OPERA models for ADME properties and toxicity endpoints

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OPERA is a free and open-source/open-data suite of QSAR models providing predictions on toxicity endpoints and physicochemical, environmental fate, and ADME properties. All OPERA models are built on curated data and standardized QSAR-ready chemical structures. OPERA follows the five OECD principles for QSAR modeling to provide scientifically valid, high accuracy models with minimal complexity that support mechanistic interpretation, when possible. The latest additions to OPERA include models for estrogenic activity, androgenic activity, and acute oral systemic toxicity developed through international collaborative modeling projects. Existing OPERA models are also updated regularly. Recently, the models predicting plasma protein binding and intrinsic hepatic clearance, two of the most important ADME parameters for in vitro to in vivo extrapolation, have been updated with the latest publicly available datasets to improve their predictivity and applicability domain coverage. Furthermore, models predicting physicochemical parameters such as logKow, water solubility, and vapor pressure have been updated to account for highly investigated groups of chemicals such as polyfluorinated substances (PFAS). In addition to predictive models, OPERA provides a tool for standardizing chemical structures, an estimate of prediction accuracy, an assessment of applicability domain, and experimental values when available. Technical and performance details are described in OECD-compliant QSAR model reporting format (QMRF) reports. OPERA predictions are available through the EPA CompTox Chemicals Dashboard and the National Toxicology Program's Integrated Chemical Environment. The OPERA application can also be downloaded from the NIEHS GitHub repository as a command-line or graphical user interface for Windows and Linux operating systems. This project was funded in whole or in part with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C. The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.