

## § 113.4

selected at random from final containers of completed product by an employee of the Department, of the licensee, or of the permittee, as designated by the administrator. Each sample shall:

(1) Consist of 5 single-dose packages, 2 multiple-dose packages, or 2 diagnostic test kits, except that, in the case of diagnostic test kits in which final packaging consists of multiple microtiter test plates or strips, a sample may consist of a specified number of test plates or strips along with all other test reagents as prescribed in a filed Outline of Production;

(2) Be adequate in quantity for appropriate examination and testing;

(3) Be truly representative and in final containers;

(4) Be held in a special compartment set aside by the licensee or permittee for holding these samples under refrigeration at the storage temperature recommended on the labels for 6 months after the expiration date stated on the labels. The samples that are stored in this manner shall be delivered to the Animal and Plant Health Inspection Service upon request.

(Approved by the Office of Management and Budget under control number 0579-0013)

[38 FR 29886, Oct. 30, 1973, as amended at 40 FR 758, Jan. 3, 1975; 40 FR 49768, Oct. 24, 1975; 41 FR 56627, Dec. 29, 1976; 48 FR 9506, Mar. 7, 1983; 48 FR 57473, Dec. 30, 1983; 50 FR 21799, May 29, 1985; 56 FR 66784, Dec. 26, 1991; 60 FR 14356, Mar. 17, 1995; 67 FR 15713, Apr. 3, 2002]

### § 113.4 Exemptions to tests.

(a) The test methods and procedures contained in all applicable Standard Requirements shall be complied with unless otherwise exempted by the Administrator and provided that such exemption is noted in the filed Outline of Production for the product.

(b) Test methods and procedures by which the biological products shall be evaluated shall be designated in the Outline of Production for such products.

[38 FR 29887, Oct. 30, 1973, as amended at 56 FR 66784, Dec. 26, 1991]

### § 113.5 General testing.

(a) No biological product shall be released prior to the completion of tests prescribed in a filed Outline of Produc-

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tion or Standard Requirements for the product to establish the product to be pure, safe, potent, and efficacious.

(b) Tests of biological products shall be observed by a competent employee of the manufacturer during all critical periods. A critical period shall be the time when certain specified reactions must occur in required tests to properly evaluate the results.

(c) Records of all tests shall be kept in accordance with part 116 of this chapter. Results of all required tests prescribed in the filed Outline of Production or the Standard Requirements for the product shall be submitted to Animal and Plant Health Inspection Service. Blank forms shall be furnished upon request to Animal and Plant Health Inspection Service.

(d) When the initial or any subsequent test is declared a "No test," the reasons shall be reported in the test records, the results shall not be considered as final, and the test may be repeated.

(e) When new test methods are developed and approved by Animal and Plant Health Inspection Service, biological products tested thereafter shall be evaluated by such methods, and if not found to be satisfactory when so tested shall not be released.

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[34 FR 18004, Nov. 4, 1969, as amended at 39 FR 25463, July 11, 1974; 40 FR 45420, Oct. 2, 1975; 40 FR 46093, Oct. 6, 1975; 41 FR 6751, Feb. 13, 1976; 48 FR 57473, Dec. 30, 1983; 56 FR 66784, Dec. 26, 1991]

### § 113.6 Animal and Plant Health Inspection Service testing.

A biological product shall with reasonable certainty yield the results intended when used as recommended or suggested in its labeling or proposed labeling prior to the expiration date.

(a) The Administrator is authorized to cause a biological product, manufactured in the United States or imported into the United States, to be examined and tested for purity, safety, potency, or efficacy; in which case, the licensee or permittee shall withhold such product from the market until a determination has been made.

(b) The final results of each test conducted by the licensee and Animal and

Plant Health Inspection Service shall be considered in evaluating a biological product. A serial or subserial which has been found unsatisfactory by a required test prescribed in a filed Outline of Production or Standard Requirement is not in compliance with the regulations and shall not be released for market.

[34 FR 18004, Nov. 7, 1969, as amended at 40 FR 45420, Oct. 2, 1975; 40 FR 53378, Nov. 18, 1975; 41 FR 6751, Feb. 13, 1976; 56 FR 66784, Dec. 26, 1991]

#### § 113.7 Multiple fractions.

(a) When a biological product contains more than one immunogenic fraction, the completed product shall be evaluated by tests applicable to each fraction.

(b) When similar potency tests are required for more than one fraction of a combination biological product, different animals must be used to evaluate each fraction except when written Standard Requirements or outlines of production make provisions and set forth conditions for use of the same animals for testing different fractions.

(c) When the same safety test is required for more than one fraction, requirements are fulfilled by satisfactory results from one test of the completed product.

(d) When an inactivated fraction(s) is used as a diluent for a live virus fraction(s), the inactivated fraction(s) may be tested separately and the live virus fraction(s) may be tested separately: *Provided*, That, the viricidal test requirements prescribed in §113.100 are complied with.

(e) Virus titrations for a multivirus product shall be conducted by methods which will quantitate each virus.

[34 FR 18004, Nov. 7, 1969, as amended at 40 FR 46093, Oct. 6, 1975; 56 FR 66785, Dec. 26, 1991]

#### § 113.8 In vitro tests for serial release.

(a) Master Seed which has been established as pure, safe, and immunogenic shall be used for preparing seed for production as specified in the Standard Requirements or in the filed Outline of Production. The Administrator may exempt a product from a required animal potency test for

release when an evaluation can, with reasonable certainty, be made by:

(1) Subjecting the master seed to the applicable requirements prescribed in §§113.64, 113.100, 113.200, and 113.300;

(2) Testing the Master Seed for immunogenicity in a manner acceptable to the Animal and Plant Health Inspection Service (APHIS);

(3) Establishing satisfactory potency for the product in accordance with the following provisions:

(i) Potency for live products may be determined by  $\log_{10}$  virus titer or determining the live bacterial count based on the protective dose used in the Master Seed immunogenicity test plus an adequate coverage for adverse conditions and test error; and

(ii) Potency for inactivated products may be determined using tests for relative antigen content by comparing the antigen content of the test serial to a reference preparation using a parallel line immunoassay or equivalent method which measures linearity, specificity, and reproducibility in a manner acceptable to APHIS.

(b) In the case of live products, each serial and subserial of desiccated product derived from an approved Master Seed and bulk or final container samples of each serial of completed liquid product derived from an approved Master Seed shall be evaluated by a test procedure acceptable to APHIS. On the basis of the results of the test, as compared with the required minimum potency, each serial and subserial shall either be released to the firm for marketing or withheld from the market. The evaluation of such products shall be made in accordance with the following criteria:

(1) If the initial test shows the count or titer to equal or exceed the required minimum, the serial or subserial is satisfactory without additional testing.

(2) If the initial test shows the count or titer to be lower than the required minimum, the serial or subserial may be retested, using double the number of samples. The average counts or titers obtained in the retests shall be determined. If the average is less than the required minimum, the serial or subserial is unsatisfactory without further consideration.