

**RECEIVED**

NOV 29 1999

NTP Interagency Center for the
Evaluation of Alternative Test MethodsAgency for Toxic Substances
and Disease Registry
Atlanta GA 30333

NOV 24 1999

William S. Stokes, D.V.M.
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, North Carolina 27709

Dear Dr. Stokes:

I am responding to Dr. Kenneth Olden's June 18 letter to Dr. Barry Johnson regarding the report, *Corrositex: A Test Method for Assessing the Dermal Corrosivity Potential of Chemicals*. Dr. Johnson retired in December, 1998, and I have since been appointed as his successor as Assistant Administrator, ATSDR. This report was prepared by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and sent to the Agency for Toxic Substances and Disease Registry (ATSDR) for comments. Specifically, ATSDR was asked to inform the ICCVAM of any applications the Corrositex Assay may have at ATSDR, as well as steps taken to inform agency scientists and others about the availability of the report.

Through our representative Dr. William Cibulas, ATSDR has provided ongoing input to the development of validation criteria for alternative test methods. The March, 1997 ICCVAM report on this subject matter provides outstanding guidance for offerors of alternative methods and the ICCVAM is to be commended for the vision used in putting in place a scientifically credible process to accomplish this task. We were also pleased that Dr. Buck Grissom from our agency was able to serve on the Corrosivity Working Group and that other agency scientists are participating on various subject matter working groups as well.

At this time, we have completed our review of the Corrositex Assay peer review report and the conclusions of the ICCVAM Corrosivity Working Group that were provided in your package and we have noted the subsequent concurrence of the full ICCVAM. As an outcome, ATSDR agrees with the conclusion that the Corrositex Assay, when used in accordance with the panel report, can be used effectively for assessing dermal corrosion potential. Furthermore, we note that the panel concluded that the Corrositex Assay should be used as part of a tiered testing strategy, such as the one endorsed by the Organization of Economic Cooperation

and Development (OECD). In this approach, positive responses do not generally require further testing, while negative responses would usually be followed by in vivo dermal irritation/corrosion testing. We also note the limitations identified by the panel, and that some corrosive chemicals and mixtures do not qualify for testing with Corrositex. Specifically, the excluded chemicals do not cause a color change in the chemical detection system. Further, we agree with the panel's conclusion that the Corrositex Assay offers several advantages with respect to animal welfare as outlined in the June 14 letter from the ICCVAM Co-Chairs Dr. Stokes and Dr. Hill to Dr. Olden. These considerations are essential to the goals of the ICCVAM.

As you are aware, ATSDR has a mandate to assure the initiation of a program of research to fill research needs for the most hazardous substances found at waste sites. To date, the agency's Substance-Specific Applied Research Program (SSARP) has identified 188 priority data needs for its top 50 substances, often including the need to assess dermal toxicity. The availability of the Corrositex Assay as a valid test method to assess dermal corrosivity will be shared with the program staff responsible for administering that program and it will be shared with various ATSDR public and private sector partners who work closely with ATSDR to fill this research agenda. Further, as a research and service organization charged with addressing the public health concerns of citizens potentially exposed to a variety of environmental contaminants, we will share the availability of the Corrositex Assay broadly with other ATSDR scientists.

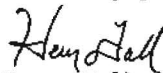
In closing, we strongly support the goal of the ICCVAM to coordinate the validation of proposed new test methods throughout the federal and scientific communities. We find ourselves in a solid position to defend new test methods, such as the Corrositex Assay, when we are assured that the methodology meets the validation criteria established by the ICCVAM and has passed the rigors of scientific peer review. Of equal importance to this process, however, are the views of the regulatory community. Without regulatory acceptance, proposed alternative methods are not likely to gain favor in the scientific community because the regulators will still require the results from traditional tests. This affects organizations such as ATSDR who have partnered with the Environmental Protection Agency (EPA), for example, to develop test rules to fill ATSDR testing needs under the Toxic Substances Control Act. Thus, in this case, if EPA chooses not to accept the Corrositex Assay as part of a tiered testing strategy to assess dermal corrosivity potential, ATSDR would not be in a position to recommend to our research partners that they use this new methodology that possibly reduces, refines, or replaces the need for some animal testing. Thus, we look forward with keen interest to your report on the acceptance status of the

Page 3 - Dr. Stokes

Corrositex Assay by regulatory agencies. On a related issue, ATSDR looks forward to the discussion of the regulatory acceptance status of the Local Lymph Node Assay (LLNA) at the Spring 2000 meeting of the NTP Advisory Committee on Alternative Toxicological Methods. We plan to send a representative.

In summary, we support the findings of the ICCVAM establishing the Corrositex Assay as a valid part of a tiered testing strategy for assessing dermal corrosion potential. ATSDR will make the protocol available to its staff as well as to our public and private sector partners.

Sincerely yours,



Henry Falk, M.D., M.P.H.
Assistant Administrator

cc:
Christopher De Rosa
William Cibulas
Buck Grissom