Towards Refined Use of Toxicity Data in Statistically Based SAR Models for Developmental Toxicity

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QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIPS

BACKGROUND

Finding from ILSI Risk Science Institute (RSI) Working Group*

Statistically based SAR models for developmental toxicity are potentially valuable for prioritizing untested substances for further study. To advance this potential, refined approaches for using toxicity data to inform SAR model training sets are needed. In order to conduct a systematic and informed exploration of data and potential approaches to using the data, a database of adequate design, scope and depth is required.

*See Birth Defects Research Part A 70:902-911, 2004

PROJECT GOAL

Bring toxicologists, SAR modelers, and database developers together to design a prototype database that, when populated, could serve as a starting point to explore biologically-based, objective and transparent approaches for utilizing the data.

KEY FEATURES OF PROTOTYPE DATABASE

- Compiles published data from oral route, C-section studies in the rat
- Captures study design information and assesses compliance with testing guidelines
- Captures data in a detailed, objective, transparent way, including:
  - offspring survival, growth, and morphology data
  - maternal toxicity data (survival, body weight, clinical signs)
- Captures data on discrete endpoints, which:
  - avoids “summary calls” from the study
  - provides flexibility to “lump” or “split” groups of endpoints
- Captures data as reported in study, with space for additional expert comment
- Adopts internationally harmonized terminology (“Terminology of Developmental Abnormalities in Common Laboratory Mammals” Wise et al. Teratology 55:249-292, 1997)

PLANNED NEXT STEPS

- Populate the database with data from at least one species
- Add chemical structure information and structure searching capability
- Continue interdisciplinary collaboration to develop enhanced approaches for using such data (e.g., to inform SAR model training sets, to complement in vitro and genomics data sets, etc.)
- Promote collaboration/synergy with other standardized data models and efforts (e.g., ToxML,ToxRef, MARTA/MTA Historical Control database, FDA-Leadscope efforts)

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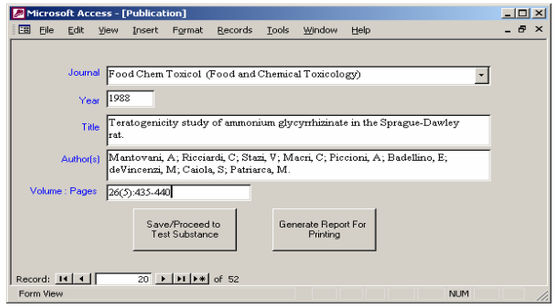

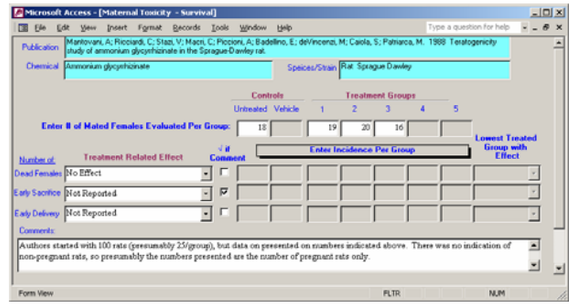

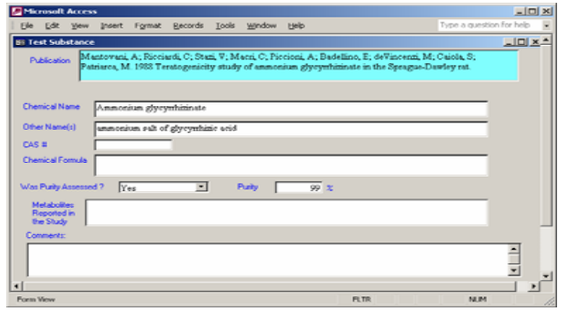

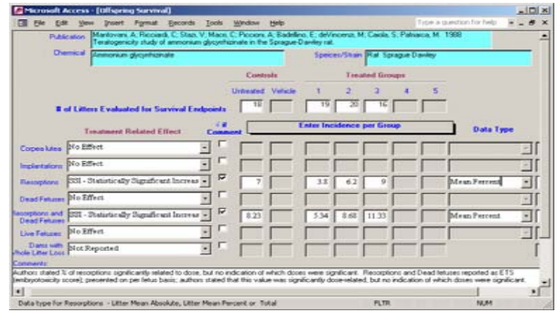

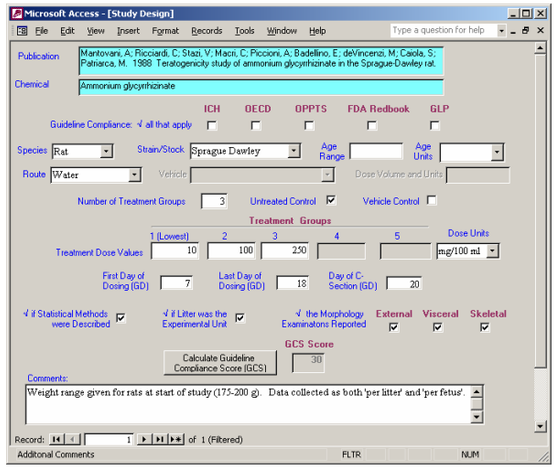

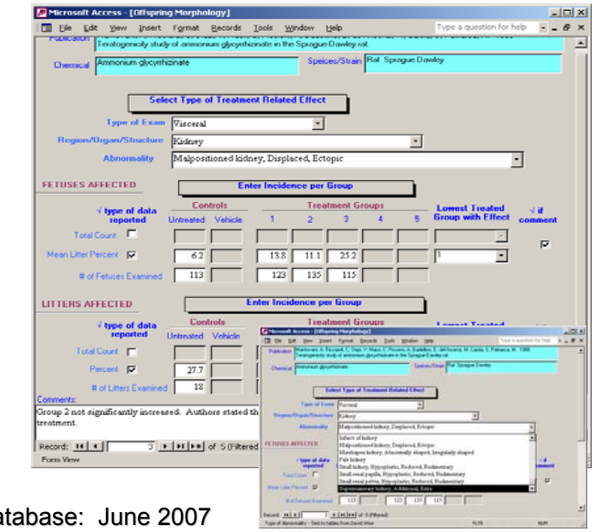

Anticipated release of publicly available prototype database: June 2007