

ICCVAM Review of the *In Vivo* Rabbit Dermal Corrosivity Test

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) has evaluated four *in vitro* test methods for assessing the dermal corrosivity potential of chemicals and chemical mixtures—Corrositex[®], EpiDerm[™], EPISKIN[™], and the rat skin Transcutaneous Electrical Resistance (TER) assay (ICCVAM 1999, 2002). ICCVAM recommended that these assays be used in a weight-of-evidence approach that is part of an internationally harmonized, integrated, and tiered testing scheme. In the weight-of-evidence approach, positive *in vitro* corrosivity responses do not generally require further testing and can be used for classification and labeling whereas negative *in vitro* corrosivity responses should be followed by *in vivo* dermal corrosion/irritation testing. This recommendation was based, in part, on the 12% to 21% false-negative rates of these *in vitro* assays. Because a false-negative result could cause irreversible and permanent injuries to persons or animals exposed to a corrosive chemical that was not labeled with the proper hazard warning, this level of error was not considered to provide adequate protection for public health and safety. ICCVAM also recommended that for certain testing circumstances (e.g., to meet United Nations transportation Packing Group classification requirements; UN 2003) Corrositex[®] “could be useful as a stand-alone assay for evaluating the corrosivity of acids, bases, and acid derivatives”.

Public comments received in response to these ICCVAM recommendations led ICCVAM to evaluate the likelihood of under-predicting a dermal corrosivity hazard when using the traditional *in vivo* rabbit skin test. With assistance from ICCVAM member agencies, the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), which provides operational and scientific support for ICCVAM and ICCVAM-related activities, has identified and compiled relevant study results for analysis. The current database now includes results on 171 test substances. However, there are potential limitations on the usefulness of this database based on the fact that some of the data were generated with only one or two animals, and some data were not generated in accordance with GLPs. Initial analyses on this database indicate that the *in vivo* test has an estimated under-prediction (“false negative”) rate that ranges between 1% and 10% and the greatest under-

prediction rate occurs for weak corrosives (i.e., test substances that produce a corrosive response in only one out of three tested animals.) ICCVAM has also requested *in vivo* corrosivity study data and results from federal agencies and the public (68 FR 42067, July 16, 2003). Once these additional data are reviewed and analyzed, they will be considered for possible inclusion into the database and the under-prediction rate analysis will be refined accordingly. ICCVAM will prepare a manuscript on this evaluation for peer reviewed publication. Once the manuscript is accepted for publication, it will be made available to the public through this web site and reprints will be available upon request.

References

1. NIEHS. 2003. NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) Request for Existing Dermal and Ocular Irritancy Chemical Test Data from Animal and Human Studies Using Standardized Testing Methods. *Federal Register* 68:42067. Available: <http://iccvam.niehs.nih.gov/methods/epiderm.htm> [accessed 20 February 2004].
2. ICCVAM. 2002. Evaluation of EPISKINTM, EpiDermTM (EPI-200), and Rat Skin Transcutaneous Electrical Resistance (TER): *In Vitro* Test Methods for Assessing Dermal Corrosivity Potential of Chemicals. NIH Publication No. 02-4502. Research Triangle Park, NC: National Institute of Environmental Health Sciences. Available: <http://iccvam.niehs.nih.gov/methods/epiderm.htm> [accessed 20 February 2004].
3. ICCVAM. 1999. Corrositex[□] An *In Vitro* Test Method for Assessing Dermal Corrosivity Potential of Chemicals. NIH Publication No. 99-4495. Research Triangle Park, NC: National Institute of Environmental Health Sciences. Available: <http://iccvam.niehs.nih.gov/methods/corrode.htm> [accessed 20 February 2004].
4. UN. 2003. Globally Harmonized System of Classification and Labelling of Chemicals (GHS). [ST/SG/AC.10/30]. United Nations, New York and Geneva. Available: <http://www.unece.org/trans/danger/publi/ghs/officialtext.html> [accessed 20 February 2004].