§ 113.311 Bovine Virus Diarrhea Vaccine.

Bovine Virus Diarrhea 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 tenth passage from the Master Seed Virus.

(a) The Master Seed Virus shall meet the applicable general requirements prescribed in §113.300.
(b) Each lot of Master Seed Virus shall meet the special requirements prescribed in this section.

(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 bovine virus diarrhea susceptible calves shall be used as test animals (20 vaccinates and five controls). Blood samples shall be drawn from these animals and individuals serum samples tested. The calves shall be considered susceptible to bovine virus diarrhea virus infection if the results are negative at a 1:2 final serum dilution in a varying serum-constant virus neutralization test with less than 500 TCID\textsubscript{50} of bovine virus diarrhea virus.

(2) A geometric mean titer of the dried vaccine produced from the highest passage of the Master Seed Virus shall be established before the immunogenicity test is conducted. The 20 calves to be used as vaccinates shall be injected with a predetermined quantity of vaccine virus and the remaining five calves held as uninjected controls. To confirm the dosage calculations, five replicate virus titrations shall be conducted on a sample of the vaccine virus dilution used.

(3) At least once during a period 14 to 28 days post-vaccination, individual serum samples shall be collected for virus-neutralization tests from each of the vaccinates. 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 per dose sufficiently greater than the titer of vaccine virus used in the immunogenicity test prescribed in paragraph (c) of this section to assure that when tested at any time within the expiration period, each serial and subserial shall have virus titer of 10^{2.5} TCID\textsubscript{50} per dose.

(5) If less than 19 of the post-injection serum samples, tested as prescribed in paragraph (c)(3) of this section, show neutralization in all tubes of the 1:8 dilution; or if more than one of the vaccinates exhibits respiratory or other clinical signs of bovine virus diarrhea post-challenge; or both, the Master Seed Virus is unsatisfactory.

(d) Test requirements for release:

(1) Purity test. The test for Brucella contamination prescribed in §113.32 shall be conducted on each batch of primary cells intended for production use.

(2) Safety test. The mouse safety test prescribed in §113.33(a) and the calf safety test prescribed in §113.41 shall be conducted.

(3) 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 each subserial shall have a virus titer per dose sufficiently greater than the titer of vaccine virus used in the immunogenicity test prescribed in paragraph (c) of this section to assure that when tested at any time within the expiration period, each serial and subserial shall have virus titer of 10^{2.5} TCID\textsubscript{50} per dose.