



# STATE OF NEW YORK DEPARTMENT OF HEALTH

Wadsworth Center

The Governor Nelson A. Rockefeller Empire State Plaza

P.O. Box 509

Albany, New York 12201-0509

Richard F. Daines, M.D.  
*Commissioner*

Wendy E. Saunders  
*Executive Deputy Commissioner*

April 30, 2009

Harry Prince, Ph.D.  
Focus Diagnostics  
5785 Corporate Ave  
Cypress, CA 90630

Re: ELISA Test for Rabies Antibody

Dear Dr. Prince:

This is to follow up the Department's March 10, 2009, notification of concern about the performance of the Focus Diagnostics ELISA test for rabies antibody. At that time, Dr. Wong presented preliminary data that suggested poor analytical specificity with clinical consequences of some people being told their vaccine immunity was adequate, when they likely needed a booster vaccination to be safe. The preliminary conclusions about assay performance have been substantiated as described below. Consequently, Focus Diagnostics must halt the processing of specimens originating from New York State for rabies serology testing. Additionally, the Department recommends that rabies vaccine recipients who have been given results of adequate titers ( $>0.50$  IU of rabies antibody) within the past two years have a repeat test performed by a laboratory that performs a virus neutralization procedure. The federal Centers for Medicare & Medicaid Services CLIA program has been informed of our findings and it may impose restrictions on patient testing outside New York State.

### **Study Design and Findings**

The Wadsworth Center's Diagnostic Immunology Laboratory sent a blinded panel of sera (90 samples) to Focus and the NYS rabies laboratory. Focus performed their ELISA procedure, and the NYS laboratory performed the virus neutralization procedure, which is the gold standard. This panel contained sera from both rabies vaccine recipients and patients with known clinical conditions.

For the rabies vaccine recipient sera, the Focus ELISA falsely identified 19.4% (7/36) of individuals as having adequate anti-rabies specific antibody levels but who were negative by the virus neutralization procedure. This is problematic for the following reason: these individuals need a booster dose of vaccine to maintain their WHO recommended minimum level of protection, but they would not receive this booster dose if they had their sera tested via the Focus ELISA. These individuals would be given a false sense of security when indeed they were not adequately protected against rabies. Given that rabies is a fatal disease, this alone is extremely dangerous.

Another concern is the substantial number of false positives. In sera from patients who had various diseases (mumps, measles, rubella, WNV, CMV, RMSF, ARBO, HSV 1&2, syphilis,

VZV, Lyme, HGA, Babesia), the Focus ELISA identified false positive anti-rabies antibodies in 50% (27/54) of the samples. This assay is designed to measure anti-rabies glycoprotein antibodies induced by rabies vaccination only; it should not be used as a tool to assess natural exposure to rabies virus. Since the ELISA test is mistakenly ordered by some hospitals when a physician wishes to test for rabies antibody, these false positives create a situation where physicians suspect a rabies infection in the sick human. There is no procedure in place to stop this testing and reporting of results to hospitals.

Finally, the results for the entire panel were confirmed by an independent laboratory using the virus neutralization test. The Diagnostic Immunology Laboratory "reblinded" the samples and sent them to the Kansas State University (KSU) laboratory for independent confirmation and again to the NYS rabies laboratory for retesting. These results showed close correlation between the KSU virus neutralization test and the NYS virus neutralization procedure, confirming the discrepancies with the Focus ELISA procedure.

Please be reminded that 10NYCRR Part 58 section 58-1.10 subdivision g requires that "All technical procedures employed in a laboratory shall be of proven reliability." The Department finds that its investigation of assay performance provides substantial evidence that the Focus Diagnostics ELISA test for rabies antibody is not of proven reliability. Please provide acknowledgment before close of business Friday, May 1, that Focus Diagnostics has ceased accepting specimens from New York State for rabies antibody testing and that it has developed a plan for the notification of rabies vaccine recipients about the probable falsely high titer results with recommendation that a repeat test be performed by a laboratory using a virus neutralization procedure. The acknowledgement and questions can be delivered to me by email at [rwj03@health.state.ny.us](mailto:rwj03@health.state.ny.us).

Sincerely,



Richard W. Jenny, Ph.D., Director  
Clinical Laboratory Evaluation Program

copy: Alfred Lui, MD  
Robert Rudd  
Susan Wong, Ph.D.