DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institute of Environmental Health Sciences (NIEHS); Corrositex®: An In Vitro Test Method for Assessing Dermal Corrosivity Potential of Chemicals, Report Now Available

SUMMARY: The report entitled ''Corrositex®: An *In Vitro* Test Method for Assessing Dermal Corrosivity Potential of Chemicals,'' NIH Publication 99–4495, is now available and may be obtained as described in this notice. The report describes the results of an independent peer review evaluation of the validation status of Corrositex® that was conducted on January 21, 1999 **Federal Register** 63 FR 57303, October 27, 1998). Corrositex® was proposed by In Vitro International, Inc., Irvine, CA, as an alternative toxicological test method for assessing the dermal corrosivity potential of chemicals and chemical mixtures. The review was coordinated by the Interagency Coordinating Committee on the Validation of Alternative methods (ICCVAM) and the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). The review was sponsored by NIEHS and the NTP.

Background

Pub. L. 103–43 directed NIEHS to develop and validate alternative methods that can reduce or eliminate the use of animals in acute or chronic toxicity testing, establish criteria for the validation and regulatory acceptance of alternative testing methods, and recommend a process through which scientifically validated alternative

methods can be accepted for regulatory use. Criteria and processes for validation and regulatory acceptance were developed in conjunction with 13 other Federal agencies and programs with broad input from the public. These are described in the document ''Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the Ad Hoc Interagency Coordinating Committee on the Validation of Alternative Methods,'' NIH publication 97–3981, March 1997, which is available on the Internet at http://ntp-server.niehs.nih.gov/htdocs/ICCVAM/iccvam.html. ICCVAM was subsequently established in a collaborative effort by NIEHS and 13 other Federal regulatory and research agencies and programs. The Committee's functions include the coordination of interagency reviews of toxicological test methods and communication with stakeholders throughout the process of test method development and validation. The following Federal regulatory and research agencies and organizations participate in this effort:

Consumer Product Safety Commission
Department of Defense
Department of Energy
Department of Health and Human Services
  Agency for Toxic Substances and Disease Registry
  Food and Drug Administration
  National Institute for Occupational Safety and Health/CDC
  National Institutes of Health
  National Cancer Institute
  National Institute of Environmental Health Sciences
  National Library of Medicine
Department of the Interior
Department of Labor
  Occupational Safety and Health Administration
Department of Transportation
  Research and Special Programs Administration
Environmental Protection Agency

ICCVAM determined that there was sufficient information available to merit an independent scientific peer review evaluation of the Corrositex® test method. Peer review is an essential prerequisite for consideration of a method for regulatory acceptance. The peer review panel was charged with developing a scientific consensus on the usefulness and limitations of the test method.

Description of the Method

Corrositex® is an *in vitro* method used to determine the dermal corrosive potential of chemicals and chemical mixtures. Corrositex® is based on the ability of a corrosive chemical or chemical mixture to pass through, by diffusion and/or destruction/erosion, a biobarrier and to elicit a color change in the underlying liquid Chemical Detection System (CDS). The biobarrier is composed of a hydrated collagen matrix in a supporting filter membrane, while the CDS is composed of water and pH indicator dyes. Test chemicals and chemical mixtures, including solids and liquids, are applied directly to the biobarrier. The time it takes for a test chemical or chemical mixture to penetrate the biobarrier and produce a color change in the CDS is compared to a classification chart to determine corrosivity/noncorrosivity and to identify the appropriate U.S. Department of Transportation (U.S. DOT) packing group. Chemicals are prescreened for compatibility with the assay by directly applying the test chemical or chemical mixture to the CDS; if a color change is not induced, then the test chemical or chemical mixture does not qualify for testing with this assay. The U.S. DOT currently accepts the use of Corrositex® to assign subcategories of corrosivity (packing groups) for specific chemical classes for labeling purposes according to United Nations (UN) Committee of Experts on the Transport of Dangerous Goods guidelines.

Conclusions and Recommendations

The peer review panel concluded that for specific testing circumstances such as that required by the U.S. DOT, Corrositex® is useful as a stand-alone assay for evaluating the corrosivity or noncorrosivity of acids, bases, and acid derivatives. In other testing circumstances, and for other chemical and product classes, the peer review panel concluded that Corrositex® may be used as part of a tiered assessment strategy. In this approach, negative responses must be followed by dermal irritation testing, and positive responses require no further testing unless the investigator is concerned about potential false positive responses. The panel recommended that in either testing strategy, an investigator may conclude that confirmation testing is necessary based on consideration of supplemental information, such as pH, structure-activity relationships, and other chemical and/or testing information. These conclusions are based on the assumption that the method will be performed in accordance with the following peer review panel recommendations:

1. The protocol should incorporate the following:

- It should be explicitly stated that the biobarrier should be allowed to harden on a level surface and to cool overnight before use.
- Guidance should be provided on how to evaluate an aberrant value, even though replicate variability has been shown to be very low.
- The IVI Corrositex® Data Sheets provided with the test kit should contain a provision for recording the performance of the positive and negative controls. This information should be used to determine the suitability of the test results.
- Description of the test protocol would benefit from the addition of a flow diagram illustrating the steps in the procedure.

2. In future studies, compliance with Good Laboratory Practice (GLP) guidelines and inclusion of quality control procedures would improve data quality and credibility.

3. Positive and negative control values should be reported concurrently with each assay to demonstrate that the test is working properly.

4. Laboratories unfamiliar with conducting the test should obtain appropriate training and conduct tests with test reference chemicals before undertaking any testing of unknown chemicals and chemical mixtures.

5. Prior to the use of Corrositex®, pH testing should be conducted, given the ease and cost effectiveness of conducting a pH test. Such information could be used in the future to re-evaluate the agreement between pH and Corrositex® in identifying corrosivity.

The peer review panel also concluded that Corrositex® offers advantages with respect to animal welfare considerations. Corrositex®, when used as a stand-alone assay for some testing applications such as transportation purposes, can replace the use of animals for corrosivity testing of qualified chemicals in some chemical classes. When used as part of a tiered testing strategy for corrrosivity, there is a reduction in the number of animals required because positive results usually eliminate the need for animal testing, and when further testing in animals is determined to be necessary, only one animal is required to confirm a corrosive chemical. Corrositex® also provides for refinement in that most of the chemicals that are identified as negative by Corrositex® or nonqualifying in the detection system are unlikely to be corrosive when tested in the in vivo test for irritation potential.

The peer review panel's report was accepted by ICCVAM and has been forwarded to Federal agencies for their determination of the regulatory

acceptability and applicability of the test method according to their statutory mandates.

Obtaining the Report

The full report contains 238 pages and includes the results of the independent peer review evaluation and supporting documentation, including the original test method submission and supporting data evaluations conducted by NICEATM.

To receive a copy of the report, please contact NICEATM at PO Box 12233, MD EC–17, Research Triangle Park, NC 27709 (mail), 919–541–3398 (phone), 919–541–0947 (fax), or iccvam@niehs.nih.gov (email). The report will also be available on the ICCVAM/NICEATM website at http://iccvam.niehs.hih.gov.

Dated: June 15, 1999.

Samuel H. Wilson,

Deputy Director, National Institute of Environmental Health Sciences.

[FR Doc. 99–15725 Filed 6–18–99; 8:45 am]

BILLING CODE 4140–01–M