

NEUROBEHAVIORAL TESTING & ANALYSIS



Accurate, Objective Answers for Pre-Clinical Trials and Toxicology

When the answers matter, trust Battelle. We offer a complete package of central nervous system (CNS) testing for safety pharmacology, drug development and industrial- and agro-chemicals. Whether you need end-to-end service or targeted support, we can help you move through the regulatory process with confidence.

At Battelle's Neurobehavioral Laboratory, you'll find state-of-the-art facilities for high-throughput animal testing and highly qualified staff with proven experience in the full range of neurobehavioral testing options. We go beyond standard testing batteries to help you solve problems and move your products to market more efficiently. We deliver:

- High-throughput testing of multiple species in a dedicated, GLP-compliant facility

- Fully automated, validated equipment with electronic data capture to expedite data collection and analysis
- Sophisticated analysis of objective, quantitative data to uncover subtle neurobehavioral effects
- Integrated CNS, cardiovascular and pulmonary testing and data collection to streamline your pre-clinical trial programs.





A Comprehensive Suite of Neurobehavioral Services

Tier I Testing (Functional Observational Battery [FOB] or Modified Irwin Test)

Tier I testing provides the initial investigation into potential neurotoxic effects. It utilizes a battery of home cage, handling and open field tests to screen for potential neurotoxicity and includes:

- ~40 tests to assess excitability, neuromuscular coordination, general activity, posture, grip strength, presence of tremors or convulsions, autonomic nervous system function, spontaneous activity, motor activity, arousal, sensory/motor reflex responses and body temperature
- Can be performed in multiple species including rats, mice, dogs non-human primates, and in juveniles and adults

Tier II Testing

More sophisticated behavioral testing is available when Tier I tests trigger concern. The goal of Tier II testing is to characterize the nature of neurotoxicity seen in Tier I tests by quantifying effects on motor function, sensorimotor function and cognitive behavior using complex tasks. These include:

Locomotor Activity Assessment: Motor Monitor System

- Automated motor activity monitoring quantifies multiple parameters of spontaneous locomotor activity, including rearing, grooming, stereotypic behavior, ambulatory activity, exploration of a novel environment and habituation. Testing can be performed in mice and rats including juveniles and adults.
- High-throughput capacity of more than 100 animals per day

Sensorimotor Gating: Acoustic Startle System

- Tests for acoustic startle response, habituation and pre-pulse inhibition to assess sensorimotor gating
- Juvenile and adult assessment in mice and rats
- High-throughput capacity of more than 200 animals per day

Motor Coordination: Rotarod/Accelarod Units

- Assessment of gait, balance, coordination and endurance in juveniles and adults
- High-throughput capacity of more than 100 animals per hour

Gait Analysis: DigiGait Imaging Device

- Sophisticated, multi-parameter gait analysis to assess spontaneous and motivated movement with parameters including gait, automated foot splay, ataxia, swing time, equilibrium, coordination, endurance and more in mice and rats, and for juvenile and adult rodents
- High-throughput capacity of approximately 100 animals per day

Learning and Memory: Morris Water Maze

- Assesses spatial orientation and memory, swimming capacity, learning and reversal learning in juvenile and adult animals
- High-throughput capacity of approximately 70 animals per day

Anxiety and Emotionality: Elevated Plus Maze

- Evaluation of anxiety-like behavior and thigmotaxis in juvenile and adult mice and rats
- Capacity of approximately 20 animals per hour

Tier III Testing

Tier III testing helps uncover the mechanisms underlying neurotoxic effects seen in Tier I and Tier II tests. At Battelle, some of these include:

- EEG with *simultaneous* behavioral monitoring capability
- Special staining for detailed neurohistopathological analysis.

Ready to learn more?

Contact us today to talk with a study design expert.

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Case Studies

Characterization of a Functional Observational Battery

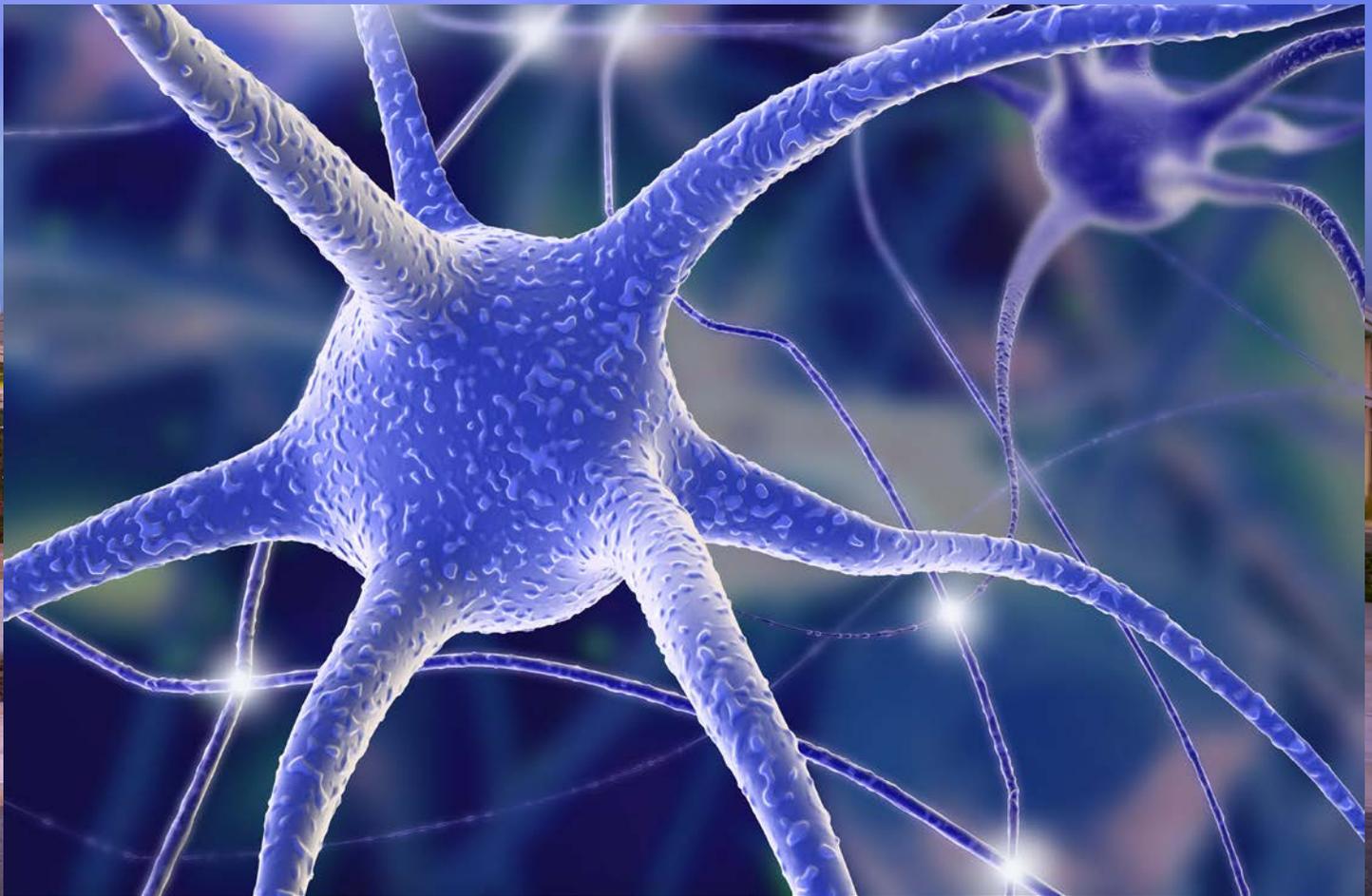
Battelle's Functional Observational Battery (FOB) was optimized across several species including the standard mouse and rat rodent models, as well as non-rodent species including dogs and non-human primates (NHPs). Positive (Amphetamine) and negative (Chlorpromazine) controls have been assessed and validated, with these species showing equivalent results. This versatility provides the capability of conducting FOBs using the most appropriate species for evaluation, for example, NHPs for testing drug safety evaluation of biologic therapeutics.

Validation of CNS Safety Pharmacology Tests

The ICH S7A and S7B guidelines for Safety Pharmacology clearly recognize the need for validated CNS SP testing in addition to the mandated Cardiovascular and Pulmonary SP testing. In response to these guidelines, Battelle developed and validated a comprehensive CNS SP/Neurobehavioral Toxicology program. This program includes the capability for testing rodents, dogs and NHPs. A Tier I screening battery has been developed and validated that consists of nearly 40 tests with elements of the classic Irwin battery, the Environmental Protection Agency Functional Observational Battery (EPA FOB) and the Expanded Clinical Observation scale (ECO). Consistent with ICH S7A and S7B guidelines, as well as with OECD and OPPTS guidelines for chemicals, Battelle also offers several Tier II neurobehavioral tests to quantitate observational results of the FOB and identify drug-induced deficits that are beyond the scope of FOBs. A Tier III test is also available that allows EEG and core temperature telemetry recording from implanted rodents, providing data related to drug-induced changes in EEG power spectra, sleep-waking and subclinical convulsive activity.

Evaluation of Cyanide Intoxication

Potassium cyanide (KCN) affects organ systems with the highest demand for energy such as the central nervous (CN), cardiovascular (CV) and pulmonary systems. Battelle validated a mouse model of oral KCN intoxication to be used for future screening and testing of CN countermeasures. Researchers evaluated sensory, motor, cognitive and behavioral changes for mice receiving an oral dose of KCN as well as controls using an FOB and Tier II CNS testing up to 42 days post-dosing. Histopathology was conducted on select tissues and telemetry was used for CV evaluations and body temperature. Our research demonstrated significant changes in FOB for mice dosed with KCN compared to controls at 30 minutes post-dose and immediate effects related to bradycardia, hypotension and hypothermia with recovery 1 to 3 hours post-dosing. Additional FOB observations and Tier II tests were conducted on Days 2, 7, 14, 28 and 42; while some FOB differences were observed between the groups, Tier II testing showed significant differences between treatment and control groups on Day 1 only. Subsequent studies will now be able to utilize this mouse model to measure the effect of treatments on KCN-induced changes in CV and CNS parameters and determine the efficacy of potential countermeasures.



Ready to learn more?

Contact us today at solutions@battelle.org or 1.800.201.2011 to talk with a study design expert.

Every day, the people of Battelle apply science and technology to solving what matters most. At major technology centers and national laboratories around the world, Battelle conducts research and development, designs and manufactures products, and delivers critical services for government and commercial customers. Headquartered in Columbus, Ohio since its founding in 1929, Battelle serves the national security, health and life sciences, and energy and environmental industries. For more information, visit www.battelle.org.

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