

Reg Tox Pharmacol 53(2):150-5
March, 2009

The transgenic mouse assay as an alternative test method for regulatory carcinogenicity studies – Implications for REACH

Wells, M.Y., and **E.S. Williams**

REACH, an EU regulation that requires the submission of safety data in support of the protection of human and environmental health, mandates that registration should be achieved with the minimum amount of animal testing possible. Under REACH, a two-year carcinogenicity assay may be required for certain chemicals produced at >1000 metric tonnes per year. In addition, some chemicals that are found to be genotoxic will also require testing. Alternative methods have been explored in an attempt to improve the predictivity of this bioassay as well as to reduce the number of animals used for such testing. This research has focused on the use of transgenic/knockout mouse models. Study results from selected models indicate that they are useful in hazard identification, even if they are not entirely suitable for risk assessment on their own. Carcinogenic hazard assessment can be greatly enhanced and animal use reduced if the traditional two-year rat bioassay is combined with a well conducted transgenic mouse assay. Importantly, the use of transgenic animals to supplement a traditional two-year carcinogenicity study may help reduce the number of false negatives, one of the unstated goals of REACH via the precautionary principle.

Keywords: REACH, Carcinogenicity, Transgenic mice, Alternative models, High production volume chemicals, Genotoxicity, ICH, NTP, HESI, Two-year rodent bioassay