

November 25, 2002

VETERINARY SERVICES MEMORANDUM NO. 800.107

Subject: Policy for Changing Cells and Cell Substrates of Licensed Vaccines

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

I. PURPOSE

This memorandum clarifies Center for Veterinary Biologics policy for obtaining approval to amend a filed Outline of Production to change the cell passage level or to change the cell lines used in the manufacture of licensed vaccines.

II. BACKGROUND

The general requirements for testing of cell lines used in the production of veterinary biological products are outlined in 9 CFR 113.51 and 113.52. When a licensee wishes to amend a filed Outline of Production to change the cell substrate(s) used for production of vaccines, e.g., increasing the passage level of the cell line, the policy (Veterinary Biologics Notice, February 26, 1993) has been to require that the Master Seed be retested for immunogenicity. However, due to current methodologies available, CVB may waive the requirement for immunogenicity testing if it can be demonstrated that the change in substrates does not alter the microbial genome and/or protein profile of the organism or product.

III. POLICY

Approval of a change in substrate or culture conditions will require a retest for immunogenicity or data demonstrating that there are no detectable changes in the microbial genome or protein profile. The *in vitro* data may be generated by using a combination of assays including sequencing, Western blot, SDS PAGE, HPLC, mass spectrometry, or other appropriate methodologies. If a firm is considering a change in the cell substrate for a product, a proposal for generating the data to support the change should be submitted to the firm's reviewer for evaluation and comment.

/s/ W. Ron DeHaven

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Veterinary Services