§ 114.8 Outline of Production required.

An Outline of Production shall be on file with Animal and Plant Health Inspection Service for each licensed biological product or for each biological product authorized to be imported into the United States for Distribution and Sale. Preparation of a biological product in a licensed establishment shall be in accordance with the Outline of Production for such product filed with Animal and Plant Health Inspection Service as provided in this section, but subject to changes as may be required under § 114.8(f).

(a) The Outline of Production shall be prepared as prescribed in § 114.9 and submitted to Animal and Plant Health Inspection Service for filing. When objectionable features, if any, are corrected and no further exceptions are taken by Animal and Plant Health Inspection Service to an Outline of Production for a biological product, such Outline of Production shall be approved for filing.

(b) Each page shall be stamped as filed on the date such action was taken in the bottom right hand corner. Although the filed outline may be referred to as an approved outline, approval for filing constitutes no endorsement by Animal and Plant Health Inspection Service of such biological product or the methods and procedures used to prepare such biological product.

(c) One copy of the Outline of Production shall be retained by the Animal and Plant Health Inspection Service and one copy returned to the licensee or permittee.

(d) Each licensee shall review each Outline of Production for accuracy and sufficiency not less frequently than once a year. Revisions necessary to bring an Outline of Production into compliance with the regulations shall be submitted to Animal and Plant Health Inspection Service.

(e) When a list of licensed products to be continued in production at a licensed establishment is requested by the Administrator in accordance with § 102.5(d) of this subchapter, the licensee shall supplement the list with information for each product as follows:

(1) The Outline of Production currently being used shall be identified as to the date when last revised and filed with Animal and Plant Health Inspection Service and the date of the last review made by the licensee.

(2) The Outline of Production to be kept in the active file shall be designated. If more than one has been filed for a product, only the Outline of Production currently being used shall be included.

(f) The Administrator may, upon the basis of information not available to him at the time the current Outline of Production for a biological product was filed, object to the methods or procedures being used in the preparation of such biological product and notify the licensee to modify the filed Outline of Production to eliminate such objections. If the licensee does not comply with the notice, the Administrator may, after affording opportunity for a hearing to the licensee, suspend the product license for the biological product involved; in which case, the licensee shall not prepare such product until subsequent notice of withdrawal.
§ 114.9 Outline of Production guidelines.

Each Outline of Production shall be prepared in accordance with the applicable directions provided in this section.

(a) General requirements. (1) All copies of each Outline of Production or special outline or revised pages of either shall be prepared on heavy paper (8.5” x 11”) of a type receptive to permanent stamp ink.
(2) The name of the biological product (or component), the establishment license number, and the date prepared shall appear on a front cover page and each page of the Outline of Production or special outline. The name of the licensee (or foreign manufacturer) shall appear on the front cover page.
(3) The pages shall be numbered in the upper center. At least 1½ inch margin shall be left at the top of the first page and a 2 inch margin at the bottom of each page for the Animal and Plant Health Inspection Service stamp.
(4) Amended pages shall be numbered the same as those being superseded. They shall bear the date prepared and refer to the date on the pages being superseded. If one replacement page supersedes more than one page, the new page shall indicate same, but if several replacement pages are added to supersede one page, the page number followed by letters shall be used.
(5) The last page of both copies of either a new or a completely rewritten Outline of Production and each page revised separately shall be signed in the lower left corner by the authorized representative of the licensee (or foreign producer). Stamped or facsimile signatures are not acceptable.
(6) A summary of changes shall appear on an attached page and refer to each page, paragraph, or subparagraph being changed.
(7) Transmittal forms shall be used for the original and subsequent revisions. Transmittal forms are available on the Internet at (http://www.aphis.usda.gov/animal_health/vet_bioligics/vb_forms.shtml).
(b) Special outline. An outline describing the preparation of a component of a biological product or an operation performed in the preparation of a biological product may be required if such special outline could be referred to in Outlines of Production to eliminate repetition. Each special outline shall be identified by number and shall not be used until accepted and filed by Animal and Plant Health Inspection Service.
(c) Outline of Production for antiserum, antitoxin, and normal serum shall be written according to the following:

OUTLINE GUIDE FOR PRODUCTION OF ANTISERUM AND ANTITOXIN AND NORMAL SERUM

License No. Name of Product Date

I. Serum animals.
A. Species, conditions, age, and general health.
B. Examination, preparation, care, quarantine, tests, and treatment of animals before injections are started.
C. Holding, handling, exercising, and monitoring the condition of animals after injections are started.

II. Antigens.
A. Composition and character of the antigen.
2. Source and date of accession of each micro-organism.
4. Proportions of each micro-organism and strain.
B. Identification methods used for each micro-organism and frequency with which these methods are applied.
C. Virulence and purity of cultures or antigen and the determination and maintenance thereof. Range of subcultures or passages to be used in production.
D. Attenuation, if any, before use for production purposes.
E. Character, size, and shape of containers used for growing micro-organisms.
F. Media used for stock, seed, and antigen cultures (composition and reaction of). May refer to a special outline by number.
G. Preparation of the antigen or toxin and toxoid. Complete and full description of each step and its manner of accomplishment and number these steps in sequence. Include all tests for each antigen, and the specifications for character, identity, virulence, concentration, and standardization.

III. Immunization of animals. A. Outline fully with special attention given to the following:
1. Character and dose of the antigen.