

§ 113.210

9 CFR Ch. I (1–12 Edition)

challenge. If one or more of the vaccinates die from rabies, all the remaining vaccines, regardless of titer, along with the five controls shall be challenged. The cumulative results from the two challenges shall be evaluated for acceptance as specified in paragraph (b)(3)(v) of this section.

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

(c) If more than 1 year duration of immunity is to be claimed, a duration of immunity test for the additional time shall be conducted and interpreted as prescribed in paragraph (b) of this section for the 1 year test. The test animals shall be monitored serologically at least every 180 days. The time of challenge may be adjusted accordingly.

(d) Test requirements for release: Each serial and each subserial shall meet the general requirements prescribed in §113.200 and special requirements in this paragraph.

(1) *Purity test.* Primary cell cultures of hamster origin or brain tissues of mouse origin used in vaccine production shall be tested for LCM virus as prescribed in §113.42. Hamster origin cells shall be disrupted and undiluted cell fluids from each lot shall be tested. Where mouse brains are used in production, at least five mice which have not been injected with rabies virus shall be sacrificed and a 10 percent suspension of brain material shall be prepared and tested.

(2) *Safety tests.* Bulk samples from each serial shall be tested for virus inactivation and safety as follows:

(i) At the end of the inactivation period, each of 20 12 to 16 gram mice shall be injected intracerebrally with 0.03 ml and two rabbits shall be injected into each cerebral hemisphere with 0.25 ml and observed each day for 21 days. The brains of animals dying between the fourth and 21st day post-injection shall be checked for rabies virus. Material from each brain recovered shall be injected into each of five mice and the mice observed each day for 14 days. The fluorescent antibody test or serum neutralization test shall be used to confirm the presence or absence or live ra-

bies virus. If live rabies virus is confirmed, the serial is unsatisfactory unless reprocessed in accordance with §114.18.

(ii) A test for safety in three young seronegative animals of the most susceptible species for which the vaccine is recommended shall be conducted. Each shall be injected intramuscularly with one recommended dose of vaccine. If unfavorable reactions attributable to the product occur during a 28 day observation period, the serial is unsatisfactory.

(3) *Potency test.* Bulk or final container samples of completed product from each serial must be tested for potency by tests conducted in accordance with the standard NIH test for potency in Chapter 37 of "Laboratory Techniques in Rabies," Fourth Edition (1996), which is incorporated by reference at paragraph (b)(1) of this section. The relative potency of each serial must be at least equal to that used in an approved host animal immunogenicity test.

[39 FR 44715, Dec. 27, 1974, as amended at 42 FR 6794, Feb. 4, 1977; 43 FR 49528, Oct. 24, 1978; 50 FR 20090, May 14, 1985. Redesignated at 55 FR 35562, Aug. 31, 1990; 56 FR 66784, 66786, Dec. 26, 1991; 61 FR 31823, June 21, 1996; 64 FR 45420, Aug. 20, 1999; 69 FR 18803, Apr. 9, 2004; 75 FR 20773, Apr. 21, 2010]

§ 113.210 Feline Calicivirus Vaccine, Killed Virus.

Feline Calicivirus Vaccine, Killed Virus, 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 seeds 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.

(b) The Master Seed shall be tested for chlamydial agents as prescribed in §113.43.

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

from the Master Seed and prepared at the minimum preinactivation titer specified in the Outline of Production.

(d) *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 (d)(2) of this section shall be observed each day during the prechallenge period. If unfavorable reactions occur, including oral lesions, 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. If the test is not repeated, the serial is unsatisfactory.

(2) *Potency.* Bulk or final container samples of completed product shall be treated for potency as follows:

(i) Eight feline calicivirus susceptible cats (five vaccinates and three controls) shall be used as test animals. Throat and nasal swabs shall be collected from each cat and individually tested on susceptible cell cultures for the presence of feline calicivirus. Blood samples shall be drawn and individual serum samples tested for neutralizing antibody. The cats shall be considered suitable for use if all swabs are negative for virus isolation and all serums are negative for calicivirus antibody at the 1:2 final dilution in a 50 percent plaque reduction test or other test of equal sensitivity.

(ii) The five cats used as vaccinates shall be administered one dose of vaccine by the method recommended on the label. If two doses are recommended, the second dose shall be given after the interval recommended on the label.

(iii) Fourteen or more days after the final dose of vaccine, the vaccinates and controls shall each be challenged intranasally with virulent feline calicivirus furnished or approved by Animal and Plant Health Inspection Service and observed each day for 14 days postchallenge. The rectal temperature of each animal shall be taken and the presence or absence of clinical

signs, particularly lesions on the oral mucosa, noted and recorded each day.

(iv) If three of three controls do not show clinical signs of feline calicivirus infection other than fever, the test is inconclusive and may be repeated.

(v) If a significant difference in clinical signs cannot be demonstrated between vaccinates and controls using a scoring system approved by Animal and Plant Health Inspection Service and prescribed in the Outline of Production, the serial is unsatisfactory.

[50 FR 433, Jan. 4, 1985. Redesignated at 55 FR 35562, Aug. 31, 1990, as amended at 56 FR 66784, 66786, Dec. 26, 1991]

§ 113.211 Feline Rhinotracheitis Vaccine, Killed Virus.

Feline Rhinotracheitis Vaccine, Killed Virus, 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 seeds 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.

(b) The Master Seed shall be tested for chlamydial agents as prescribed in §113.43.

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

(d) *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 test.* Vaccinates used in the potency test in paragraphs (d)(2) of this