

Tox21: Toxicology Testing in the 21st Century

The Toxicology in the 21st Century program, or Tox21, is a unique collaboration between several federal agencies to develop new ways to rapidly test whether chemicals may affect human health.

What is the goal of Tox21?

Since traditional chemical testing using animals is expensive and time consuming, Tox21 is developing alternative methods to measure the ways a chemical might affect human health.¹ Ultimately, these new strategies will help to quickly evaluate thousands of chemicals and inform regulatory decisions about the safety of chemicals.

Tox21 aims to:

- Develop new testing methods to identify if and how a chemical will affect biological processes.
- Expand the number of chemicals that are tested.
- Reduce testing time, effort, and costs.
- Minimize the number of laboratory animals used.

Why do we need to change how we test chemicals?

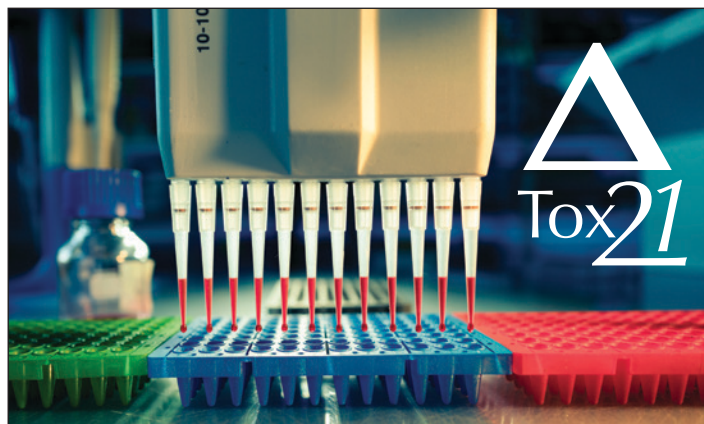
Identifying chemicals that may be hazardous to human health has traditionally relied on animal testing. This approach has taught us much about the potential for chemicals to harm humans, but animal testing is generally slow, expensive, and the results don't always translate easily from animals to humans.

How is Tox21 different from past approaches?

These new approaches move away from animal testing and aim to identify biological pathways that, when altered by a chemical, may lead to an adverse effect or disease in humans. A biological pathway is a series of biochemical steps in a cell that lead to a change in the cell.

Toxicity or disease pathways are biological pathways that may result in an adverse health effect when sufficiently disturbed or compromised. An example of an adverse health effect might be exposure to a chemical that results in the formation of a tumor.

Scientists are working to identify and map as many of these pathways as they can. They will then use these approaches to test whether chemicals interact with various important pathways, in order to predict their toxicity.



Some of the tools scientists are using to predict toxicity include:

- Biochemical-based or cell-based assays, or tests, conducted using robotics.
- Measurements on 3-D models of different human tissues and organs.
- Tests on organisms that are simpler than rats and mice, but still complex, like fish.
- Computational methods to analyze and interpret the data generated, a process called predictive modeling.

What are some of the successes of Tox21?

Tox21 has generated data on pharmaceuticals and thousands of chemicals that we know little about. This allows scientists to develop a better understanding of their interaction with biology. With the public deposit of this data, scientists world-wide are able to evaluate and potentially incorporate the data, models, and methods into regulatory processes.

Specific Tox21 successes:

- Screened more than 10,000 chemicals – including industrial and consumer products, food additives, drugs, and chemical mixtures – in approximately 70 high-throughput tests covering over 125 important processes in the body, generating more than 120 million data points.
- Published more than 200 scientific peer-reviewed articles in approximately 55 journals.
- Identified approximately 2,800 human, rat, mouse, and zebrafish genes in cells and tissues that are particularly useful in studying responses to toxic chemicals.



In ongoing studies, Tox21 scientists are studying changes in levels of ribonucleic acid (RNA) messages, called transcripts, which carry information from our DNA to make proteins necessary for cells to live. Tox21 scientists are measuring the RNAs within a cell, together called the transcriptome, in a low-cost, high-throughput manner. This analysis may help shed light on how chemicals affect the function of our genes using one testing system.

Five-year strategic vision

Tox21 plans to expand the focus of research activities to address the challenges in toxicology. These include:

- Developing an expanded portfolio of alternative testing systems that can predict human toxicity.
- Addressing technical limitations in these testing systems.
- Curating legacy animal toxicity data.
- Establishing scientific confidence in the test systems.
- Refining alternative methods that characterize how chemicals move and distribute in the body using non-animal models.

Ultimately, Tox21 aims to create reliable approaches to better predict whether a chemical might be toxic to humans. Using these alternative methods, scientists are also grouping chemicals with similar toxicity data patterns, as well as similar chemical structure, to predict chemical class toxicity. With these computational models, chemical testing might be reduced significantly in the future.

Who are the federal partners involved in Tox21?

Four government agencies bring their unique expertise, resources, and tools to the Tox21 collaboration:

- [National Institute of Environmental Health Sciences \(NIEHS\)/National Toxicology Program \(NTP\)](#), National Institutes of Health (NIH), U.S. Department of Health and Human Services
- [National Center for Advancing Translational Sciences \(NCATS\)](#), National Institutes of Health (NIH)
- [Center for Computational Toxicology and Exposure \(CCTE\)](#), Office of Research and Development, U.S. Environmental Protection Agency (EPA)
- [U.S. Food and Drug Administration \(FDA\)](#), U.S. Department of Health and Human Services

What is the history of Tox21?

The Tox21 collaboration was formalized in 2008 through a memorandum of understanding (MOU) between the NIH, including the NTP and National Human Genome Research Institute's National Chemical Genomics Center (NCGC, now a part of NCATS), and the EPA's National Center for Computational Toxicology (now part of CCTE). In 2010, the FDA joined the Tox21 collaboration. The Tox21 Consortium recommitted to the collaboration in 2015 by signing a new MOU.



Watch the Tox21 robot in action on the [Tox21 webpage](#).

Access to current information, data, and web applications can be found at <https://tox21.gov>

The National Toxicology Program is an interagency program headquartered at the **National Institute of Environmental Health Sciences** that tests and evaluates chemicals in our environment.

For more information on NTP, go to <https://ntp.niehs.nih.gov>.

¹ Thomas RS, Paules RS, Simeonov A, Fitzpatrick SC, Crofton KM, Casey WM and Mendrick DL. 2018. The US Federal Tox21 Program: A Strategic and Operational Plan for Continued Leadership. ALTEX 35(2):163-168 doi:10.14573/altex.1803011