

An Open-source IVIVE Workflow Integrating QSAR and PK Models

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Many chemicals in commerce lack safety information. Accurate estimates of in vivo toxicity for these chemicals are needed to inform decisions on safe handling and use as well as accidental exposure responses. To address this need, we have developed an open-source in vitro to in vivo extrapolation (IVIVE) workflow incorporating pharmacokinetic (PK) models with differing complexities. The IVIVE workflow allows prediction of external dose corresponding to a predefined plasma concentration derived from in vitro assay data, or estimation of plasma concentration following a given dose. We developed a set of QSAR models and embedded them in the workflow to provide PK model input parameters such as fraction unbound to plasma proteins, partition coefficients, and Henry's constant. Evaluation of these models' performance yields R² values of 0.742-0.861 compared to experimental measurements. This project was funded with U.S. Federal funds from NIEHS/NIH/HHS under Contract HHSN273201500010C.