

International Workshop on Alternative Methods for Human and Veterinary Rabies Vaccine Testing: State of the Science and Planning the Way Forward

Rabies in humans is a uniformly fatal disease, with infections killing over 55,000 people worldwide each year. Rabies vaccines serve a vital role in preventing further deaths and controlling the disease in certain animal populations. According to the World Health Organization, an estimated 15 million people receive post-exposure vaccine prophylaxis annually due to actual or suspected exposures to the rabies virus. In the U.S. and other developed countries, rabies vaccines have effectively eliminated domestic canine rabies virus strains. However, determining the safety and effectiveness of rabies vaccines requires large numbers of laboratory animals and involves significant pain and distress. New methods and approaches are sought that: 1) are more humane and use fewer or no animals, 2) are faster, cheaper, and more accurate, and 3) are safer for laboratory workers.

A recent international workshop organized by NICEATM, ICCVAM, and its international partners identified rabies vaccines as one of the three highest priorities for future research, development, and validation of alternative test methods that could further refine, reduce, and ultimately replace animal use for potency and safety testing. One of the highest priority implementation activities was organization of an international workshop on alternative methods for rabies vaccine potency testing. Based on recent scientific and technological advances, several alternative approaches have been proposed or are currently available. For example, scientists at the Paul-Ehrlich-Institut recently conducted an international collaborative study for the validation of a serological potency assay for rabies vaccine (inactivated) for veterinary use. A single-dilution assay that significantly reduces the number of mice utilized for the current *in vivo* NIH test has been proposed for human and veterinary rabies vaccine potency testing. Protective antigen quantification methods that do not require animals or the use of live rabies virus are now available and may be applicable to batch release testing for rabies vaccines.

This workshop will bring together international scientific experts from government, industry, and academia to review these methods and to define efforts necessary to achieve global acceptance and implementation. The workshop will identify critical components of manufacturing processes necessary to demonstrate batch-to-batch consistency and how monitoring these components can be used with *in vivo* and *in vitro* potency tests in an integrated approach to reduce and replace animal use for rabies batch release. Finally, workshop participants will identify the most appropriate source(s) for reference reagents to ensure standardization of *in vitro* rabies potency testing methods.