UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 27, 1999

Dr. William S. Stokes
National Institute of Environmental
Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Dear Dr. Stokes:

I am responding to the letter on Corrositex® from Dr. Ken Olden to EPA Administrator Carol Browner concerning the report and recommendation from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). As with the first test method reviewed by ICCVAM, this one is very clearly presented, and positions espoused are carefully justified.

The EPA test method group, including members from the pesticides, toxic substances and research and development offices, met on December 15 to consider the acceptability of Corrositex®. Although not represented at the meeting, the Office of Solid Waste has already approved the test for the optional identification of hazardous wastes. The Office of Research and Development also concluded that the method could be used in accordance with the recommendations in the ICCVAM report.

The pesticides and toxics programs currently have a harmonized test guideline for dermal corrosives and irritants that is performed in rabbits; this guideline is in agreement with that utilized by OECD. The guideline states that if a chemical has a pH of $\leq 2$ or $\geq 11.5$, the in vivo test need not be conducted. If in vivo test data are not also submitted, the pesticide program uses pH information to classify agents as corrosives (toxicity category I).

The data base on Corrositex® has both strengths and weaknesses. It is a benefit that the method is simple to use and less expensive than the animal test. It is also an in vitro test, which obviates the need for animal testing for potentially corrosive materials. However, there is a high percentage of chemicals that do not qualify for the test, which greatly limits its applicability to the universe of chemicals. This finding is somewhat counterbalanced by the fact that of the substances evaluated, relatively few are corrosive in the pH range where the test does not qualify. We are also concerned that there is a lack of data for many classes of materials, including pesticides and mixtures. Use of pH extreme of a chemical ($\leq 2$ and $\geq 11.5$) already picks up most of the materials testing positive in Corrositex®, although it is noted that the test is somewhat better than pH alone. Both measures have a rather high false positive rate.

The Office of Pesticide Programs will accept data on Corrositex® for registration purposes under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) with certain restrictions. Non-qualifying chemicals need to be tested in vivo in at least one rabbit. Qualifying chemicals that test negative would also require in vivo testing. Materials testing positive in Corrositex® would be classed in toxicity category I. However, if there is other information on the chemical that suggests that the material is not corrosive to the skin (e.g., dermal sensitization test results), rabbit testing may be needed before a decision is made about dermal irritation hazard classification.

The Office of Pollution Prevention and Toxics (OPPT) only rarely requires that dermal corrosion and irritation studies be conducted on new or existing chemicals under the Toxic Substances Control Act (TSCA). OPPT has received in the new chemicals program (TSCA §5) about 6000 skin corrosion/irritation tests over the last 20 years. In recent times, it has been receiving annually about 12 Corrositex® tests. For testing conducted under TSCA §4 Enforceable Consent Agreements or TSCA §5(e) Consent Orders there is a role for Corrositex® within a tiered evaluation approach to identify corrosive agents. Qualifying positives would need not undergo animal testing, while qualifying negatives and non-qualifying chemicals would need to be tested in the rabbit as described above.

The newly-approved OECD harmonized hazard classification for dermal corrosion and irritation includes a tiered evaluation of effects, including the use of validated and approved screens. Corrositex® could be applied within this context for EPA regulatory programs under FIFRA and TSCA.

Significant work has been achieved with alternatives to the dermal corrosion and irritation test beyond that with Corrositex® per se (e.g., TER assay). EPA supports the recommendation made by the ICCVAM peer review group that further inquiry should be given to their possible incorporation into the testing of dermal effects.

Sincerely,

Richard D. Hill, for

Steven K. Galson, M.D., MPH
Director, Office of Science Coordination & Policy

cc: S. Wayland, J. Aidala, S. Johnson, J. Andersen, A. Lindsay, V. Turner, F. Sanders, S. Sterling, D. Keehner, M. Stasikowski, R. Schmitt, J. Jones, L. Rossi