give the egg source, age, and route of inoculation. If cell lines are being used, give dates of testing and approval as specified in 9 CFR 113.52.

C. Describe procedures used for extracting and characterizing the antigen.

D. Describe the method used to standardize the antigen.

E. If the antigen is purchased, identify the supplier and describe the criteria for acceptable material, including all tests performed by the producer and/or the recipient to determine acceptability.

III. *Preparation of Standard Reagents*

A. Describe the positive and negative controls included in the kit. If purchased, list suppliers and criteria for acceptance.

B. Describe the preparation and standardization of the conjugate(s). If purchased, list suppliers and criteria for acceptance.

C. Describe the preparation and standardization of the substrate(s). If purchased, list suppliers and criteria for acceptance.

D. Identify buffers, diluents, and other reagents included in the kit. The preparation of these components may be described in this section or in filed Special Outlines.

IV. *Preparation of the Product*

Fully describe methods used to standardize antigens, reference standards, positive control serum, negative control serum, and standard reagents from production/purchase to completion of finished product in final containers, including the following:

1. Composition and quantity of preservative in each.

2. Method of filling, plating, or attaching the antigen or antibody component to a solid phase.

3. Minimum and maximum acceptable fill volumes for each final container of reagent included in the kit.

4. The disposition of unsatisfactory material.

V. *Testing*

Refer to all applicable standard requirements.

A. Purity.

Describe all tests of the kit for purity or specify the exemption as provided in 9 CFR 113.4.

B. Safety.

In vitro products are exempt from safety tests.

C. Potency.

Provide details of tests used to determine the relative reactivity of the kit including minimum requirements for a satisfactory test. Reference standards and control serum used for this purpose should be identified by unique codes or lot numbers.

VI. *Postpreparatory Steps*

A. Describe the form and size of final containers of each reagent/component included in the kit.

B. Describe the collection, storage, and submission of representative samples. Refer to 9 CFR 113.3(b)(7).

C. Specify the expiration date. Refer to 9 CFR 114.13.

D. Provide details of recommendations for use, including all limitations, qualifications, and interpretation of results.

E. Submit confidentiality statement identifying specific parts of the outline containing information, the release of which would cause harm to the submitter.

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

[39 FR 16869, May 10, 1974, as amended at 48 FR 57473, Dec. 30, 1983; 56 FR 20124, May 2, 1991; 56 FR 66784, Dec. 26, 1991]

§ 114.10 Antibiotics as preservatives.

Antibiotics are authorized for use as preservatives for biological products if used within the limitations as to kinds and amounts prescribed in this section.

(a) When an antibiotic or combination of antibiotics, with or without a fungistat is to be used in the preparation of a biological product, the kind(s) and amount(s) of each shall be specified in the outline for such product in such a way that the concentration in the final product may be calculated. Except as may be approved by the Administrator, only those individual antibiotics or combinations of antibiotics listed in paragraphs (b) and (c) of this section shall be used.

(b) Permitted individual antibiotics:

(1) The antibiotic level of a specified individual antibiotic in one ml. of a biological product, when prepared as recommended for use, shall not exceed the amounts listed in this paragraph: *Provided,* That in the case a desiccated biological product is to be used with an indefinite quantity of water or other menstruum, the determination shall be based on 30 ml. per 1,000 dose vial or equivalent.

(2) Except as prescribed in paragraph (c) of this section, only one antibiotic shall be used as a preservative in a biological product. The kind and maximum amount per ml. of such antibiotic shall be restricted to:

Amphotericin B	2.5 mcg.
Nystatin (Mycostatin)	30.0 units
Tetracyclines	30.0 mcg.

Penicillin	30.0 units
Streptomycin	30.0 mcg.
Polymyxin B	30.0 mcg.
Neomycin	30.0 mcg.
Gentamicin	30.0 mcg.

(c) Permitted combinations:

(1) Penicillin and streptomycin.

(2) Either amphotericin B or nystatin, but not both, may be used with one of the other antibiotics listed in paragraph (b) of this section, or with a combination of penicillin and streptomycin, or with a combination of polymyxin B and neomycin.

(3) The maximum amount of each antibiotic in a combination shall be the amount prescribed for such antibiotic in paragraph (b) of this section.

(d) Antibiotics used in virus seed stock purification are not restricted as to kind or amounts provided carryover into the final product is controlled and specified in outlines of production.

[39 FR 16869, May 10, 1974, as amended at 56 FR 66784, Dec. 26, 1991

§ 114.11 Storage and handling.

Biological products at licensed establishments shall be protected at all times against improper storage and handling. Completed product shall be kept under refrigeration at 35 °to 45 °F. (2 °to 7 °C.) unless the inherent nature of the product makes storage at a different temperature advisable, in which case, the proper storage temperature shall be specified in the filed Outline of Production. All biological products to be shipped or delivered shall be securely packed.

§ 114.12 Expiration date required.

Each serial or subserial of biological product prepared in a licensed establishment shall be given an expiration date determined in accordance with the requirements provided in §114.13 or §114.14. A licensed biological product shall be considered worthless under the Virus-Serum-Toxin Act subsequent to the expiration date appearing on the label.

[41 FR 44687, Oct. 12, 1976]

§ 114.13 Expiration date determination.

Unless otherwise provided for in a Standard Requirement of filed Outline of Production, the expiration date for each product shall be computed from the date of the initiation of the potency test. Prior to licensure, stability of each fraction shall be determined by methods acceptable to Animal and Plant Health Inspection Service. Expiration dates based on this stability data shall be confirmed as follows:

(a) *Products consisting of viable organisms.* Each serial shall be tested for potency at release and at the approximate expiration date until a statistically valid stability record has been established.

(b) *Nonviable biological products.* Each serial presented in support of licensure shall be tested for potency at release and at or after the dating requested.

(c) Subsequent changes in the dating period for a product may be granted, based on statistically valid data submitted to support a revision of the Outline of Production.

[50 FR 24903, June 14, 1985, as amended at 56 FR 66784, Dec. 26, 1991]

§ 114.14 Extension of expiration date for a serial or subserial.

(a) Unless otherwise provided for in a filed Outline of Production for the product, the expiration date shall not be extended:

(1) If all fractions of the product are not evaluated for potency by tests designated in the filed Outline of Production for such product in accordance with §113.4(b) of this subchapter.

(2) For any serial or portion of any serial which has left licensed premises: *Provided,* That product which has been shipped from one licensed premises to another licensed premises shall be exempt from this requirement.

(3) For a serial or portion of a serial if the expiration date has been extended previously, unless otherwise authorized in accordance with §114.1.

(b) An extension of the expiration date may be granted by Animal and Plant Health Inspection Service if a request from the licensee is substantiated by valid test data which demonstrate the potency of the product meets or exceeds the requirements for release. The new expiration date shall be calculated from the date the latest satisfactory potency test was initiated. The extension of the expiration date shall not exceed the maximum dating