

## UNITED STATES FEDERAL GOVERNMENT COLLABORATION TOXICOLOGY IN THE 21ST CENTURY (TOX21) TESTING THOUSANDS OF ENVIRONMENTAL CHEMICALS USING NON-ANIMAL METHODS

### Overview

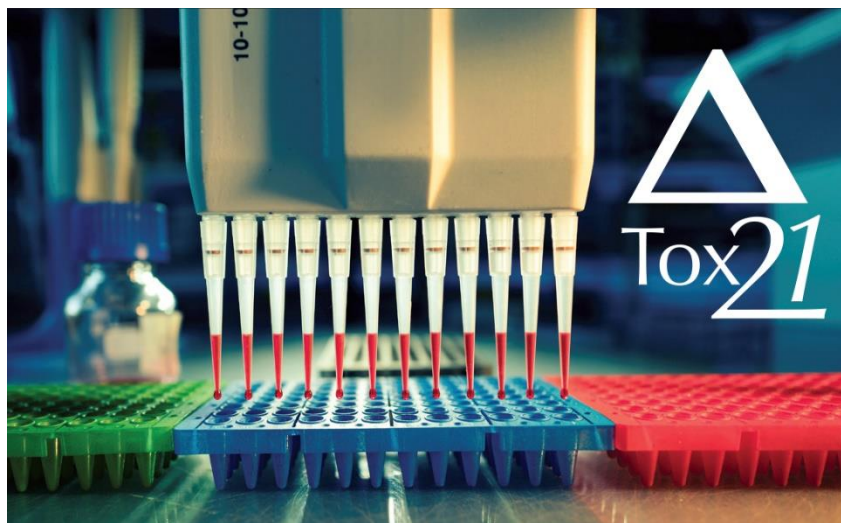
Toxicology in the 21st Century (Tox21) is a US federal research collaboration that is developing alternative, non-animal methods to quickly and efficiently test thousands of chemicals for potential health effects. These approaches use advances in robotics technology to test chemicals for their potential to disrupt processes in the human body, which may lead to negative health effects.

Since its formation in 2008, Tox21 has screened approximately 10,000 chemicals in more than 70 rapid tests called “qualitative high-throughput screening assays”. This includes chemicals used in industrial processes and consumer products as well as food additives, approved and investigational drugs, and chemical mixtures.

### Accomplishments

#### *Tox21 methods inform policy and regulatory decisions made about the safety of chemicals*

- US EPA’s Endocrine Disruption Screening Program (EDSP) is using Tox21 assays as part of a panel of 18 high-throughput screening assays that measure activity across different parts of the estrogen receptor pathway. The results from the panel of 18 tests are incorporated into a computational model to identify chemicals that have the potential for estrogenic activity which could lead to endocrine disruption.



The computational model and assays have been reviewed by a Scientific Advisory Panel and were accepted as alternative tests within the current EDSP Tier 1 testing requirements.

- The European Chemicals Agency’s document “Scenarios to be implemented for searching for potential substances of concern” highlights Tox21 assays that can be used for identifying potential endocrine disrupting chemicals.
- The California Environmental Protection Agency has incorporated Tox21 data in select pesticide assessments, and the Minnesota Department of Health is using Tox21 data for assessing health risks associated with water contaminants.
- The World Health Organization’s International Agency for Research on Cancer (IARC) has used Tox21 data as one area of evidence within a larger framework for assessing the evidence of carcinogenesis.

- Companies are using Tox21 data when they submit European chemical registration dossiers.

#### *Greater acceptance of Tox21 methods by the scientific community*

- Tox21 has published over 200 scientific peer-reviewed articles in approximately 55 journals. Articles were most frequently published in Toxicological Sciences, Environmental Health Perspectives, Chemical Research in Toxicology, and Environmental Science and Technology.
- The top 5 Tox21 articles have been cited an average of more than 100 times.
- Over 80 Tox21 publications have been cited in U.S. National Academy of Sciences Reports.



**Millions of Tox21 data points are publicly available to inform science and decisions**

- Tox21 has screened thousands of chemicals in approximately 70 high-throughput assays covering over 125 important processes in the body and generating more than 70 million data points.
- The Tox21 data is publicly available through the National Library of Medicine's PubChem, the EPA's Computational Toxicology Dashboard and NTP's Chemical Effects in Biological Systems.
- Detailed assay annotations, protocols, and performance statistics are publicly available on the EPA's Computational Toxicology website ([www.epa.gov/comptox](http://www.epa.gov/comptox)) and the NIH tripod web site (<https://tripod.nih.gov/tox21>).

**Strategic Vision for the Next Five Years**

The predominant research activities of the Tox21 collaboration have been developing and applying high-throughput screening to toxicity testing. In 2017, the Tox21 collaborators developed a new strategic vision and operational

plan that broadened the scope of the collaboration to include other emerging toxicology approaches and a focus on incorporating these scientific advances into policy and regulatory decisions.

The primary goal of the Tox21 collaboration remains focused on developing new tools and methods that more efficiently and reliably predict whether a chemical might be toxic to humans. Further development and usage of these approaches will continue to significantly reduce the use of animals for chemical testing and provide data to better protect public health.

Research activities under the new strategic vision and operational plan will be focused on the following areas:

1. Developing and deploying alternative test systems that are predictive of human toxicity and dose response.
2. Addressing key technical limitations of current high-throughput screening systems.
3. Consolidating chemical library management and developing more focused libraries.
4. Curating and characterizing legacy animal toxicity studies for continued comparison to high-throughput screening results.
5. Validating high-throughput assays, integrated assay batteries, computational models, 3-D organ-like model systems, and other emerging Tox21 approaches.
6. Refining and deploying high-throughput methods for characterizing pharmacokinetics to better predict the relationship between target tissue concentrations and external doses of chemicals.

**History**

The Tox21 collaboration was formalized in 2008 through a memorandum of understanding (MOU) between the National Institutes of Health, including the National Toxicology Program (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](#). The Food and Drug Administration (FDA) joined the Tox21 collaboration in 2010.

**More information available – [www.tox21.gov/](http://www.tox21.gov/)**

