

§ 113.100

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are negative for pneumonitis antibody in a complement fixation test or other test of equal sensitivity.

(2) A geometric mean titer of the dried vaccine produced from the highest passage of the Master Seed shall be established before the immunogenicity test is conducted. The 20 cats used as vaccinates shall be administered a predetermined quantity of vaccine by the method to be recommended on the label and the remaining 10 cats shall be held as controls. To confirm the dosage calculations, five replicate titrations shall be conducted on a sample of the vaccine dilution used. If two doses are used, five replicate confirming titrations shall be conducted on each dose.

(3) Fourteen or more days after the final dose of vaccine, the vaccinates and controls shall each be challenged intranasally with a minimum of 10,000 yolk sac LD50 of virulent feline pneumonitis furnished or approved by the Animal and Plant Health Inspection Service and observed each day for 28 days postchallenge. The rectal temperature of each animal shall be taken and the presence or absence of clinical signs noted and recorded each day.

(i) If less than 8 of 10 controls show clinical signs of feline pneumonitis infection other than fever, the test is inconclusive and may be repeated.

(ii) If a significant difference in clinical signs other than fever or chlamydia shedding cannot be demonstrated between vaccinates and controls using a scoring system approved by the Animal and Plant Health Inspection Service, the Master Seed is unsatisfactory.

(4) The Master Seed shall be retested for immunogenicity in 3 years unless use of the lot previously tested is discontinued. Either 10 vaccinates and 6 controls or 5 vaccinates and 3 controls shall be used in the retest.

(i) If less than five of six or three of three of the controls in the retest show clinical signs of feline pneumonitis infection other than fever, the test is inconclusive and may be repeated.

(ii) A significant difference in clinical signs shall be demonstrated between vaccinates and controls in a valid test as prescribed in paragraph (c)(3)(ii) of this section.

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

(c) *Test requirements for release.* Except for §113.300(a)(3)(ii), each serial and subserial shall meet the requirements prescribed in §113.300 and in this paragraph. Final container samples of completed product shall be tested. Any serial or subserial found unsatisfactory by a prescribed test shall not be released.

(1) The test for pathogens prescribed in §113.37 shall be conducted on each serial or one subserial of avian origin vaccine.

(2) *Chlamydia titer requirements.* Final container samples of completed product shall be tested for chlamydia titer using the titration method used in paragraph (b)(2) of this section. To be eligible for release, each serial and each subserial shall have a titer sufficiently greater than the titer of vaccine used in the immunogenicity test prescribed in paragraph (b) of this section to assure that when tested at any time within the expiration period, each serial and subserial shall have a titer 0.7 greater than that used in such immunogenicity test but not less than 2.5 ID50 per dose.

[55 FR 35561, Aug. 31, 1990, as amended at 56 FR 66786, Dec. 26, 1991]

INACTIVATED BACTERIAL PRODUCTS

§ 113.100 **General requirements for inactivated bacterial products.**

Unless otherwise prescribed in an applicable Standard Requirement or in the filed Outline of Production, an inactivated bacterial product shall meet the applicable requirements in this section.

(a) *Purity tests.* (1) Final container samples of completed product from each serial and each subserial shall be tested for viable bacteria and fungi as provided in §113.26.

(2) Each lot of Master Seed Bacteria shall be tested for the presence of extraneous viable bacteria and fungi in accordance with the test provided in §113.27(d).

(b) *Safety tests.* Bulk or final container samples of completed product

from each serial shall be tested for safety in young adult mice in accordance with the test provided in §113.33(b) unless:

(1) The product contains material which is inherently lethal for mice. In such instances, the guinea pig safety test provided in §113.38 shall be conducted in place of the mouse safety test.

(2) The product is recommended for poultry. In such instances, the product shall be safety tested in poultry as defined in the specific Standard Requirement or Outline of Production for the product.

(3) The product is recommended for fish, other aquatic species, or reptiles. In such instances, the product shall be safety tested in fish, other aquatic species, or reptiles as required by specific Standard Requirement or Outline of Production for the product.

(c) *Identity test.* Methods of identification of Master Seed Bacteria to the genus and species level by laboratory tests shall be sufficient to distinguish the bacteria from other similar bacteria according to criteria described in the most recent edition of "Bergey's Manual of Systematic Bacteriology" or the American Society for Microbiology "Manual of Clinical Microbiology". If Master Seed Bacteria are referred to by serotype, serovar, subtype, pilus type, strain or other taxonomic subdivision below the species level, adequate testing must be used to identify the bacteria to that level. Tests which may be used to identify Master Seed Bacteria include, but are not limited to:

- (1) Cultural characteristics,
- (2) Staining reaction,
- (3) Biochemical reactivity,
- (4) Fluorescent antibody tests,
- (5) Serologic tests,
- (6) Toxin typing,
- (7) Somatic or flagellar antigen characterization, and
- (8) Restriction endonuclease analysis.

(d) *Ingredient requirements.* Ingredients used for the growth and preparation of Master Seed Bacteria and of final product shall meet the requirements provided in §113.50. Ingredients of animal origin shall meet the applicable requirements provided in §113.53.

(e) Only serials tested for viricidal activity in accordance with the test

provided in §113.35 and found satisfactory by such test shall be packaged as diluent for desiccated fractions in combination packages.

(f) If formaldehyde is used as the inactivating agent and the serial has not been found satisfactory by the viricidal activity test, bulk or final container samples of completed product from each serial shall be tested for residual free formaldehyde content using the Basic Fuchsin Test.

(1) The residual free formaldehyde content of biological products containing Clostridial antigens shall not exceed the equivalent of 0.5 percent formaldehyde solution (1,850 parts per million formaldehyde.)

(2) The residual free formaldehyde content of bacterins, bacterin-toxoids, and toxoids other than those containing Clostridial antigens, shall not exceed the equivalent of 0.2 percent formaldehyde solution (740 parts per million formaldehyde.)

[39 FR 16862, May 10, 1974. Redesignated at 55 FR 35562, Aug. 31, 1990, as amended at 60 FR 14355, Mar. 17, 1995]

§ 113.101 *Leptospira Pomona* Bacterin.

Leptospira Pomona Bacterin shall be produced from a culture of *Leptospira pomona* which has been inactivated and is nontoxic. Each serial of biological product containing *Leptospira pomona* fraction shall meet the applicable requirements in §113.100 and shall be tested for purity, safety, and potency as prescribed in this section. A serial found unsatisfactory by any prescribed test shall not be released.

(a) *Purity test.* Final container samples of completed product from each serial and each subserial shall be tested for viable bacteria and fungi as provided in §113.26.

(b) *Safety test.* Bulk or final container samples of completed product from each serial shall be tested for safety as provided in §113.38.

(c) *Potency test.* Bulk or final container samples of completed product shall be diluted with physiological saline so that each 0.25 ml contains not more than 1/800th of the dose recommended on the label and shall be tested for potency, using the two-stage test provided in this paragraph.