"Profiling the Reproductive Toxicity of Chemicals from Multigeneration Studies in the Toxicity Reference Database (ToxRefDB)"

This manuscript by Martin et al. was published April 2009 in *Toxicological Sciences* (http://toxsci.oxfordjournals.org/cgi/reprint/kfp080), by EPA's Office of Research and Development, and is the third publication of data from EPA's Toxicity Reference Database (ToxRefDB). It presents toxicity profiles on over 300 chemicals based on results from the multigeneration reproduction study. Currently, ToxRefDB primarily consists of toxicity studies submitted as part of the registration process for conventional pesticide actives. In the future, ToxRefDB will be expanded to a broader range of chemical categories and uses. This Martin et al. paper focuses on the reproductive toxicity endpoint selection for predictive modeling. ToxRefDB serves as a primary source of in vivo toxicity data for EPA's ToxCast™ research program (http://www.epa.gov/ncct/toxcast/) in predictive toxicology. ToxCast and ToxRefDB were developed as part of EPA's commitment to modernize toxicity testing, and are committed to transparency and public access. ToxRefDB data will be made public through scientific papers, and the EPA ToxRefDB website (http://www.epa.gov/ncct/toxrefdb/). The ToxCast program's success will lead to more efficient and effective assessment and management of the hazard, and ultimately the risks of chemicals when these results are evaluated in an appropriate human exposure context. An ancillary but important benefit of this approach may be a reduction in the use of animal testing, while at the same time increasing the numbers of chemicals that can be evaluated.

A thorough quality control (QC) process is in place for ToxRefDB, and the accuracy of data entered so far has exceeded 99%. The QC review process is ongoing, and includes both internal and external peer review. ToxRefDB is an actively growing database that continues to add new and updated information. While pesticide toxicity data currently predominates in ToxRefDB, the database is being expanded to a broader range of chemical categories and uses. ToxRefDB web address: http://www.epa.gov/ncct/toxrefdb/

Finally, the underlying data represented in ToxRefDB has been evaluated by the Agency in prior pesticide registration decisions, and the presence of effects in high-dose animal studies do not translate directly into significant human risk stemming from registered uses of the pesticide. It should be noted that the EPA uses animal toxicology studies, like those entered into ToxRefDB, as well as other sources of information such as effects on wildlife populations, mechanisms of action, use patterns, environmental fate and persistence, food residue levels, and human exposure potential in its determinations to register pesticides and to establish acceptable levels of pesticide residues for uses in the United States. Full descriptions of the available data and conclusions as to the potential for the pesticides to cause harm to humans or the environment, risk mitigation measures, and the regulation of pesticides can be found at the U.S. EPA Office of Pesticide Programs websites: http://www.epa.gov/pesticides/regulating/index.htm; http://www.epa.gov/pesticides/reregistration/status.htm; http://www.epa.gov/oppsrrd1/registration_review/; http://www.epa.gov/oppsrrd1/reregistration/index.htm

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