March 21, 2006

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Computational Toxicology at the US. EPA: Developing New Tools to Screen Chemicals for Toxic Effects and to Understand the Biological Mechanisms Underlying Dose- and Time-Response Behaviors

An overview will be presented of the organization and activities of the U.S. EPA's National Center for Computational Toxicology (NCCT). The NCCT is charged with integrating modern computing and information technology with molecular biology to improve the EPA's prioritization of data requirements and risk assessment of chemicals. NCCT activities include 3-dimensional structural modeling of proteins to study ligand-receptor interactions, development of high-throughput screens for potential in vivo toxicity, and computational modeling of pharmacokinetic mechanisms (i.e., physiologically based pharmacokinetic [PBPK] modeling) and biochemical mechanisms of toxic action. Much of the work in the NCCT is motivated by developments in systems biology where high-throughput laboratory studies and associated database development are coordinated with development of computational models of biological systems. Understanding health risks potentially associated with exposure to environmentally relevant concentrations of chemicals requires, for example, an understanding of how normal signal transduction and genetic regulatory circuits function and of how toxicants perturb these functions. The expected outcomes of these efforts are more efficient screening of potential toxicants and an improved ability to accurately predict health risks associated with exposures to toxicants in the environment. *This presentation may not reflect official policies of the U.S. EPA.*