



United States
Department of
Agriculture

SEP 22 2003

Marketing and
Regulatory
Programs

Animal and Plant
Health Inspection
Service

Washington, DC
20250

Dr. Kenneth Olden
Director, National Institute
of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709

Dear Dr. Olden:

Thank you again for your letter of March 21, 2003, to the U.S. Department of Agriculture (USDA) concerning toxicological test recommendations forwarded from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). Our Agency received this letter April 7, 2003, and provided a preliminary response on May 2, 2003.

The test recommendations on *in vitro* methods for predicting acute systemic toxicity were distributed to, and reviewed by, scientists at our Center for Veterinary Biologics (CVB). The CVB regulates veterinary biologics (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin) to ensure they are pure, safe, potent, and effective. The CVB is the only regulatory unit within USDA that requires animal testing. They determined these test methods:

1. A cytotoxicity assay procedure used to select an appropriate starting dose for testing the acute oral lethality potential of chemicals in humans and animals, and
2. the revised Up-and-Down Procedure, a substitute for an existing LD₅₀ test for assessing the acute oral toxicity of chemicals, — do not apply to the safety testing done under the mandates of the Virus-Serum-Toxin Act for veterinary biologics. As noted by the absence any USDA regulations listed in Appendix F of the National Institutes of Health (NIH) Publication No. 01-4499, *Report of the International Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity* and Appendix Q of NIH Publication No. 02-4501, *The Revised Up-and-Down Procedure: A Test Method for Determining the Acute Oral Toxicity of Chemicals*, our Agency does not recommend or require this type of testing.

We appreciate the effort put forth by ICCVAM to generate these recommendations. Links to these test methods have been posted on the website of the Animal Welfare Information Center (National Agricultural Library, Agricultural Research Service) at <http://www.nal.usda.gov/awic/alternatives/alternat.htm#> as a resource for investigators considering alternatives to painful or distressful procedures in animals.



APHIS - Protecting American Agriculture


An Equal Opportunity Employer

Dr. Kenneth Olden
Page 2

We encourage the development and use of methods that reduce, refine, or replace animal testing while ensuring the scientifically valid results necessary for regulatory testing requirements. We look forward to receiving more such recommendations.

Sincerely,

(/s/

 Bobby R. Acord
Administrator

cc:
Rick Hill, VS/CVB, 510 S. 17th Street, Suite 104, Ames, IA 50010