

Translational Biomarkers of Neurotoxicity (NeuTox)



Our Mission

The committee's mission is to identify (i) biomarkers for improving the prediction of neurotoxicity and (ii) seizurogenic compounds using microelectrode array (MEA).

Chairs

Public Chair

Dr. Tucker Patterson (US Food and Drug Administration)

Private Chair

Dr. Ruth Roberts (Apconix)

HESI Staff

Jennifer B. Pierson, MPH (jpierson@hesiglobal.org)

Webpage

<https://hesiglobal.org/committee-on-translational-biomarkers-of-neurotoxicity/>

2022 Committee Highlights



Participating Organizations

7 government/regulatory agencies,
11 academic/research institutes, 11 industry



Publications

2 in progress



Outreach

1 oral presentation

IUTOX/EUROTOX 2022

- Symposium presenting minimally invasive biomarkers of central nervous system toxicity. Ruth Roberts, Greet Tuens, Serguei Liachenko, and Tucker Patterson presented, including highlights from the HESI NeuTox Committee work.



Geographic Representation

Belgium, Germany, Japan, Netherlands,
Portugal, Switzerland, United Kingdom,
United States

Working Groups



Translational Biomarkers of Neurotoxicity. Working toward identifying biomarkers of improving the prediction of neurotoxicity and identifying correlations in behavioral, imaging, and neuropathological endpoints. A phase 2 study was launched to validate a set of biomarkers of neurotoxicity.

- **Microelectrode Array Subteam.** Working toward characterizing the predictivity of seizurogenic activity using MEA technology. A final analysis of data generated from a multi-site study is expected by early 2023.



Think Tank Planning Subteam. A subteam was formed to plan a small Think Tank workshop where participants will discuss possible new areas of focus and next steps.

Areas of Focus for 2023

- Complete the phase 2 study to validate biomarkers of neurotoxicity.
- Finalize and publish the analysis of the MEA data for seizure prediction.
- Think tank workshop around related ideas to scope potential future projects.

Strategic Impact Areas

Enhanced efficiency and accuracy in safety assessment practice

The utilization of biomarkers of neurotoxicity may enhance our ability to efficiently and accurately identify neurotoxicity. The NeuTox Committee aims to validate sensitive, reliable, and easily measurable biomarkers of neurotoxicity. Such biomarkers could prove invaluable for drug development research ranging from preclinical studies to clinical trials and may prove to assist with monitoring of the severity or neuronal and CNS damage.



Catalysis of new science

Current biomarkers of neurotoxicity require invasive sampling or behavioral monitoring and can lack in specificity and accuracy. Identifying noninvasive biomarkers of neurotoxicity would result in an improved drug development process as well as a better understanding of chemical toxicity. Additionally, the team is working to characterize predictive power for an *in vitro* assay for use in safety assessment of seizure prediction.



Publications

In Progress

Imam et al. Study to investigate circulating biomarkers that predict central & peripheral neurotoxicity resulting from exposure to trimethyltin (TMT).

Shafer et al. Detection of seizurogenic compounds using neural networks grown on microelectrode arrays; a multi-laboratory, multi-model assessment.



Participating Organizations

Government/Regulatory Agencies

National Centre for the Replacement,
Refinement, and Reduction of Animals in
Research (NC3Rs, UK)

National Institute of Health Sciences (Japan)

Swiss Center for Applied Toxicology

US Army

US Centers for Disease Control and Prevention,
National Institute for Occupational Safety
and Health

US Environmental Protection Agency (EPA)

US Food and Drug Administration (FDA)

Academic/Research Institutes

Albert Einstein College of Medicine

Colorado State University

Duke University

Gunma University

Natural and Medicines Institute (NMI),

University of Tubingen

Newcastle University

Tohoku Institute of Technology

Tokyo, Graduate School of Pharmaceutical Sciences

University of Lisbon

Utrecht University

Virginia Tech

Industry

Apconix

Bristol-Myers Squibb

Fujifilm Cellular Dynamics, Inc.

Cyprotex

GSK

Janssen Pharmaceuticals

Neucyte

Neurocrine Bioscience

Pfizer, Inc.

Takeda Pharmaceutical Company, Ltd.

Wave Life Sciences