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Using Alternative Approaches to Prioritize Testing for the Universe of Chemicals with Potential for Human Exposure

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One use of alternative methods is to target animal use at only those chemicals and tests that are absolutely necessary. We discuss prioritization of testing based on high-throughput screening assays (HTS), QSAR modeling, high-throughput toxicokinetics (HTTK), and exposure modeling. Concentration-response HTS provides lowest effective concentrations (LEC), the lowest concentrations at which relevant biological perturbations occur. From the HTS data, QSAR models can be developed to provide predicted LEC (pLEC) values for the remainder of a chemical library. HTTK allow us to convert from an LEC to a lowest effective level / dose (LEL) that can be compared directly with exposure estimates. Results of this approach will be illustrated using work on the Human Exposure Universe (HEU), a set of 32K distinct chemicals with evidence for potential human exposure. We focus on the estrogen receptor, for which 1800 chemicals have been assayed using HTS, while the remainder of the 32K have been modeled using a crowd-sourced battery of QSAR models. Exposure estimates have been calculated using far-field and near-field models. Finally, HTTK data for selected chemicals are used to quantitatively compare exposure with activity to set priorities for further testing for estrogenicity.
This abstract does not necessarily reflect Agency policy.