

## Curation and Analysis of a Rodent Uterotrophic Database: Insights on Data Quality and Reproducibility

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High-quality *in vivo* reference data are critical to understanding the biological relevance of Tox21 and ToxCast *in vitro* assay data. The rodent uterotrophic bioassay, validated by OECD as a short-term screening test for assessing the estrogenic potential of chemicals, is included in the EPA's Endocrine Disruptor Screening Program as an *in vivo* Tier 1 screen. We performed a comprehensive literature review for uterotrophic bioassays conducted on 1812 chemicals in the EPA ToxCast screening program. Over 700 articles were identified as potentially relevant. Protocols used in each article were evaluated by two independent reviewers for conformity to six predefined criteria based on EPA and OECD uterotrophic test guidelines, with overall compliance determined by consensus. Studies meeting all criteria were considered guideline-like (GL). Information on 442 GL bioassays extracted from 92 articles and containing data for 98 ToxCast chemicals was compiled into a database of uterotrophic outcomes. The database includes data on 42 descriptors, including species/strain, number of animals per group, route of administration, duration of dosing, number of doses, maximum dose tested, lowest effect level, and test outcome. The immature rat model was used for 80% of the reported studies, with 72% of these using injection as the route of administration. Active outcomes were more common in rat models (74% active) compared to mouse models (36% active). Of the 70 chemicals in the database with at least two reported GL uterotrophic bioassays, 18 (26%) had discordant outcomes, many of which may be attributable to differences in study design (e.g. injection vs. oral dosing). This database provides a valuable resource for evaluating the performance of *in vitro* assays that measure key events in the estrogen receptor signaling pathway. *This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No.HHSN27320140003C.*