United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

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CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 07-07

Subject: Post-Challenge Observation Periods for Efficacy Studies

To: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics

I. PURPOSE

This notice provides clarification to licensees, permittees, and applicants of current Center for Veterinary Biologics (CVB) policy regarding post-challenge observation periods in efficacy studies. This policy pertains to pivotal efficacy studies conducted to support product label claims, as well as routine efficacy studies intended to qualify or requalify potency reference preparations.

II. BACKGROUND

Animal vaccination-challenge studies are frequently performed to demonstrate product efficacy. The CVB approves label claims for efficacy upon the demonstration of statistically significant, clinically relevant differences in post-challenge disease between vaccinated test animals vs. placebo-vaccinated control animals. Label claims are based on disease prevention or a meaningful reduction in disease severity or duration. Claims are not typically granted for products that merely delay disease onset or increase the time to peak disease severity.

Protocols for efficacy studies should include the period of time that the animals will be observed for signs of disease after exposure to challenge. This period is typically based on the expected incubation period of the disease agent and the expected duration of clinical disease. Many study-specific factors, however, can impact the actual time that elapses from challenge-exposure to the resolution of clinical disease. In individual cases, the post-challenge observation period proposed in the study protocol may be insufficient to evaluate all of the relevant post-challenge manifestations of disease, and protocol deviations to increase the observation period may be justified.

III. ACTION

Studies should be designed to have an appropriate observation period. The length of the observations period specified in the protocol should be the same for all subjects and appropriate for the disease course and study objective.

The post-challenge observation period stated in the study protocol should be considered a *minimum* interval during which all study subjects will be evaluated for relevant signs of disease. The presence of clinical signs of disease at the end of the planned observation period may indicate that the planned observation period is not long enough to properly assess the study objectives. The best course of action in such cases is usually to extend the observation period until clinical signs resolve. All reports describing studies in which the post-challenge observations are terminated prior to the resolution of relevant clinical signs and other substantive features of the disease should include a justification why continued observation would not have materially affected the conclusions drawn from the study.

/s/Richard E. Hill, Jr.

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