toxicology Program



The NTP's Structure

The NTP is made up of three core agencies:

1. The National Center for Toxicological Research (NCTR). The NCTR is part of the Food and Drug Administration (FDA).
2. The National Institute of Environmental Health Sciences (NIEHS). The NIEHS is part of the National Institutes of Health (NIH).
3. The 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.

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 regulatory and research agencies including Agency for Toxic Substances and Disease Registry/National Center for Environmental Health (ATSDR/NCEH), Consumer Product Safety Commission (CPSC), Environmental Protection Agency (EPA), FDA, 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 Department of Health and Human Services (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, and 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 Work

The NTP has a broad mandate to evaluate the toxicity of substances of public health concern. Selection of substances for research and testing is achieved through a nomination review process that is open to all interested individuals and groups. The NTP strives to balance its selection of substances for study and initiates studies as time and resources permit.

NTP studies follow approaches accepted by federal regulatory authorities and generally use rodent models and evaluate substances for a variety of health-related effects, including general toxicity, reproductive and developmental toxicity, genotoxicity, immunotoxicity, neurotoxicity, and carcinogenicity. NTP research and testing activities are carried out in contract laboratories and at the NCTR or NIOSH.

The results from the NTP's studies are published in the peer-reviewed scientific journals and NTP Technical Report series. Completed reports are available on the NTP Web site at http://ntp.niehs.nih.gov/go/reports or in hard copy from Central Data Management (for contact information, see page 22).

The NTP Archives

The NTP Archives houses the nation's premiere resource for toxicology research. The NTP Archives has research specimens and supporting data from over 1,100 NTP studies, as well as a world-class collection of education and training materials on rodent pathology. It is open to all scientists and provides a unique opportunity for researchers to:

- Examine rare or unusual lesions
- Compare disease processes that occur spontaneously or are chemically induced
- Explore the cellular or molecular basis of a pathologic response

To gain access to the archives, submit a request to the NTP Archives (for contact information, see page 22).

NTP Training Programs

The NTP offers postdoctoral trainees opportunities to build their careers by helping to create a safer world. Trainees in applied toxicology and carcinogenesis actively participate as study scientists in the design, conduct, analysis, and reporting of NTP studies. Pathology fellows gain expertise in diagnostic pathology and related techniques, and animal medicine trainees obtain experience in laboratory animal veterinary care. Each program helps ready its trainees for board certification exams. The postdoctoral training programs fund fellowships at the NIEHS for up to five years. Information about these programs is available on the NTP Web site at http://ntp.niehs.nih.gov/go/33381.

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 (for contact information, see page 22).

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

The NTP welcomes the nomination of substances for evaluation by the NTP's research and testing program, CERHR, or RoC or alternative test methods for evaluation by ICCVAM. 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 (for contact information, see page 22) or through the NTP Web site at http://ntp.niehs.nih.gov/go/opensolicitations.

Central Data Management distributes substance-specific study information and other NTP documents on request, including the NTP Annual Report, NTP study status reports, background documents for substances nominated to the NTP for study, and NTP Technical Reports, NTP Toxicity Reports, and NTP Genetically Modified Models Reports. Access these reports on the NTP Web site or contact Central Data Management (for contact information, see page 22).

Contact Information

Primary Contact

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

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For information about NTP studies, go to: http://ntp.niehs.nih.gov

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