§ 113.303  

Bluetongue Vaccine.  

Bluetongue Vaccine shall be prepared from virus-bearing cell culture fluids. Only Master Seed which has been established as pure, safe, and immunogenic shall be used for preparing the seeds for vaccine production. All serials of vaccine shall be prepared from the first through the tenth passage from the Master Seed.

(a) The Master Seed shall meet the applicable general requirements prescribed in §113.300 and the requirements in this section.

(b) Each lot of Master Seed shall be tested for transmissibility and reversion to virulence in sheep using a method acceptable to Animal and Plant Health Inspection Service. If reversion to virulence is demonstrated, the Master Seed is unsatisfactory.

(c) Each lot of Master Seed used for vaccine production shall be tested for immunogenicity. The selected virus dose from the lot of Master Seed shall be established as follows:

(1) Twenty-five lambs, susceptible to the bluetongue virus serotype contained in the vaccine, shall be used as test animals (20 vaccinates and 5 controls). Blood samples shall be drawn from these animals and individual sera tested. A lamb shall be considered susceptible if there is no neutralization at a 1:2 final serum dilution in a constant virus varying serum neutralization test with 60 to 300 TCID₅₀ of bluetongue virus or another method acceptable to Animal and Plant Health Inspection Service.

(2) A geometric mean titer of the vaccine produced from the highest passage from the Master Seed shall be established before the immunogenicity test is conducted. The 20 lambs to be used as vaccinates shall be administered a predetermined quantity of vaccine virus by the method recommended on the label. To confirm the virus dosage administered, five replicate virus titrations shall be conducted on a sample of the vaccine used.

(3) At least once during the period of 14 to 18 days postvaccination, individual serum samples shall be collected from each of the vaccinates and tested for virus neutralizing antibody using the 60 to 300 TCID₅₀ of bluetongue virus.

(4) Twenty-one to twenty-eight days postvaccination the vaccinates and the controls shall each be challenged with virulent bluetongue virus and observed for 14 days. The rectal temperature of each animal shall be taken and recorded for 17 consecutive days beginning 3 days prechallenge. The presence
or absence of lesions or other clinical signs of bluetongue noted and recorded on each of 14 consecutive days postchallenge.

(i) If at least four of the five controls do not show clinical signs of bluetongue and a temperature rise of 3 °F or higher over the prechallenge mean temperature, the test shall be considered inconclusive and may be repeated.

(ii) If at least 19 of the 20 vaccinates tested as prescribed in paragraph (c)(3) of this section do not have bluetongue neutralizing antibody titers of 1:4 final serum dilution or higher, or if more than one of the vaccinates shows a temperature rise of 3 °F or higher than its prechallenge mean temperature for 2 or more days, or if more than one of the vaccinates exhibits clinical signs of bluetongue, the Master Seed is unsatisfactory.

(5) An Outline of Production change shall be made before authority for use of a new lot of Master Seed shall be granted by Animal and Plant Health Inspection Service.

(d) Test requirements for release. Each serial and subserial shall meet the applicable general requirements prescribed in §113.300 and the requirements prescribed in this section. Final container samples of completed product shall be tested. Any serial or subserial found unsatisfactory by a prescribed test shall not be released.

(1) Safety test. The mouse safety test prescribed in §113.33(a) and the lamb safety test prescribed in §113.45 shall be conducted.

(2) Virus titer requirements. Final container samples of completed product shall be tested for virus titer using the titration method used in paragraph (c)(2) of this section. To be eligible for release, each serial and subserial shall have a virus titer sufficiently greater than that used in such immunogenicity test.

$\frac{50 \text{ FR } 23796, \text{ June 6, 1985. Redesignated at } 55 \text{ FR } 35562, \text{ Aug. } 31, 1990, \text{ as amended at } 56 \text{ FR } 66784, 66786, \text{ Dec. } 26, 1991; 72 \text{ FR } 72564, \text{ Dec. } 21, 2007}$

§113.304 Feline Panleukopenia Vaccine.

Feline Panleukopenia Vaccine shall be prepared from virus-bearing cell culture fluids. Only Master Seed Virus which has been established as pure, safe, and immunogenic shall be used for preparing the production seed virus for vaccine production. All serials of vaccine shall be prepared from the first through the fifth passage from the Master Seed Virus.

(a) The Master Seed Virus shall meet the applicable general requirements prescribed in §113.300 and the requirements prescribed in this section.

(b) The lot of Master Seed Virus shall be tested for other agents as follows:

(1) To detect virulent feline panleukopenia virus or virulent mink enteritis virus, each of two feline panleukopenia susceptible cats, as determined by the criteria prescribed in paragraph (c)(1) of this section, shall be injected subcutaneously with the equivalent of one cat dose each and the cats observed each day for 21 days. If either or both cats show signs of disease or reduced white blood cell counts below 50 percent of the normal level established by an average of three or more counts taken prior to injection, the Master Seed Virus is unsatisfactory.

(2) To detect chlamydial agents, the Master Seed Virus shall be tested as prescribed in §113.43.

(c) Each lot of Master Seed Virus used for vaccine production shall be tested for immunogenicity. The selected virus dose from the lot of Master Seed Virus shall be established as follows:

(1) Twenty-five feline panleukopenia susceptible cats shall be used as test animals (20 vaccinates and 5 controls). Blood samples drawn from each cat shall be individually tested for neutralizing antibody against feline panleukopenia virus to determine susceptibility.