§ 113.215 Bovine Virus Diarrhea Vaccine, Killed Virus.

Bovine Virus Diarrhea Vaccine, Killed Virus, 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 seed cultures for vaccine production. All serials of vaccine shall be prepared from the first through the fifth passage from the Master Seed.

(a) The Master Seed shall meet the applicable general requirements prescribed in §113.200 and the requirements of this section.

(b) The immunogenicity of vaccine prepared from the Master Seed in accordance with the Outline of Production shall be established by a method acceptable to the Animal and Plant Health Inspection Service. Vaccine used for this test shall be at the highest passage from the Master Seed and at the minimum preinactivation titer provided in the Outline of Production.

(c) *Test requirements for release.* Each serial and subserial shall meet the applicable general requirements prescribed in §113.200 and the special requirements provided in this paragraph. Any serial or subserial found unsatisfactory by a prescribed test shall not be released.

(1) *Safety.* Vaccinates used in the potency test in paragraph (c)(2) of this section shall be observed each day during the prechallenge period. If unfavorable reactions occur, including respiratory signs, which are attributable to the vaccine, the serial is unsatisfactory. If unfavorable reactions occur which are not attributable to the vaccine, the test is inconclusive and may be repeated one time. If results of the second test are not satisfactory, or if the test is not repeated, the serial is unsatisfactory.

(2) *Potency.* Bulk or final container samples of completed product shall be tested for potency using the method described in this paragraph.

(i) Eight bovine virus diarrhea susceptible calves (five vaccinates and three controls) shall be used as test animals. Individual serum samples shall be collected, inactivated, and individually tested for neutralizing antibody.

(ii) A constant virus decreasing serum neutralization test in cell culture using 50–300 TCID50 of virus shall be used. Calves shall be considered susceptible if there is no neutralization at 1:2 final serum dilution. Other tests of equal sensitivity approved by the Animal and Plant Health Inspection Service may be used.

(iii) The five calves used as vaccinates shall be administered one dose of vaccine as recommended on the label. If two doses are recommended, the second dose shall be given according to the interval recommended on the label.

(iv) Fourteen days or more after the last vaccination, blood samples shall be drawn and the individual serum samples inactivated and tested for bovine virus diarrhea virus neutralizing antibody by the same method used to determine susceptibility.

(v) *Test interpretation.* If the controls have not remained seronegative at 1:2, the test is a No Test (NT) and may be repeated. If at least four of the five vaccinates in a valid test have not developed 50 percent endpoint titers of 1:8 or greater, the serial is unsatisfactory, except as provided in paragraph (c)(2)(vi) of this section.

(vi) *Virus Challenge Test.* If the results of a valid serum neutralization test are unsatisfactory, the vaccinates and controls may be challenged with virulent bovine virus diarrhea virus furnished or approved by the Animal and Plant Health Inspection Service. The animals shall be observed for 14 days post-challenge. If two of the three control calves do not show a temperature rise to 104.5 °F and develop respiratory or clinical signs of bovine virus diarrhea, the test is inconclusive and may be repeated one time. If two or more vaccinates show a temperature of 104.0 °F for 2 or more days and develop respiratory or clinical or other signs, the serial is unsatisfactory.

(vii) The prevaccination and postvaccination sera from a satisfactory potency test shall be submitted to the National Veterinary Services Laboratories for confirmatory testing.

[55 FR 35562, Aug. 31, 1990]