



Submission Compliance

Submitting Complete and Accurate License Applications, Outlines, and Labels

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Table of Contents

General Guidance for Submitting License & Permit Applications.....	1
General Guidance for Submitting Outlines of Production.....	2-6
Outline Cover Page Example.....	3
Outline Page 1 Example.....	4
General Guidance for Submitting Labels.....	7-10
Label Mounting Sheet Example.....	10
PEL Work Flow.....	11
L.I.E. Review of Applications.....	12
L.I.E. Review of Outlines.....	12-13
L.I.E. Review of Labels.....	13
L.I.E. and CVB Contact Information.....	14

General Guidance for Submitting License and Permit Applications (APHIS Forms 2001, 2003, and 2005)

Reference 9 CFR, Parts 102 (Licenses) and 104 (Permits). *Detailed instructions are located on the reverse sides of Form 2001 and Form 2003.* These forms are available as fillable documents found on the CVB website at:

http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalhealth/sa_vet_biologics/ct_vb_forms

In this section, we will try to define application items (blocks) on APHIS Form 2005 that may need further clarification. Attachments to applications are acceptable if the space provided in the blocks is not sufficient; if used, please refer to the block number.

2005 – Application for United States Veterinary Biological Product Permit

Fill out only those blocks pertaining to a Permit for *General Sale and Distribution*.

Product Permit Number (above Block 1) - If a company is applying for the first time, APHIS will assign this number and enter the number in this block. If you are updating a current permit, in most cases, the number will be the same so the assigned number should be entered into this blank block.

Blocks 1 and 18 - These dates should be the date that you are sending the application to CVB.

Block 3 -This is the legal name and address as stated on the Articles of Incorporation.

Block 4 -This is the legal name and address of the foreign manufacturer.

Block 8 – Leave blank.

General Guidance for Submitting Outlines of Production (Outlines)

- ❖ Indicates items required by 9 CFR 114.9

Please reference Veterinary Services Memorandum (VS Memo) No. 800.206 for complete instructions on preparing Outlines of Production.

Please submit:

- ❖ 1 APHIS Form 2015 (2015)
- ❖ 2 copies of the Outline, each with an original signature by an authorized representative
 - ❖ Sign in the lower left corner
 - Sign with blue ink (to differentiate from black and white photocopies)

Distribution:

- One copy is filed with the Center for Veterinary Biologics-Policy Evaluation and Licensing (CVB-PEL) as the official record.
- The remaining copy is returned to the establishment for their records.

Cover Page:

- ❖ Name of Biological Product (or component)
- Code 0000.00 (when assigned)
- ❖ Preparation Date of the Outline
- ❖ Name of the Licensee or Permittee
- ❖ APHIS-assigned Establishment Number

(Do not number the cover page.)

Content Pages:

- ❖ The pages shall be numbered in the upper center. Each page header shall contain the name of the biological product, the establishment license number, and the date prepared.
- ❖ A 2-inch margin is required at the **bottom** of **each page** for the “Animal and Plant Health Inspection Service” (APHIS) stamp.

On pages 3 and 4 are examples of a cover page and page 1 of an Outline.

(Cover Page Example)

Biological Product True Name

APHIS Code No. 0000.00

Preparation Date: January 10, 2014

“New” or “Complete Revision”

Supersedes: Date

(If a Complete Revision, use date from previous cover sheet)

“Establishment Name”

U.S. Veterinary License No. XXX

(Page 1 of Outline Example)

-1-

Est. Name	Biological Product True Name	Prepared: January 7, 2014
U.S. Vet. Lic. No. XXX	APHIS Code No. 0000.00	“Complete Revision” or “New” (or Supersedes Date if page is amended)

1. VS Memo 800.206 is applicable to this section.
 - A. Use an outline format. Continuation designations on subsequent pages, if applicable, are helpful (example: I.C.1. continued). Make sure all tabs are aligned, and watch for hard returns that could cause unintended repagination or alignment problems.
 - B. The 9 CFR 114.9 (c) through (f) has specifications for headings and subheadings:
 1. Outline Guide for Production of Antiserum and Antitoxin and Normal Serum
 2. Outline Guide for Vaccines, Bacterins, Antigens, and Toxoids
 3. Outline Guide for Allergenic Extracts
 4. Outline Guide for Diagnostic Test Kits
 - C. These guides are specific to the nature of the product.

Amended or Added Pages - 9 CFR 114.9(a)(4)

Amended pages are numbered the same as those being superseded. They shall bear the date prepared and refer to the date on the pages being superseded. Inserting a page, designated with a number and a letter, is acceptable to accommodate overflow of text due to changes. As an example, if an addition causes page 3 to overflow, a page 3a may be added.

Every amended page needs a signature (see details under **Signature** listed below)

Do not submit a new cover page when pages are amended.

Original Signatures - 9 CFR 114.9(a)(5)

The **last page of complete** Outlines of Production and **each page** amended **separately** shall be **signed in the lower left corner** by the authorized representative of the licensee or permittee. ***Stamped or facsimile signatures are not acceptable.***

Signatures completed in blue ink help us to distinguish original signatures from those that are photocopied.

Summary of Changes - 9 CFR 114.9(a)(6)

A summary of changes shall appear on an attached page(s), preferably behind the Outline, and refer to each **page, paragraph, or subparagraph** being changed and the reason for the change.

The summary of changes is separate; it is not a continuation of the Outline. It (if numbered) has its own set of numbers when consisting of more than one page.

Transmittal Form - APHIS Form 2015 (*full instructions on back of form*)

A single transmittal form shall be used for each new or subsequent submission. The 2015 is available on the CVB web site (see address on last page) under “Veterinary Biologic”, “Biologics Forms”.

If the product has not been licensed at the time of the submission, place an “X” in Block 7. This will serve as a priority flag for review.

Block 10 - “Complete Revision” is checked only if an entire Outline of Production is being submitted to replace the Outline of Production currently on file with APHIS.

Special Outlines - 9 CFR 114.9(b)

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 used if such a Special Outline could be referred to in multiple Outlines of Production to eliminate repetition. Each Special Outline shall be identified by number and shall not be used until approved and filed by APHIS.

These are structured the same as Product Outlines with:

- A cover page
- Pages structured in outline format
- A summary of changes for revised or amended pages
- Requirement for signatures

A Special Outline needs to be approved before referencing in a Product Outline.

General Guidance for Submitting Labels

Labels and sketches submitted on the same date for the same product code can be accompanied by a single APHIS Form 2015. *Detailed instructions are located on the reverse side of the form. **Labels and outlines need separate 2015s.***

Two copies of each label are required (CVB Notice 02-02).

When two final containers are packaged in the form of a combination package, the labels must be submitted together on a single mounting sheet. For diagnostic test kits, the labels for use on the individual reagent containers to be included in the kit shall be mounted together on a single sheet of paper, if possible. If necessary, a second sheet of paper may be used. The carton label and enclosure shall be mounted on separate mounting sheets.

Mounting Labels -9 CFR 112.5(d)(2)

Each label or sketch shall be securely fastened to a separate mounting sheet of heavy bond paper (8½” by 11”) in such a manner that all information is available for review. Computer generated labels are also acceptable as long as they are exact replicas with respect to size, color, and content. See page 10 for an example of a mounting sheet.

Subsidiary and Division Use on Labels - 9 CFR 112.4

The Subsidiary, as listed on the establishment license, may be listed as the manufacturer without reference to the licensee. Divisions, as listed on the establishment license, may only be listed in addition to the licensee’s name and address. The relationship of the division to the licensee shall appear prominently on the label by use of the term “division of” or equivalent.

For Further Manufacture Labels - VS Memorandum No. 800.54

When submitting labels For Further Manufacture, the following must appear on the labels:

- ❖ True name of the product
- ❖ “For Further Manufacture” phrase
- ❖ Serial Number
- ❖ Name, address, and establishment license number of the manufacturer
- ❖ Volume of contents
- ❖ Storage conditions

Container Labels – 9 CFR 112.2(a)(5)

- ❖ On a container label, full instructions for use and all required warning/caution statements must appear unless the resultant print size render them illegible. In this case, a reference to the box label or circular must then be included.

Distributor Labels – 9CFR 112.4 (c)

- ❖ If a distributor’s logo is used, the manufacturer’s logo must appear in equal or greater prominence.
- ❖ The distributor’s name and address must not be more conspicuous than the manufacturer’s.

Export Labels – 9 CFR 112.8 and references below

- ❖ Final containers of Products, labeled or unlabeled, may be exported in sealed shipping boxes, adequately identified as to contents with an approved label, and plainly marked “**For Export Only**”.
- ❖ Completed inactivated liquid products, antiserums, and antitoxins, may be exported in large multi-dose containers identified with an approved label that contains the words “**For Export Only**” prominently displayed.
- ❖ Concentrated inactivated liquid product, completed except for dilution to the proper strength for use, may be exported in large multiple-dose containers identified with an approved label that contains the words “**For Export Only**” prominently displayed.
- ❖ When label requirements of a foreign country conflict with APHIS requirements, **Special Labels** may be approved for use on biological products to be exported to such country per 9 CFR 112.2 (e) and VS Memorandum 800.208.

Firms requesting approval of **Special Labels for products for export** to a foreign country must submit a copy of the proposed special label along with documentation demonstrating the approval of the importing country. See VS Memo 800.208 for detailed instructions.

Foreign Language Labels – 9 CFR 112.5(e)

The foreign language portion of a bilingual label must be a direct translation of the English portion. If a label is entirely in a foreign language, an accurate English translation must be provided. It is most efficient for the CVB if an English translation is enclosed with the label submission. Alternatively, the mounting sheet may cite a previously approved English label and verify that the foreign language label is a direct translation of the cited label. See VS Memo 800.208 as it relates to foreign language labels for export products.

Standards for Displaying True Names - VS Memorandum 800.54

- ❖ The True Name of the product must appear on the label as it appears on the license, including the principal part of the True Name and descriptive terms such as “Killed Virus”. 9 CFR 112.2(a)(1)

Each term of the principal part of the True Name must receive equal emphasis with regard to size, boldness, color, etc.

Standards for Displaying Trade Names – VS Memorandum 800.54

- The trade name lettering must not exceed that of the True Name in size or boldness.
- Colors used must not render the trade name more prominent than the true name.
- The True Name must not be overshadowed by any logo, trademark, design, or company name.

Nonbiologic Sterile Diluents

When a desiccated biological product is packaged with a nonbiologic, sterile diluent, final container, both labels should be mounted on the same mounting sheet.

Experimental Biological Products - 9 CFR 103.3

Labels for experimental biological products should **not** be submitted with APHIS Form 2015 but as a part of the package required in 9 CFR 103.3. Requests to ship experimental product may be submitted electronically, preferably under cover of APHIS Form 2071.

The following must appear on experimental biological product labels:

- ❖ True Name of the product
- ❖ Storage conditions
- ❖ Name and address of the manufacturer
- ❖ Volume of contents
- ❖ Number of doses
- ❖ The statement “**Notice: For Experimental Use Only-Not For Sale**” or the equivalent.
- ❖ The United States Veterinary License legend must **NOT** appear on these labels per 9 CFR 103.3(d).

(Mounting Sheet Example)

To appear at the top of each mounting page per 9 CFR 112.5 (d) (3):

- ❖ **True Name and product code number** of product as it appears on the license or permit
- ❖ **Designation of the specimen:** - Label or Master Label - Sketch, Final Container Label, Carton Label, or Enclosure (also referred to as a circular or insert)
- ❖ **Size of package** for which the labels or enclosures are to be used

Heading Example:

Bronchitis Vaccine, Mass Type, Live Virus
Code 1231.12
Master Label: Final Container Label
200 mL - 100 doses

Label

The label is attached or printed directly on the mounting sheet. Printed labels must be an exact version of the actual label.

If true/applicable, a **direct translation statement for foreign labels** should be on the mounting sheet. See 9 CFR 112.5 (e).

To appear in the lower left corner of each page, if relevant, per 9 CFR 112.5 (d) (4):

Some firms may have a template that includes all items, but only fill in the appropriate blank(s).

- ❖ **Master label dose sizes approved for code:** *List no. of doses in each size of container or carton.* For example, a container with a total volume of 100 mL for a product that specifies a 2 mL dose would have 50 doses ($100 \div 2 = 50$). The firm should calculate this for all container/carton sizes.
- ❖ **Replacement for label, master label, and/or sketch no.:** *List APHIS-assigned label number of the label being replaced.*
- ❖ **Addition to label no.:** *List APHIS-assigned label number of the “in addition to” label.*
- ❖ **License application pending.** *List for prelicense products.*
- ❖ **Foreign language copy of label no.:** *List APHIS-assigned label number of the approved English version.*

Leave room for the APHIS stamp in the lower right corner (~ 2”H x 3”W)

PEL Workflow

1. When the mail arrives, it is opened.
2. Every piece of incoming mail is stamped with the received date.
3. The mail is then logged into the PEL mail log database.
4. For revised Outlines and labels, the currently approved documents are pulled from the files.
5. Outlines and labels are then distributed to the Legal Instruments Examiner (L.I.E.) assigned to the submitting firm.
6. Protocols, correspondence, and other reports go to the assigned Reviewer.
7. Data is reviewed by Statistics and other program personnel, as applicable, and samples received at the laboratory are tested.
8. The L.I.E. examines each Outline of Production and label submission for compliance and any applicable changes.
9. After L.I.E. review, submissions go to the Reviewer for action (response, approval, etc.).
10. After the Reviewer's determination, the documents are then passed on to an alternate Reviewer for review and a Section Leader for final approval. After that, the Support Staff performs final processing on the documents and obtains the Reviewer's signature.
11. Support staff processes the documents further by logging out of the PEL database and mailing the firm copy.

Legal Instruments Examiners (L.I.E.) Review of License Applications, Outlines, and Labels

Applications

New APHIS Forms 2001 (licensee), 2003 (products), and 2005 (product permits) are examined for completeness, accuracy of legal information (addresses, entities/companies) as compared to the Articles of Incorporation, and timeliness of the dates provided by the applicant. Updated 2001s or 2005s, submitted for establishment or permit changes, will be examined as above and compared against current records on file.

Outline of Production

The L.I.E. examines the structural form of the Outline and completes an initial review of compliance with respect to regulations so the Reviewer can concentrate on the “scientific” content and requirements.

The L.I.E. is responsible for the following examination of each document before giving it to the Reviewer.

New Outlines (also relates to Special Outlines)

Reviews the Outline to make certain pages are numbered correctly and a 2-inch margin has been left on the bottom of each page so the APHIS stamp will not cover any text on the page.

Reads for context, and checks spelling, punctuation, and grammar. Also checks for consistency of the formatting throughout the document.

Verifies the True Name of the Product and the Code Number, once assigned.

Ensures that the requirements in the 9 CFR 114, and the guidelines in the VS Memos, and CVB Notices have been followed.

Examines the outline structure per the 9 CFR.

Complete Revision of Outlines or Special Outlines

Reviews the Outline and ensures a Summary of Changes is attached and is in compliance with the 9 CFR, stating page number, paragraphs, and subparagraphs that have been changed (preferably the page number of the revised Outline). The L.I.E. confirms that all changes stated in the Summary have been made, notes any changes made that are not in the Summary, and checks to re-affirm all prior pen-and-ink changes have been made. They reference pen and ink changes not made as requested and, if provided, the firm's explanation. If only a few changes are made, but the Outline is submitted as a complete revision, it is still necessary to examine the complete document to ensure the Outline is in compliance with the 9 CFR and that all changes are noted for review.

Amended Outline Pages

When amended pages are received, the L.I.E. examines each amended page following the same guidelines as above. In this case, only amended pages, not the entire Outline, are examined.

Labels

Ensures that the information on the APHIS Form 2015 reflects the submitted label and other accompanying documents if applicable.

Checks the mounting sheet for required information (see mounting sheet example on page 10).

When new labels are submitted, checks the content for compliance according to regulations and consistency with an approved Outline, once on file.

Checks to see that Subsidiaries and Divisions are listed correctly.

Checks the font size and print clarity to make sure the label is legible.

Checks and notates if the trade name overshadows the True Name of the product.

Notates any changes from previous labels designated as replacements or any discrepancies with approved text in Section VI of the Outline of Production.

Ensures that foreign translations and approvals are provided as applicable.

Contact Information

Contact us if you have any questions regarding format, regulations, memorandums, notices, or the status of your submissions.

Request priorities through your assigned CVB-PEL Reviewer.

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To reach the current CVB Notices, VS Memos, and 9 CFR from our Home Page, click on *Veterinary Biologics* and *Biologics Regulations & Guidance*.