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Recent Developments in Toxico-Cheminformatics: Supporting a New Paradigm for Predictive Toxicology

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EPA's National Center for Computational Toxicology is building capabilities to support a new paradigm for toxicity screening and prediction through the harnessing of legacy toxicity data, creation of data linkages, and generation of new high-content and high-thoughput screening data. In association with EPA's ToxCast™, ToxRef DB, and ACToR projects, the DSSTox project provides cheminformatics support and, in addition, is improving public access to quality structure-annotated chemical toxicity information in less summarized forms than traditionally employed in SAR modeling, and in ways that facilitate data-mining and data read-across. The latest DSSTox version of the Carcinogenic Potency Database file (CPDBAS) illustrates ways in which various summary definitions of carcinogenic activity can be employed in modeling and data mining. The DSSTox Structure-Browser provides structure searchability across all published DSSTox toxicity-related inventory, and is enabling linkages between previously isolated toxicity data resources associated with environmental and industrial chemicals. The public DSSTox inventory also has been integrated into PubChem, allowing a user to take full advantage of PubChem structure-activity and bioassay clustering features. Phase I of the ToxCast™ project is generating high-throughput screening data from several hundred biochemical and cell-based assays for a set of 320 chemicals, mostly pesticide actives with rich toxicology profiles. Incorporating traditional SAR concepts into this new data-rich world poses conceptual and practical challenges, but also holds great promise for improving predictive capabilities. *This work was reviewed by EPA and approved for publication, but does not necessarily reflect EPA policy.*