Abstract Proposal – Poster Session

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Tentative Title: **Translational Biomarkers of Neurotoxicity: An ILSI-HESI Consortium Perspective on Identifying and Assessing Biomarkers**

Authors:
Russ Bialecki
David Calligaro
Joe Hanig
David Herr
Thomas Hudzik
Andreas Jeromin
Serguei Liachenko
James Lynch
Merle Paule
Ruth Roberts
William Slikker

Environmental toxicants such as mercury, manganese, pesticides and others; contaminants in designer drugs of abuse such as MPTP; and a vast and growing inventory of industrial chemicals have been linked to neurological damage and a significant number of progressive neurological diseases such as Parkinson's and other CNS degenerative syndromes. In addition, attrition due to neurotoxicity represents a significant issue in all stages of drug development. Traditionally, neurotoxicity testing has relied on composite data sets of functional assessments (e.g., behavior, activity, seizures) and conventional neuropathological evaluations (e.g., organ weights, gross observations, histopathology of neural tissue). Current histopathologic analyses often suffer from constrained spatial sampling and limited translational capability and microscopic findings often do not correlate with the functional and/or neurochemical evidence typically collected. In addition, most neurotoxicants produce very specific cellular changes, restricted to either cellular compartments (e.g., somatic, axonal, or dendritic) and/or cell populations in different regions of the brain with distinct temporal profiles. These toxicities may also be species specific, further confounding the challenge of translation to humans. Thus far, few non-invasive biomarkers for neuropathologies have been qualified.

In late-2012, ILSI-HESI approved a proposal for identifying and assessing new biomarkers of neurotoxicity and a consortium was formed to carry out this investigation. This poster will review

recommendations from a recent ILSI-HESI workshop and highlight new approaches for identifying translational biomarkers in neurotoxicity. These innovations include fluid-based biomarkers and non-invasive imaging and functional measures. Two neurotoxicants, trimethyl tin and MPTP, were used as initial prototypic compounds to help focus a discussion around current best practices, assessment gaps and potential new biomarkers.