April 1, 2004

CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 04-09

Subject: Use of Humane Endpoints in Animal Testing of Biological Products

To: Biologics Licensees, Permittees, and Applicants
Veterinary Services Management Team
Directors, Center for Veterinary Biologics
Deputy Administrator, Animal Care

I. PURPOSE

This notice informs licensees, permittees, and applicants of current Center for Veterinary Biologics (CVB) policy concerning the use of humane endpoints in animal challenge tests.

II. BACKGROUND

Title 9 Code of Federal Regulations (9 CFR) Part 117.4(e) indicates that animals used in testing of biological products may be treated or humanely destroyed if illness has progressed to a point where death is certain to occur. The definition of that point (herein called the humane endpoint) is to be included in the Outline of Production. This notice clarifies the humane endpoint for all animal challenge potency tests codified in 9 CFR Part 113. It also provides guidance on establishing humane endpoints for potency tests that do not follow Standard Requirements.

III. POLICY

All codified potency tests (with the exception of the rabies challenge test discussed below) that are conducted by administering viable virus, bacteria, or a bacterial toxin to animals in a dose that is expected to be lethal may be modified to include the following wording:

> Moribund animals exhibiting clinical signs consistent with the expected disease pathogenesis that are unable to rise or move under their own power may be humanely euthanized and considered as deaths as outlined in 9 CFR 117.4.

In the case of the rabies challenge described in 9 CFR 113.209, 9 CFR 113.312, and Supplemental Assay Method 308, acceptable wording is:

> Animals exhibiting paresis, paralysis, and/or convulsions may be humanely euthanized and considered as deaths as outlined in 9 CFR 117.4.

Similar definitions may be incorporated into non-codified potency tests and efficacy study protocols. Proposed endpoints will be reviewed on a case-by-case basis and will be acceptable unless the CVB identifies a compelling reason why the proposed endpoint would not be appropriate.

When implementing humane endpoints, equal treatment must be given to both vaccinated and control animals; ideally, observers should be blinded to treatment group assignment. Criteria should be as objective as possible, to minimize differences in individual interpretation.

/s/ Richard E. Hill, Jr.

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Director
Center for Veterinary Biologics