

LABELS

Overview

Labeling materials (e.g., container and box labels, inserts or circulars) are regulated items and must be approved by the CVB prior to use. Likewise, stocks of labeling materials are under controlled access at the firm and are subject to inventory controls.

Regulations and guidance regarding labeling materials are found in the following documents:

[9CFR 101.4](#)

Labeling terminology

[9CFR 112](#)

Main regulatory section for packaging and labeling

[VS Memorandum 800.54](#)

Guidelines for the Preparation and Review of Labeling Materials

[VS Memorandum 800.98](#)

Advertising and Promotional Materials

[VS Memorandum 800.110](#)

Exemption from Label Warning

Concerning Use of modified live IBR vaccine in pregnant cows or calves

[VS Memorandum 800.208](#)

nursing pregnant cows, 9 CFR 112.7(e)

Special Labels for Export

APHIS Final Rule 2008-0008

Labeling and Packaging Rule

APHIS Final Rule 2011-0049

Single Label Claims Rule

Definitions

Label: All written, graphic or printed matter appearing on a final container, any immediate carton or box, or any accompanying enclosures (leaflets, inserts, circulars).

Sketch: A preliminary draft of a label OR a label considered unsuitable for approval

Special Label for Export: Label approvable only under the provisions described in VS Memorandum 800.208. Practically speaking, these labels contain variances to USDA regulations regarding claims and use and therefore would not be allowable solely under the flexibility provided in 9CFR 112.2(e).

Master Label: Finished carton, container, or enclosure label for the smallest size final container, which serves as a Master template applicable to other designated size containers

Subsidiary: A corporation in which the licensed corporation owns in excess of 50% of the voting stock.

Division: A marketing unit established by the licensee

Distributor: One who sells, trades, or markets products he does not produce or import

Flow of Information

1. Labeling materials must be submitted via the portal by portal enabled firms, but may be submitted on paper for non-portal enabled firms. Instructions for processing labels electronically may be found under “PEL Guide to Processing Labels Submitted Electronically,” [REDACTED] [REDACTED] Paper submissions require an accompanying APHIS Form 2015, but portal submissions do not. Two paper copies must be submitted, although some firms may submit additional copies for their own use. The Program Assistants (PA)s automatically return any extra copies of the paper labels to the firm, after retaining 1 copy for the CVB.

Labels may be submitted as preliminary sketches or in final format. Note: Colored computer-generated images (label proofs) that are identical to, and to the same scale as, the actual label are acceptable for consideration as final labels.

2. After log-in, labeling materials are routed to the LIE. Supporting documents, such as a previously filed sketch of the label, an Outline of Production, or a foreign regulatory authorization, are used to aid in review of the current submission.

3. The LIE will do a line-wise comparison of the newly submitted label with applicable supporting documents. The LIE will also review the label for general style and compliance with the Outline and 9 CFR 112. Notations may be made on the PEL copy of the paper label or on an electronic version, in which case the LIE mark-up will be uploaded to the ML. He/She will record his/her initials and the date on the bottom left corner of the paper label mounting sheet.

4. When the LIE has completed his/her review, the label submission is forwarded to the Reviewer. The Reviewer does his/her own technical review (taking into account the notations made by the LIE) and scientific evaluation of the label. It is the Reviewer’s role to decide what is supported by filed data and what may need to be changed. [Stepwise instructions for processing electronic labels](#) are found in the [REDACTED]. The instructions for “writing” in the following instructions apply only to paper submissions.

5. After reviewing, the reviewer determines what type of processing stamp should be applied to the label. There are 4 CVB label stamps, which have been assigned numbers for easy internal reference: #1 (returned as a sketch; not approved for use), #2 (permanent approval), #3 (approved for temporary use), and #4 (special label for export). See Appendix I for examples.

5.1 If a final label is acceptable without modification, write “#2” on the mounting sheet to indicate that the #2 stamp should be added. This includes labels that meet all USDA regulations, whether for domestic or export use. See the section of this chapter named “Labels for Export Only” for additional instructions on the proper stamp for labels that meet foreign regulatory requirements but contain variances to USDA regulations.

5.2 Labels submitted as preliminary sketches are always returned as sketches, as are any other labels deemed unsuitable for processing or being returned “unprocessed” at the request of the firm. Write “#1” on the mounting sheet.

5.3 If a final format label requires immediate revision, process it as a sketch (use #1 stamp). At reviewer discretion, certain minor revisions may be deferred for a limited period of time, in which case temporary use may be granted instead.

5.4 If a final label is acceptable for temporary use, write #3 on the mounting sheet and ensure that the reviewer comments specify the expiration date. For consistency, the expiration date is expressed as the last day of the desired month.

5.5 If multiple labels are submitted in the same ML, it is acceptable to return some of the labels as sketches, and some as approved labels, if necessary. You do not have to sketch all the labels back to the firm, if only one of the labels requires revision. An explanation regarding the sketches should be provided and returned to the firm.

5.6 Labels acceptable for defined transitory periods (e.g., interim true names containing old and new taxonomy) should be assigned a #3 stamp, even though the expiration date may be years away. Likewise, assign a #3 stamp to labels that should be updated at the next printing. (Have the firm estimate how long they anticipate the initial printing to last.) If such labels are assigned #2 stamps, there is no mechanism to flag them for archival at the end of their allowable use period, nor is there any mechanism to identify these labels for follow-up if they are not replaced in a timely manner.

5.7 Unless other arrangements are made, when a submitted label replaces or supersedes an old one, the old label becomes obsolete and is archived as soon as the new one is approved. Often, however, the firm will request permission to use existing inventories of the replaced label. The firm will specify on the mounting sheet the CVB-issued identification numbers of the labels being replaced. If submitting paper, the firm will use Block 8D of the APHIS Form 2015 to request permission to use the remaining inventories of superseded labels. If this is permissible without modification, do not make a comment. An authorized CVB signature on the processed submission indicates CVB concurrence with the stated request. The default period to use superseded labels is one year. Expiration dates are standardized to

the last day of the 12th month after the date on the processed label (Date returned). Either the new or superseded labeling may be used before, or on the expiration date. If the request is denied or is acceptable only with modification, provide an explanation in a reviewer comment. These “extended use” labels remain in our active files until the expiration date, after which they are automatically archived.

Firms may designate that a label is “in addition to” a previously filed label. “In addition to” should be reserved for cases where there is no intention to retire the related label. If the firm indicates a submitted label is to be used “in addition to” an existing one (instead of as a replacement), but you suspect that the firm simply wants to use existing inventory, contact the liaison to confirm and edit the information accordingly.

5.8 Labels and sketches should never be returned “unprocessed,” unless they are submitted improperly (e.g., no APHIS Form 2015). In cases where it may seem intuitively appropriate to return a submission unprocessed, always return the submission as a sketch. This ensures that we retain a copy of the submission in our labeling files.

6. The reviewer prepares the text that will be appended as reviewer comments to the submission.

6.1 Prepare the text as a word processing document. Use the template 


6.2 Name the document according to the naming convention described in the Office Procedures section of this manual (e.g., Est_ProdCode_YYMMDD_LBL).

6.3 The document should begin with the standard wording found in Appendix II of this section of the Reviewer Manual.

6.4 If there are no comments, write “NC” on the paper mounting sheet next to the reviewer initials. This provides positive confirmation to the support staff that they do not need to be looking for a comment document.

7. Upload the reviewer comments document as Outgoing Correspondence to the mail log. If no comments, add the “No Return Form Comments” tag to the mail log. Forward the submission to the super-reviewer electronically in the mail log, and place the physical (paper) submission, if applicable, on the desk of the responsible super-reviewer.

8. After the submission has been approved by the super-reviewer, and the section leader, the PA will process paper labels:

8.1 If there are exceptions, the “CVB Exceptions Attached” box is checked in Block 16 of APHIS Form 2015 and the exceptions will be printed.

8.2 Each label mounting sheet will be stamped with the appropriate stamp. Attachments to the mounting sheet (e.g., foreign language translations, foreign government approvals) are

not typically stamped but will be stapled to the label. These documents are available in the “File Room” on Sharepoint.

8.3 Each different label in the submission will be given a unique number, automatically generated by LSRTIS. The number is written in red ink on the designated line on the CVB stamp. If a #3 stamp is used, the appropriate expiration date also will be entered.

8.4 If applicable, replaced paper labels will be stamped (see Appendix I) to indicate that existing inventories may be used through a certain date.

8.5 The signature line will be prepared on the paper 2015. The date in Block 17 of the 2015 should match the date of the stamp on the label mounting sheet.

8.7 The paper submission will be returned to the Reviewer for final signature.

9. When the processed submission is returned to the Reviewer, the Reviewer should:

9.1 Confirm that each paper copy of each label or sketch has been stamped with the proper stamp. Ensure that the correct label number has been added; this number should coincide with the label number written in Block F of APHIS Form 2015. Ensure that temporary use labels bear the correct expiration date.

9.2 Confirm that replaced labels for which the firm has requested extended use are properly stamped and dated.

9.3 Confirm that the proper reviewer comments have been attached to the 2015. Ensure the Exceptions checkbox has been checked in Block 16.

9.4 When each of the above is confirmed, sign the 2015 in Block 16. Return the submission to the PA that did the initial processing.

10. The labels will be further processed and filed as described in Step 9 of “Flow of Information” for the Outlines of Production chapter, except that obsolete labels for currently licensed products are filed in the Label Correspondence file for the firm and not in individual product files. Any extra copies submitted by the firm are returned to the firm. Supporting documents associated with foreign approvals and/or language translations are filed with the label, not the 2015. (Electronically submitted labels are not printed, so they are not found in the paper file room. The ML serves as archival storage.)

Reviewing Labels and Sketches

1. All label claims and recommendations for administration and use must be supported by data on file at the CVB. No statement may be false or misleading. Labels must meet labeling requirements which have recently been updated. For a summary of the impact of the new labeling rules, see Appendix 3.

1.1 Label claim: Labels for each product must have a claim that describes the expected efficacy of the product. There must be a claim for each antigen in the true name of the product. The claim is based on the results of the pivotal efficacy study for the given product fraction. Historically, the claim had at least 2 components: degree of protection and disease. Single tier labeling is now required for most products (vaccines, bacterins, toxoids, and immunomodulators). The syntax for the single claim is codified:

- This product has been shown to be effective for the vaccination of healthy (insert name of species) X weeks of age or older against (insert name of agent or disease). For more information regarding efficacy and safety data, see productdata.aphis.usda.gov.

1.1.1 In the case of agents that cause multiple disease syndromes, the syndrome for which efficacy has been proven must be included. Example: “Is effective against reproductive disease due to porcine respiratory and reproductive syndrome virus.”

Diseases accepted as Syndromes for purposes of single-tier labeling:

Agent	Syndromes
PRRS virus	Respiratory vs. reproductive forms
E. coli	Enteric disease vs. edema disease
Mycoplasma bovis	Respiratory vs. mastitis vs. arthritis
BVD virus	Respiratory vs. persistently infected calves
Calicivirus	Respiratory vs. systemic hemorrhagic
Campylobacter jejuni	Enteric vs. abortion
Chlamydia psittaci	Respiratory vs. abortion
Bovine coronavirus	Respiratory vs. enteric
Equine rhinopneumonitis	Respiratory vs. abortion
Haemophilus somnus	Respiratory vs. neurological
Streptococcus suis	Arthritis vs. pneumonia vs. meningitis

1.1.4 In the case of agents with multiple types or strains that are not necessarily highly cross-protective, the claim must specify the type/strain for which efficacy was demonstrated (e.g., effective against of persistently infected calves due to bovine virus diarrhea type 1).

1.1.5 Old claim syntax is *not* acceptable for new products. Ensure that all labels meet current standards before recommending a product for licensure.

1.1.6 For legacy labels, single tier wording is required by October 31, 2020.

1.1.7 When working with labels with single tier wording, follow the guidance in Reviewer Manual Chapter 4.2.2 which describes business processes associated with single tier label claims.

1.1.8 Send all Labels with single tier wording to the single tier confirmation of wording activity for review to ensure consistent review.

1.2. Route(s) of administration, number of doses, dose volume, and time interval between doses in the initial vaccination series: This must correspond to the protocol used in the pivotal efficacy study.

It is not permissible to state on a domestic-use label that a product may be co-administered or mixed with another product, even though there may be data on file to support the statement. This claim is considered to recommend the use of an unlicensed combination package.

1.3 Minimum age at vaccination: All new labels should specify a minimum age at vaccination, *unless the product is for use only in mature breeding animals*, but some historical labels lack this information. The minimum age should correspond to the age of the animals used in the field safety and efficacy studies. In cases where SPF animals with no maternal antibody are used in efficacy studies, the label may recommend revaccination at frequent intervals until maternal antibody has waned.

Historically, equine and bovine efficacy studies were often conducted using older animals after maternal antibodies have waned. Labels for these products could recommend vaccination of younger animals *provided* that the field safety study was conducted in animals of that age. In those cases, the labels recommended revaccination at 6 months of age. We are allowing firms to format their single tier labeling as follows if the supporting studies were conducted prior to the requirement to use minimum-age animals in the licensing studies:

“This product has been shown to be effective for the vaccination of healthy <insert species> against disease X. This product was licensed prior to the requirement to define a minimum age for use. For more information regarding efficacy and safety data, see productdata.aphis.usda.gov.”

1.4. Revaccination interval (after initial vaccination series): Each label must specify recommendations for revaccination beyond the initial vaccination series, as appropriate.

When supported by data, the label may disclose the proven duration of immunity. This may be expressed indirectly as a recommended revaccination interval, or the label may expressly state that the duration of immunity is at least X days.

If there are no data to support a particular revaccination interval, the label must state that the interval is unknown.

If firms request being able to maintain a connection to historical recommendations, this is the recommended format for a 2nd paragraph under the indications statement:

“Historically this product was labeled with a recommendation for revaccination at 6 months if used in animals under 6 months, and for annual revaccination thereafter, but no specific revaccination schedule has been determined.”

1.5. Slaughter withdrawal period: For products intended for food-producing animals (including horses), a slaughter withdrawal period (required time elapsed between final vaccination and slaughter) of at least 21 days must be specified, per 9CFR 112.2(a)(8). This interval is based on data (gross lesions and histopathology) provided by the firm that characterizes the vaccination site at various time periods after vaccination. See the reviewer manual chapter on adjuvants, and [Veterinary Services Memorandum 800.51](#), for more information.

Withdrawal statements are not required on oral antibody products intended solely for neonatal use. Although technically these products are subject to slaughter withdrawal times, they are used in such a manner that an acceptable withdrawal period (at least 21 days) would elapse before the animal was slaughtered.

1.6 Safety precautions: As the result of minor post-vaccination reactions noted during the pre-license field safety study or because of public health concerns, it may be appropriate to include a safety statement. Examples: “Transient swelling may be observed at the vaccination site” or “Accidental injection in humans may cause severe inflammation and necrosis.”

2. Besides the data-driven elements described above, final container labels have several other required elements. See 9CFR 112.2(a) and VSM 800.54 for details. Note that for very small containers, some of the requirements are exempted. [VSM 800.54](#) lists the minimum requirements for very small container labels.

The subtopics below contain additional information not specifically stated in either 9 CFR 112 or VSM 800.54:

2.1 Name and address of manufacturer (licensee) if produced in the United States. If imported, the name and address of the permittee, as well as the name of the foreign manufacturer, must be included. See also 9CFR 112.4.

2.1.1 Subsidiary names may be used interchangeably with the licensee name.

2.1.2 Division and distributor names must be clearly specified as such, and the licensee name also must appear. Specific guidance for distributor labels is found in VS Memorandum 800.80.

2.1.3 According to 9 CFR 112.4(b) the relationship of the division or marketing unit to the licensee shall appear prominently on the label by use of the term “division of” or equivalent. The CVB interprets the d/b/a (doing business as) designation as an equivalent method of listing the marketing unit relationship.

2.1.4 The manufacturer’s telephone number must appear on the labels. The contact number is necessary to enable the consumer to contact someone who knows about the manufacture of the product and the published licensing study data. If the firm can provide adequate assurances that the distributor is equipped and willing to handle any question

about the product, and not just adverse event reports, then the firm could potentially get an exemption to list only the distributor telephone number. If the firm cannot provide such assurances, but would still like to list the distributor telephone number, then 2 telephone numbers may be listed on the labels, one for the manufacturer, and one for the distributor.

2.2 USDA Establishment Number: This number must appear on all labels, even those used solely for export, as it is recognized by our international trading partners as evidence that the label has been approved by APHIS. Imported product must contain the USDA Permit Number. The only exceptions are Special Labels for Export, labels for experimental product, and labels for unlicensed products exported under FDA-EREA, all of which must not bear the license number.

2.3 Serial number. Do not use the word “Lot” in lieu of Serial on domestic labels. In the U.S., Lot is used to identify individual components of test kits so that they are not confused with the serial number of the overall kit.

2.4 Permitted expiration date for the serial: The label for this information should be “Expiration” or “Exp.” on labels for domestic use.

2.5 The label must be legible. If the label is electronic, it should display at 100% size unless there is a statement to the contrary on the mounting sheet. Review at an equivalent of 100% to assess readability.

2.6 Per VSM 800.54 , certain internationally recognized symbols may be used on diagnostic kit labels. The [list of currently approved symbols](#) is on the CVB website. Additional symbols may be considered with appropriate justification, provided the symbol has not been disallowed in previous communication.

2.7 Bilingual or foreign-language labels are permissible, provided that a direct English translation is provided. If the label is intended for domestic use, however, English must be one of the languages on it.

3. Carton labels also have required elements and packaging restrictions, described in 9CFR 112.2(b) and [VSM 800.54](#).

4. Inserts have content expectations described in [VSM 800.54](#).

5. Products containing certain antigens are subject to additional requirements. See 9CFR 112.7 for requirements for the following:

- live Newcastle disease virus
- infectious bronchitis virus

- Marek's disease virus
- rabies virus
- modified live infectious bovine rhinotracheitis virus
- *Clostridium hemolyticum*
- *Clostridium botulinum Type C*
- *Erysipelothrix rhusiopathiae*
- canine adenovirus type 2
- feline panleukopenia virus
- autogenous biologics
- Conditional licenses
- wart vaccine
- normal serum, antiserum
- diluents not tested for viricidal activity

Considerations should also be made for other specific antigens, including those that may be used in program disease eradication efforts.



Note that other products may have license restrictions that should be reflected on the label.

Examples:

- Products for further manufacture (FFM)
- Other restrictions that pertain to product use (e.g., diagnostic test kits that are to be used with a specific marker vaccine, products that are to be used only upon the approval of APHIS).

Submission Format

Each label or circular must be mounted on an appropriately labeled mounting sheet. See 9CFR 112.5(d)(1) for specific requirements. Electronic labels should be mounted on the [CVB label template](#); substitutes are not currently allowed.

The top of a paper mounting sheet should contain:

- true name and product code
- label type (label/master label/sketch; container, carton, or circular)
- package size(s) (doses/ml/cc/units) for which the labels will be used

The lower left corner of a paper mounting sheet should contain:

- Explanation of the submission (i.e., what label(s) it replaces or is in addition to, if the license application is pending)

The following should appear somewhere on the paper mounting sheet:

- if the label is for Export Only
- For foreign language labels, a statement that the text is a direct translation of approved English text (or an explanation for differences can be provided)

Labels for Export Only

Firms often submit labels that are used only for serials exported to foreign countries. Use of such labels must be authorized by the CVB if the labels are applied to the product while it is in the U.S. See 9CFR 112.8 and [VSM 800.208](#) for additional detail. Such labels also undergo review and approval in the receiving country, which may have different labeling requirements, or allow different labeling statements, than does APHIS. In such cases, labels that do not meet the requirements of the 9CFR may be approved for export purposes either under our regular processing workflow (i.e., with a #2 or #3 stamp) or as a Special Label for Export (i.e., #4 stamp).

The following items are needed to approve an export label containing variances to APHIS regulations:

- Copy of foreign regulatory authorization from receiving country is required only for special labels for export. Copy of foreign regulatory authorization is not required for export only labels that include minor variances from current labeling requirements in the United States. Minor variances may include disclosure of preservatives, or slaughter withdrawal times. The content and appearance of such documentation varies greatly from country to country. It may, or may not, include an actual label approved by foreign regulators.
- A direct translation of any foreign text, if applicable
- Statement on the mounting sheet that the label is for EXPORT ONLY

The reviewer must determine whether the variances on an export label are “cosmetic” or pertain to claims or product use. Cosmetic changes include formatting or text elements required in APHIS regulations but, without which, the label maintains acceptable descriptions of product expectations (claims) and proper use. Labels containing only cosmetic differences should be processed with a #2 or #3 stamp under the flexibilities provided in 9CFR 112.2(e). Those with statements for claims or use that have not been approved by the CVB are approvable only under the additional flexibility provided in VS Memorandum 800.208 and must be processed with a #4 stamp.

A list of potential variances is maintained in [Chapter 4.2.1](#) Precedents for International Label Non-Compliance. The spreadsheet identifies the stamp under which the variance has previously been approved and describes any variance-specific instructions for processing. It is the responsibility of the reviewer to process labels consistent with those precedents and to request that the spreadsheet be updated when new variances arise.

Labels processed with a #2 or #3 stamp must include the USDA Establishment Number. If a label otherwise eligible for a #2 or #3 stamp is submitted without a USDA Establishment Number, contact the firm to discuss adding the Establishment Number. The number is a required element for approval unless the firm can provide documentation that the foreign regulatory authority does not allow it. (This differs from simply providing a foreign approval of a label that does not bear the number, as this does not prove that the regulators would have rejected a label that did contain the number.)

Labels processed with a #4 stamp must NOT bear the USDA Establishment Number. These labels also are not eligible for Certificates of Licensing and Inspection.

The regulatory authorizations from some countries are for a finite period and/or are subject to periodic renewal. If a label is processed with a #4 stamp, the CVB approval of the label should terminate when the current foreign regulatory authorization expires. There is a space on the #4 stamp to insert an expiration date (i.e., “Use permitted until...”). If the foreign authorization does not expire and is not subject to renewal, then insert the phrase “further notice” in the date blank on the #4 stamp (“Use permitted until further notice.”) If an export label is processed with a #2 or #3 stamp, it is not necessary to define a CVB expiration date solely because the foreign authorization has an expiration.

Note that not all labels designated by the firm as Export Only will be unacceptable for domestically marketed product; it simply may be that this is the only intended use that they have.

When a label is approved as an export only label, the submission must include clarification regarding which countries are applicable. The phrase “for export only to (name of the country)” should appear on the mounting sheet, or the submission description, or clarified in the synopsis of the reviewer response.

Labels for Permitted (Imported) Product

If a label is approved for a product imported under a Permit for General Sale and Distribution, add the following comment to the Exceptions section of the APHIS Form 2015:

This label is to be used only on containers and packaging imported into the United States. Use of this label on serials (or portions thereof) not imported into the United States is prohibited.

This comment is intended to remind foreign manufacturers that they are not to use labels identifying the product as licensed by the USDA on any containers of product that they may distribute in countries other than the US. The veterinary permit number implies not only that the

product is licensed (permitted) in the US, but also that the individual serial (or portion thereof) has undergone serial release by APHIS. Only those containers that have been imported into the US may bear this assurance.

Master Label Concept

To reduce the amount of paperwork associated with label submissions, the Master Label concept (9CFR 112.5(d)(1)) was adopted. Many products are marketed in various package sizes; the labels for each size are often identical except for physical size and the text regarding the number of doses and recoverable volume. In those cases, it is permissible for the licensee or permittee to submit only the label for the *smallest* package size. This label becomes the Master Label and serves as a template for other larger package sizes, which are specified on the mounting sheet. It is not necessary to submit the other related presentations; such labels are approved concurrently with the submitted Master Label.

Minor Label Changes

Although most label changes must be approved prior to using the modified labels on licensed product, there are certain minor changes (9CFR 112.5(c)(2)) that do not require prior approval, provided that they do not render the label false or misleading and do not affect legibility. Labels containing minor changes, however, must be submitted within 60 days of label use. Currently accepted minor changes include:

- Change in physical dimensions
- Change in color of label print or background
- Addition or deletion of Trade Mark or Registered symbol
- Correction of typographical errors
- Adding or changing barcodes/label control numbers/contact numbers
- Revising or updating logos
- Changing an Est # after an approved merger/acquisition
- Change distributor

Diluent Labels

There are special requirements, described in 9CFR 112.3, for labels placed on inert (i.e., contains no biological agents) diluents that are used to reconstitute lyophilized biological products. The following must be included:

- The name (Sterile Diluent)
- True name of biological product with which the diluent is packaged (unless the firm has another method of matching the correct diluent to the product)
- Recoverable volume, in cc or ml
- Serial number
- Name and address of licensee or permittee

Additional requirements, described in 9CFR 112.3(f), apply if the diluent and desiccated portions will come into contact while the diluent is in its original container.

Approval of labels before a product is licensed or permitted

Approved labeling materials must NOT be returned to the license or permit applicant before the license or permit is issued. Sketches may be returned at any time, according to the procedure described above. When a final label suitable for use on licensed product is submitted, add a “Hold Pending Licensure” tag to the mail log item and, the label is paper, put it in the prelicensing file. The label is processed with a #2 (or #3) stamp *at the time the license is prepared for signature*. The PA who prepares the license will process the label.

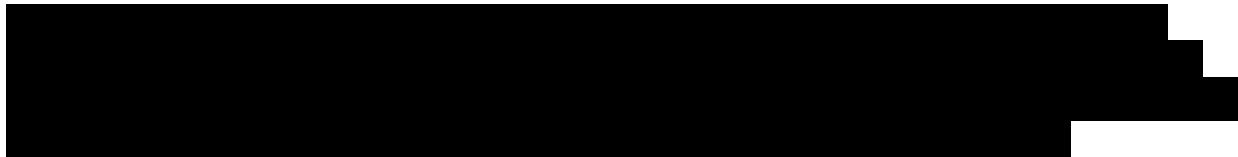
Experimental Use Labels

Labels used on unlicensed product for experimental use have specific requirements that are discussed in the chapter, “Experimental Shipment of Biological Product.” Such labels do NOT undergo the same approval process as labels for licensed product and are not stamped with any of the CVB stamps.

Packaging

Specific packaging requirements are described in 9CFR 112.6 for the following products:

- Multiple-dose containers that require a diluent for administration
- Single-dose products that require a diluent for administration
- Poultry products for mass administration (including, but not limited to, administration through the drinking water)
- Marek’s Disease Vaccine
- Poultry vaccines administered to individual birds via automatic equipment



Appendix I. CVB Stamps Used on Paper Labeling Materials

#1 stamp—used for sketches

SKETCH NO. _____
USDA-APHIS-VS
CENTER FOR VETERINARY BIOLOGICS
OCT 06 2010
POLICY, EVALUATION, AND LICENSING
FINISHED LABEL MUST NOT BE
USED UNTIL AUTHORIZED

2 stamp—used for permanently approved labels

LABEL NO. _____
USDA-APHIS-VS
CENTER FOR VETERINARY BIOLOGICS
OCT 06 2010
POLICY, EVALUATION, AND LICENSING
USE PERMITTED UNTIL FURTHER NOTICE

#3 Stamp; used to approve labels for temporary use (expiration date is entered at the bottom)

LABEL NO. _____
USDA-APHIS-VS
CENTER FOR VETERINARY BIOLOGICS
SEP 29 2010
POLICY, EVALUATION, AND LICENSING
TEMPORARY USE UNTIL

#4 Stamp; used to process Special Labels for Export

SPECIAL EXPORT LABEL _____
USDA-APHIS-VS
CENTER FOR VETERINARY BIOLOGICS

AUTHORIZED SOLELY ON BASIS OF
IMPORTING COUNTRY'S CONSENT

NOT FOR USE ON PRODUCT
DISTRIBUTED IN THE UNITED STATES

USE PERMITTED UNTIL

Extended use stamp; used when firms request continued use of current inventories of labels that have been replaced

EXTENDED USE
EXPIRES

FEB 28 2014





3 9CFR 112 Integrated Version Showing Impact of Single Tier and Packaging/Labeling Rules (inclusive of technical amendments)

§ 112.1 General.

(a) Unless otherwise authorized or directed by the Administrator, each biological product prepared at a licensed establishment, or imported, shall be packaged and labeled as prescribed in this part before it is removed from the licensed establishment or presented for importation: *Provided*, That biological products to be imported for research and evaluation shall be subject to packaging and labeling requirements in § 112.9. *Provided further*, That, unless otherwise exempted, all preparation, including packaging and labeling, of biological products shall only be performed in a licensed establishment under an approved Outline of Production.

(b) No person shall apply or affix to or include with, or cause to be applied or affixed to or included with, any carton or final container of a biological product, any label, stamp, mark or statement that is

false or misleading in any particular, is not in compliance with the regulations, or is not approved by APHIS.


(c) No person shall alter, mark or remove any approved labeling affixed to or included with any biological product prior to selling or otherwise distributing such product. In addition, no person shall mark any carton, other container, or final container of a biological product so as to falsify the labeling, make it misleading, or cause it to be illegible.

(d) Labels that are stamped, printed or glued directly on cartons, other containers, or final containers shall be legible throughout the dating period. Biological products bearing labels, which have been altered, mutilated, destroyed, obliterated or removed, shall be withheld from the market.

§ 112.2 Final container label, carton label, and enclosure.

(a) Unless otherwise provided, final container labels, carton labels, and enclosures (inserts, circulars, or leaflets) shall include the information specified in this section.

New	Old
<p>(1) The complete true name of the biological product which name shall be identical with that shown in the product license under which such product is prepared or the permit under which it is imported, shall be prominently lettered and placed giving equal emphasis to each word composing it. Descriptive terms used in the true name on the product license or permit shall also appear. Abbreviations of the descriptive terms may be used on the final container label if complete descriptive terms appear on the carton label and enclosure. The following exceptions are applicable to small final containers, and containers of interchangeable reagents included in diagnostic test kits:</p> <ul style="list-style-type: none"> (i) For small final containers, an abbreviated true name of the biological product, which shall be identical with that shown in the product license under which the product is prepared or the permit under which it is imported, may be used: <i>Provided</i>, That the complete true name of the product must appear on the carton label and enclosures; (ii) In addition to the true name of the kit, the functional and/or chemical name of the reagent must appear on labeling for small final containers of reagents included in diagnostic kits: <i>Provided</i>, That the true name is not required on labeling for small final containers of interchangeable (noncritical) components of diagnostic kits. 	<p>(1) The principal part of the true name of the biological product which name shall be identical with that shown in the product license under which such product is prepared, or the permit under which it is imported, shall be prominently lettered and placed giving equal emphasis to each word composing it. Descriptive terms used in the true name on the product license or permit shall also appear. Abbreviations of the descriptive terms may be used on the final container label if complete descriptive terms appear on a carton label and enclosures;</p>
<p>(2) For biological product prepared in the United States or in a foreign country, the name and address of the producer (licensee, or subsidiary) or permittee and of the foreign producer, and an appropriate consumer contact telephone number: <i>Provided</i>, That in the case of a biological product exported from the United States in labeled final containers, a consumer contact telephone number is not required; however, small single dose containers marketed</p>	<p>(2) If the biological product is prepared in the United States, the name and address of the producer (licensee or subsidiary) or if the biological product is prepared in a foreign country, the name and address of the permittee and of the foreign producer.</p>

New	Old
<p>in the United States must include contact telephone information on carton and enclosures.</p> <p>(3) The United States Veterinary Biologics Establishment License Number (VLN) or the United States Veterinary Biological Product Permit Number (VPN), and the Product Code Number (PCN) assigned by the Department, which shall be shown only as "VLN/PCN" and "VPN/PCN," respectively, except that:</p> <ul style="list-style-type: none"> (i) Only the VLN or VPN is required on container labels of interchangeable (non-critical) components of diagnostic kits and container labels for individual products packaged together for coadministration. (ii) The PCN may be used in lieu of the true name of the kit on small container labels for critical components of diagnostic kits. (iii) Container labels for individually licensed biological products, when marketed as components of combination packages, must include a statement referring the consumer to the carton or enclosure for the PCN of the combination package. 	
<p>(3) The United States Veterinary Biologics Establishment License Number (VLN) or the United States Veterinary Biological Product Permit Number (VPN), and the Product Code Number (PCN) assigned by the Department, which shall be shown only as "VLN/PCN" and "VPN/PCN," respectively, except that:</p> <ul style="list-style-type: none"> (i) Only the VLN or VPN is required on container labels of interchangeable (non-critical) components of diagnostic kits and container labels for individual products packaged together for coadministration. (ii) The PCN may be used in lieu of the true name of the kit on small container labels for critical components of diagnostic kits. (iii) Container labels for individually licensed biological products, when marketed as components of combination packages, must include a statement referring the consumer to the carton or enclosure for the PCN of the combination package. 	<p>(3) The license or permit number assigned by the Department which shall be shown only in one of the following forms respectively: "U.S. Veterinary License No. _____," or "U.S. Vet. License No. _____," or "U.S. Vet Lic. No. _____," or "U.S. Veterinary Permit No. _____," or "U.S. Permit No. _____."</p>
<p>(4) Storage temperature recommendation for the biological product stated as 2 to 8 °C or 35 to 46 °F, or both.</p>	<p>(4) Storage temperature recommendation for the biological product stated as not over 45 °F. or stated as not over 7 °C. or stated as not over 45 °F. or 7 °C.</p>

New	Old
<p>(5) Full instructions for the proper use of the product, including indications for use, target species, minimum age of administration, route of administration, vaccination schedule, product license restriction(s) that bear on product use, warnings, cautions, and any other vital information for the product's use; except that in the case of limited space on final container labels, a statement as to where such information is to be found, such as "See enclosure for complete directions," "Full directions on carton," or comparable statement.</p>	<p>(5) An indications statement to read, "This product has been shown to be effective for the vaccination of healthy (insert name of species) ___ weeks of age or older against ___. <i>Provided</i>, That in the case of very small final container labels or carton, a statement as to where such information is to be found, such as "See enclosure for complete directions," "Full directions on carton," or comparable statement; (This was moved to subsection 12.)</p>
<p>6) No changes</p>	<p>(6) In the case of a multiple-dose final container, a warning to use entire contents when first opened: <i>Provided</i>, That a diagnostic or a desensitizing antigen packaged in a multiple-dose final container is exempt;</p>
<p>(7) The following warning statements, or equivalent statements, shall appear on the labeling as applicable:</p> <ul style="list-style-type: none"> (i) Products other than diagnostic kits: "Do not mix with other products, except as specified on this label." (ii) Injectable products and other products containing hazardous components: "In case of human exposure, contact a physician." (iii) Products containing viable organisms: "Inactivate unused contents before disposal." 	<p>(7) If the biological product contains viable or dangerous organisms or viruses, a warning to "Burn this container and all unused contents," except that in the case of a small one-dose container, the statement "Burn this container" or "Burn this vial" may be used.</p>
<p>(8) No change</p>	<p>(8) In the case of a biological product recommended for use in domestic animals, the edible portion of which may be used for food purposes, a withholding statement of not less than 21 days to read: "Do not vaccinate within (insert number) days before slaughter" or "Do not vaccinate food-producing animals within (insert number) days before slaughter": <i>Provided</i>, That longer periods shall be stated when deemed necessary by the Administrator. Very small final container labels are exempted from this requirement.</p>

New	Old
<p>(9) Same as old version except for addition of subsection (v):</p> <p>(v) A statement similar to “For more information regarding efficacy and safety data, go to <i>productdata.aphis.usda.gov</i>.”</p>	<p>(9) The following information shall appear on the final container label and carton label, if any, but need not appear on the enclosure:</p> <ul style="list-style-type: none"> (i) A permitted expiration date; (ii) The number of doses where applicable; (iii) The recoverable quantity of the content of each final container stated in cubic centimeters (cc.) or milliliters (ml.) or units. (iv) A serial number by which the product can be identified with the manufacturer's records of preparation: <i>Provided</i>, That when a liquid antigenic fraction is to be used instead of a water diluent for one or more desiccated antigenic fractions in a combination package, a hyphenated serial number composed of a serial number for the desiccated fraction and the serial number for the liquid fraction shall be used on the carton;
<p>(10) In the case of a product that contains a preservative that is added during the production process and is not reduced to undetectable levels in the completed product through the production process, the statement “Contains [name of preservative] as a preservative” or an equivalent statement must appear on cartons and enclosures, if used. If cartons are not used, such information must appear on the final container label.</p>	<p>(10) In the case of a product which contains an antibiotic added during the production process, the statement “Contains ___ as a preservative,” or an equivalent statement indicating the antibiotic added shall appear on cartons and enclosures if used: <i>Provided</i>, That if cartons are not used, such information shall appear on the final container label;</p>
<p>No change</p>	<p>(11) The number of final containers of biological product and the number of doses in each final container shall be stated on each carton label for all cartons containing more than one final container of biological product. The number of final containers of diluent, if any, and the quantity in each shall also be stated on each carton label.</p>
<p>(12) An indications statement to read, “This product has been shown to be effective for the vaccination of healthy (insert name of species) ___ weeks of age or older against ___.” <i>Provided</i>, That in the case of very small final container labels or carton, a statement as to where such information is to be found, such as “See enclosure for complete directions,” “Full directions on carton,” or comparable statement.</p>	<p>No prior #12. What now is in #12 used to be in subsection 5..</p>

(b) Labels may also include any other statement which is not false or misleading and may include factual statements regarding variable response of different animals when vaccinated as directed but may not include disclaimers of merchantability, fitness for the purpose offered, or responsibility for the product.

(c) Labels of biological products prepared at licensed establishments or imported shall not include any statement, design, or device, which overshadows the true name of the product as licensed or which is false or misleading in any particular or which may otherwise deceive the purchaser.

New	Old
<p>d) Carton labels and enclosures shall be subject to paragraph (d)(1), (d)(2), and (d)(3) of this section.</p> <p>(1) The statement, "Restricted to use by or under the direction of a veterinarian" or "Restricted to use by a veterinarian," shall be used on all carton labels and enclosures when such restriction is prescribed on the product license.</p> <p>(2) If the licensee states on the carton labels and enclosures of a product that its sales are restricted to veterinarians, then the entire production of that particular product in the licensed establishment shall be so restricted by the licensee.</p> <p>(3) The statement "For use in animals only" may appear on the labeling as appropriate for a product to indicate that the product is recommended specifically for animals and not for humans.</p>	<p>(d) Carton labels and enclosures shall be subject to paragraph (d)(1), (d)(2), and (d)(3) of this section.</p> <p>(1) The statement, "Restricted to use by or under the direction of a veterinarian" or "Restricted to use by a veterinarian," shall be used on all carton labels and enclosures when such restriction is prescribed on the product license.</p> <p>(2) If the licensee states on the carton labels and enclosures of a product that its sales are restricted to veterinarians, then the entire production of that particular product in the licensed establishment shall be so restricted by the licensee.</p> <p>(3) The statement "For veterinary use only" or an equivalent statement may appear on the carton labels and enclosures for a product if such statement is being used to indicate that the product is recommended specifically for animals, and not for humans</p>
<p>(e) When label requirements of a foreign country differ from the requirements as prescribed in this part, special labels may be approved by APHIS for use on biological products to be exported to such country upon receipt of written authorization, acceptable to APHIS, from regulatory officials of the importing country, provided that:</p> <p>(1) If the labeling contains claims or indications for use not supported by data on file with APHIS, the special labels for export shall not bear the VLN.</p> <p>(2) All other labels for export shall bear the VLN unless the importing country provides documentation that the VLN is specifically prohibited. When laws, regulations, or other requirements of foreign countries require exporters of biological products prepared in a licensed establishment to furnish official certification that such products have been prepared in accordance with the Virus-Serum-Toxin Act and regulations issued pursuant to the Act, such certification may be made by APHIS.</p>	<p>(e) When label requirements of a foreign country conflict with the requirements as prescribed in this part, special labels may be approved for use on biological products to be exported to such country. When laws, regulations, or other requirements of foreign countries require exporters of biological products prepared in a licensed establishment to furnish official certification that such products have been prepared in accordance with the Virus-Serum-Toxin Act and regulations issued pursuant thereto, such certification may be made by Animal and Plant Health Inspection Service upon request of the licensee.</p>

<p>(f) Multiple-dose final containers of liquid biological product and carton tray covers showing required labeling information are subject to the requirements in this paragraphs.</p> <p>(1) If a carton label or an enclosure is required to complete the labeling for a multiple-dose final container of liquid biological product, only one final container, with a container of diluent if applicable, shall be packaged in each carton: <i>Provided</i>, That if the multiple dose final container is fully labeled without a carton label or enclosure, two or more final containers, and a corresponding number of diluent containers, may be packaged in a single carton which shall be considered a shipping box. Labels or stickers for shipping boxes shall not contain false or misleading information, but need not be submitted to APHIS for approval.</p> <p>(2) When required labeling information is shown on a carton tray cover, it must be printed on the outside face of such tray cover where it may be read without opening the carton. The inside face of the tray cover may contain information suitable for an enclosure.</p>	<p>(f) If a carton label or an enclosure is required to complete the labeling for a multiple-dose final container of liquid biological product, only one final container shall be packaged in each carton: <i>Provided</i>, That if the multiple-dose final container is fully labeled without a carton label or enclosure, two or more final containers may be packaged in a single carton which shall be considered a shipping box. Labels or stickers for shipping boxes shall not contain false or misleading information but need not be submitted for approval.</p>
---	---

§ 112.3 Diluent labels. Each final container of diluent, other than a liquid biological product, packaged with desiccated biological products shall bear a label that includes the following:

- (a) The name—Sterile Diluent.
- (b) True name of the biological product with which the diluent is packaged, except that when the firm packages all desiccated biological products with the same diluent, or two or more types of diluent are used, and the licensees' methods of identification and storage insure that all products are packaged with the correct type of diluent, labels affixed to the containers of diluent are exempt from this provision.
- (c) The recoverable quantity of contents in cubic centimeters (cc) or milliliters (ml).
- (d) A serial number by which the diluent can be identified with the manufacturer's records of preparation;
- (e) Name and address of the licensee or the permittee;
- (f) In the case of a diluent with which a desiccated biological product is to come in contact while the diluent is in its original container; and,
 - (1) Is in a multiple-dose container, a positive warning that all of the biological product shall be used at the time the container is first opened; and/or

New	Old
(2) The biological product is composed of viable or dangerous organisms or viruses, the notice, "Inactivate unused contents before disposal."	(2) The biological product is composed of viable or dangerous organisms or viruses, the notice, "Burn this container and all unused contents," except that, in the case of a small one-dose container, the statement "Burn this container" or "Burn this vial" may be used.

(g) The establishment license number or the permit number, as the case may be, in one of the forms provided in § 112.2(a)(3).

§ 112.4 Subsidiaries, divisions, distributors, and permittees. Labels used by subsidiaries, divisions, distributors, and permittees shall be affixed by the licensee in a licensed establishment where the product is produced. Such labels shall comply with requirements for their review, approval, and filing as provided in the regulations.

(a) *Subsidiaries*. Labels to be used on a licensed biological product prepared by a subsidiary operating in a licensed establishment shall be submitted in accordance with § 112.5. Only labels approved for use on such product shall be used by the subsidiary.

(b) *Divisions*. Labels to be used on a licensed biological product prepared in a licensed establishment for distribution by a division or marketing unit of the licensee shall be submitted in accordance with § 112.5. The name, address, and license number of the licensee shall be prominently placed on such labels. The relationship of the division or marketing unit to the licensee shall appear prominently on the label by use of the term “division of” or equivalent.

(c) *Distributors*. The name and address of the distributor or any statement, design, or device shall not be placed on the labels or containers of a licensed biological product in a manner which could be false or misleading or which could indicate that the distributor is the manufacturer of such product or operating under the license number shown on the label. The manufacturer shall be identified by name, address, and license number with the term “manufactured by,” “produced by,” or an equivalent term prominently placed in connection therewith. The name and address of the distributor may be placed on labels or containers if the term “distributor,” or “distributed by,” or an equivalent term is prominently placed in connection therewith.

(d) *Permittees*. The name and address of the permittee and any statement, design, or device shall not be placed on the labels or containers of a biological product imported for sale and distribution in accordance with § 104.5 in a manner which could be false or misleading or which could falsely indicate that the permittee is the manufacturer of such product. The manufacturer shall be identified by name and address with the term “manufactured by,” “produced by,” or an equivalent term prominently placed in connection therewith. Reference to the permittee shall be made by name, address, and permit number with the term “imported by,” “produced for,” or an equivalent term prominently placed in connection therewith.

§ 112.5 Review and approval of labeling. Labels used with biological products prepared at licensed establishments or imported for general distribution and sale must be submitted to the Animal and Plant Health Inspection Service for review for compliance with the regulations and approval in writing prior to use, except as provided in paragraph (d) of this section and under the master label system provided in paragraph (e) of this section.

New	Old
<p>(a) Transmittal forms, available on the Internet at https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/veterinary-biologics/sa_bio_forms/ct_vb_forms, shall be used with each submission of sketches (including proofs) and labels. Separate forms shall be used for each biological product but only one copy of the form shall be used for all sketches and labels submitted at the same time for the same biological product.</p>	<p>(a) Transmittal forms, available on the Internet at (http://www.aphis.usda.gov/animallhealth/vetbiologics/vblforms.shtml), shall be used with each submission of sketches (including proofs) and labels. Separate forms shall be used for each biological product but only one copy of the form shall be used for all sketches and labels submitted at the same time for the same biological product.</p>
<p>(b) A data summary, available on the Internet at productdata.aphis.usda.gov, shall be used with each submission of efficacy and safety data in support of a label claim. Manufacturers will submit the efficacy and safety data information with either the efficacy and safety studies or at the time of label submission. This information will be posted</p>	<p>This subsection did not exist prior to 2016. When the new subsection b was added, old sections b through g were redesignated as c through h.</p>

New	Old
<p>at productdata.aphis.usda.gov to allow public disclosure of product performance.</p>	
<p>No change other than redesignating the Sketch reg as (c). [REDACTED]</p>	<p>(b) Sketches may be submitted for comment to Animal and Plant Health Inspection Service by the licensee or permittee before preparing the finished label. Such sketches shall be returned to the licensee or permittee with comments, if any. Failure of the reviewer to take exception to a sketch shall not constitute approval of a finished label subsequently prepared.</p>
<p>(d)</p> <p>(1) Labels must be submitted to the Animal and Plant Health Inspection Service for review and written approval. Only labels which are approved as provided in paragraph (e) of this section may be used. When changes are made in approved labels, the new labels shall be subject to review and approval before use: <i>Provided</i>, That certain minor changes may be made in labels for products with approved labels or master labels, and the revised labels may be used prior to review by APHIS, with the provision that a new label or master label bearing these changes is submitted to APHIS for review and written approval within 60 days of label use, and that such minor changes do not render the product mislabeled or the label false and misleading in any particular.</p> <p>(2) Minor label changes that may be made under the provision for products with approved labels or master labels are:</p> <ul style="list-style-type: none"> (i) Changes in the physical dimensions of the label provided that such change does not affect the legibility of the label; (ii) Change in the color of label print or background, provided that such change does not affect the legibility of the label; (iii) The addition or deletion of a Trade Mark (TM) or Registered (R) symbol; (iv) The correction of typographical errors; (v) Adding, changing, or deleting label control numbers of bar codes; and (vi) Revising or updating logos. (vii) Changing the telephone contact number; (viii) Adding, changing, or deleting an email and/or Web site address; (ix) Changing the establishment license or permit number assigned by APHIS, and/or changing the name and/or address of the manufacturer or permittee, provided that such changes are identical to information on the current establishment license or permit; 	<p>(c)</p> <p>(1) Labels must be submitted to the Animal and Plant Health Inspection Service for review and written approval. Only labels which are approved as provided in 112.5(d) may be used. When changes are made in approved labels, the new labels shall be subject to review and approval before use: <i>Provided</i>, That certain minor changes may be made in labels for products with approved labels or master labels, and the revised labels may be used prior to review by APHIS, with the provision that a new label or master label bearing these changes is submitted to APHIS for review and written approval within 60 days of label use, and that such minor changes do not render the product mislabeled or the label false and misleading in any particular.</p> <p>(2) Minor label changes that may be made under the provision for products with approved labels or master labels are:</p> <ul style="list-style-type: none"> (i) Changes in the physical dimensions of the label provided that such change does not affect the legibility of the label; (ii) Change in the color of label print, provided that such change does not affect the legibility of the label; (iii) The addition or deletion of a Trade Mark (TM) or Registered (R) symbol; (iv) The correction of typographical errors; (v) Adding or changing label control numbers of bar codes; and (vi) Revising or updating logos.

New	Old
<p>and (x) Adding or changing the name and/ or address of a distributor.</p>	
<p>(e) Labels and sketches submitted shall be prepared in the number and manner prescribed in this paragraph.</p> <p>(1) Copies required:</p> <p>(i) For label sketches, submit two copies of each sketch of a final container label, carton label, and enclosure. Sketches must be legible, and must include all information specified in § 112.2. One copy of each sketch will be returned with applicable comments, and one copy will be held on file by APHIS for no more than one year after processing, until replaced by a finished label: <i>Provided</i>, That sketches submitted in support of an application for a license or permit shall be held as long as the application is considered active.</p> <p>(ii) For master label sketches, submit for each product two copies of each sketch of an enclosure, label for the smallest size final container, and carton label; <i>Provided</i>, That labels for larger size containers and/or cartons that are identical, except for physical dimensions, need not be submitted. One copy of each master label sketch will be returned with applicable comments, and one copy will be held on file by APHIS for one year after processing, until replaced by a finished master label that is submitted according to paragraph (e)(1)(iii) of this section: <i>Provided</i>, That master label sketches submitted in support of an application for license or permit shall be held as long as the application is considered active.</p> <p>(iii) For finished labels, submit two copies of each finished final container label, carton label, and enclosure: <i>Provided</i>, That when an enclosure is to be used with more than one product, one extra copy shall be submitted for each additional product. One copy of each finished label will be retained by APHIS. One copy will be stamped and returned to the licensee or permittee. Labels to which exceptions are taken shall be marked as sketches and handled under paragraph (e)(1)(i) of this section.</p> <p>(iv) For finished master labels, submit for each product two copies each of the enclosure and the labels for the smallest</p>	<p>(d) Labels and sketches submitted shall be prepared in the number and manner prescribed in this paragraph.</p> <p>(1) Copies required:</p> <p>(i) For label sketches, submit two copies of each sketch of a final container label, carton label, and enclosure. Sketches must be legible, and must include all information specified in § 112.2. One copy of each sketch will be returned with applicable comments, and one copy will be held on file by APHIS for no more than one year after processing, until replaced by a finished label: <i>Provided</i>, That sketches submitted in support of an application for a license or permit shall be held as long as the application is considered active.</p> <p>(ii) For master label sketches, submit for each product two copies of each sketch of an enclosure, label for the smallest size final container, and carton label; <i>Provided</i>, That labels for larger size containers and/or cartons that are identical, except for physical dimensions, need not be submitted. One copy of each master label sketch will be returned with applicable comments, and one copy will be held on file by APHIS for one year after processing, until replaced by a finished master label that is submitted according to paragraph (e)(1)(iii) of this section: <i>Provided</i>, That master label sketches submitted in support of an application for license or permit shall be held as long as the application is considered active.</p> <p>(iii) For finished labels, submit two copies of each finished final container label, carton label, and enclosure: <i>Provided</i>, That when an enclosure is to be used with more than one product, one extra copy shall be submitted for each additional product. One copy of each finished label will be retained by APHIS. One copy will be stamped and returned to the licensee. Labels to which exceptions are taken shall be marked as sketches and handled under paragraph (d)(1)(i) of this section.</p> <p>(iv) For finished master labels, submit for each product two copies each of the enclosure and the labels for the smallest size final container and carton. Labels for</p>

New	Old
<p>size final container and carton. Labels for larger sizes of containers or cartons of the same product that are identical, except for physical dimensions, need not be submitted. Such labels become eligible for use concurrent with the approval of the appropriate finished master label, provided that the marketing of larger size final containers is approved in the filed Outline of Production, and the appropriate larger sizes of containers or cartons are identified on the label mounting sheet. When a master label enclosure is to be used with more than one product, one extra copy for each additional product shall be submitted. One copy of each finished master label will be retained by APHIS. One copy will be stamped and returned to the licensee or permittee. Master labels to which exception are taken will be marked as sketches and handled under paragraph (e)(1)(ii) of this section.</p> <p>(2) Mounting:</p> <p>(i) Each label or sketch shall be securely fastened to a separate sheet of heavy bond paper (8 1/2" × 11") in such a manner that all information is available for review.</p> <p>(ii) Two-or three-part cartons, including "sleeves," shall be considered as one label. All parts shall be submitted together.</p> <p>(iii)</p> <p>(A) When two final containers are packaged together in a combination package, the labels for each shall be mounted on the same sheet of paper and shall be treated as one label. 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 individual sheets.</p> <p>(B) If either final container label is also used alone or in another combination package, sets of separate labels for each biological product with which it is used shall be submitted for review.</p>	<p>larger sizes of containers or cartons of the same product that are identical, except for physical dimensions, need not be submitted. Such labels become eligible for use, concurrent with the approval of the appropriate finished master label: <i>Provided</i>, That the marketing of larger sizes of final containers is approved in the filed Outline of Production, and the appropriate larger sizes of containers or cartons are identified on the label mounting sheet. When a master label enclosure is to be used with more than one product, one extra copy for each additional product shall be submitted. One copy of each finished master label will be retained by APHIS. One copy will be stamped and returned to the licensee. Master labels to which exceptions are taken will be marked as sketches and handled under paragraph (e)(1)(ii) of this section.</p> <p>(2) Mounting:</p> <p>(i) Each label or sketch shall be securely fastened to a separate sheet of heavy bond paper (8 1/2" × 11") in such a manner that all information is available for review.</p> <p>(ii) Two-or three-part cartons, including "sleeves," shall be considered as one label. All parts shall be submitted together.</p> <p>(iii)</p> <p>(A) When two final containers are packaged together in a combination package, the labels for each shall be mounted on the same sheet of paper and shall be treated as one label. 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 individual sheets.</p> <p>(B) If either final container label is also used alone or in another combination package, sets of separate labels for each biological product with which it is used shall be submitted for review.</p> <p>(iv) When the same final container label is applied by different methods such as</p>

New	Old
<p>(iv) When the same final container label is applied by different methods such as paper or screen printing, one of each shall be mounted on the same sheet of paper as one submission.</p> <p>(3) To appear on the top of each page:</p> <p>(i)</p> <p>(A) Name and product code number of the biological product as it appears on the product license or permit.</p> <p>(B) Extra copies of enclosures to be used with another product shall bear the name and code number of the product affected.</p> <p>(ii)</p> <p>(A) Designation of the specimen as a label or master label: sketch, final container label, carton label, or enclosure.</p> <p>(B) If two final container labels or multiple parts are on one sheet, each shall be named, and the label or part being revised shall be designated.</p> <p>(iii) Size of package (dose, ml., cc., or units) for which the labels or enclosures are to be used.</p> <p>(4) To appear on the bottom of each page in the lower left hand corner, if applicable:</p> <p>(i) The dose size(s) to which the master label applies.</p> <p>(ii) The APHIS assigned number for the label or sketch to be replaced.</p> <p>(iii) The APHIS assigned number for the label to be used as a reference for reviewing the submitted label.</p>	<p>paper or screen printing, one of each shall be mounted on the same sheet of paper as one submission.</p> <p>(3) To appear on the top of each page:</p> <p>(i)</p> <p>(A) Name and product code number of the biological product as it appears on the product license or permit.</p> <p>(B) Extra copies of enclosures to be used with another product shall bear the name and code number of the product affected.</p> <p>(ii)</p> <p>(A) Designation of the specimen as a label or master label: sketch, final container label, carton label, or enclosure.</p> <p>(B) If two final container labels or multiple parts are on one sheet, each shall be named, and the label or part being revised shall be designated.</p> <p>(iii) Size of package (dose, ml., cc., or units) for which the labels or enclosures are to be used.</p> <p>(4) To appear on the bottom of each page: The reason for and information relevant to the submission shall be stated in the lower left hand corner as:</p> <p>(i) Master label dose sizes approved for code _____.</p> <p>(ii) Replacement for label, master label, and/or sketch No. _____.</p> <p>(iii) Reference to label or master label No. _____.</p> <p>(iv) Addition to label No. _____.</p> <p>(v) License Application Pending _____.</p> <p>(vi) Foreign Language copy of Label No. _____.</p>
<p>(f) Special requirements for foreign language labels:</p> <p>(1) An accurate English translation must accompany each foreign language label submitted for approval. A statement affirming the accuracy of the translation must also be included.</p> <p>(2) If the foreign language label is not a direct translation of an approved domestic label, an English version shall be submitted with an explanation for the difference in texts.</p> <p>(3) Foreign language portion of a bilingual label shall be a true translation of the English portion. Reference to additional information on the enclosure shall not be made unless that enclosure is also bilingual.</p>	<p>(e) Special requirements for foreign language labels:</p> <p>(1) If true, a statement that the label is a direct translation from a corresponding approved domestic label.</p> <p>(2) If the foreign language label is not a direct translation of an approved domestic label, an English version shall be submitted with an explanation for the difference in texts.</p> <p>(3) Foreign language portion of a bilingual label shall be a true translation of the English portion. Reference to additional information on the enclosure shall not be made unless that enclosure is also bilingual.</p>

New	Old
<p>No change except redesignating as section g</p>	<p>(f) When a request is received from Animal and Plant Health Inspection Service, the licensee or permittee shall submit a list of all approved labels currently being used. Each label listed shall be identified as to:</p> <ul style="list-style-type: none"> (1) Name and product code number as it appears on the product license or permit for the product; and (2) Where applicable, the size of the package (doses, ml., cc., or units) on which the label shall be used; and (3) Label number and date assigned; and (4) Name of licensee or subsidiary appearing on the label as the producer. <p>(h) At the time of an inspection, or when requested by APHIS, licensees or permittees shall make all labels and master labels, including labels approved for use but exempted from filing under the master label system, available for review by authorized inspectors. Such labels shall be identical to the approved label or master label except for physical dimensions, reference to recoverable volume or doses and/or certain minor differences permitted in accordance with paragraph (d) of this section.</p>

§ 112.6 Packaging biological products.

New	Old
<p>(a) Multiple-dose final containers of a biological product with final container labeling including all information required under the regulations may be packaged one or more per carton with a container(s) of the proper volume of diluent, if required, for that dose as specified in the filed Outline of Production: Provided, That cartons containing more than one final container of product must comply with the conditions set forth in paragraphs (c)(1) through (4) of this section. Multiple-dose final containers of a product that require a carton or enclosure in order to provide all information required under the regulations shall be packaged one container per carton with the proper volume of diluent, if required, for that dose as specified in the filed Outline of Production.</p>	<p>(a) Each multiple-dose final container of a biological product which requires a diluent for administration shall be packaged in an individual carton with a container of the proper volume of diluent for that dose as specified in the filed Outline of Production. Each multiple-dose final container of a product which does not require a diluent for administration need not be packaged in an individual carton unless the final container labeling does not contain all information required by the regulations. Such information must be included in or on a carton. Exceptions are provided in paragraphs (c) and (d) of this section and § 112.8.</p>

(b) Single-dose final containers of a product need not be packaged one per carton. For single-dose products which require a diluent for administration, the number of containers of the proper amount of diluent specified in the filed Outline of Production for the number of doses contained in the carton shall be included in each carton.

(c) Poultry products for mass administration (including but not limited to administration through drinking water and spray) and products used in automatic vaccinating systems (including but not limited to pneumatic beak injectors and automated needle injectors) may be packaged in multiple-dose final containers as specified in the filed Outline of Production. Poultry products for manual administration to individual birds shall not exceed 1,000 doses in each final container. Diluent need not be packaged with the final container(s) of the product, but the licensee shall provide the required number of containers of diluent as specified in the filed Outline of Production. The following requirements apply to cartons containing more than one final container of poultry product:

- (1) They shall be sealed prior to leaving the licensed establishment.
- (2) The contents may not be repackaged.
- (3) The contents of such cartons may not be sold in fractional units.
- (4) The following statement must appear in a prominent place on the carton label: "Federal regulations prohibit the repackaging or sale of the contents of this carton in fractional units. Do not accept if seal is broken."

(d) Diluent for the following products need not be packaged with the final container(s) of the product, but the licensee shall provide the consumer with the required number of containers of the proper amount of diluent as specified in the filed Outline of Production:

- (1) Marek's Disease Vaccine.
- (2) Poultry vaccines administered to individual birds using automatic vaccinating equipment.

(e) Final containers of biological product prepared at a licensed establishment, or imported, in cartons or other containers shall not be removed from such cartons or containers for sale or distribution, unless each final container bears, or is packaged in a carton with, complete and approved labeling which is affixed to or included with each container by the licensed establishment producing the product or by the producer in the case of imported product: *Provided*, That this paragraph is not intended to apply to licensed veterinary practitioners administering or dispensing biological products in the course of their practice under a veterinary-client-patient-relationship as that term is used in § 107.1.

(f) Labels which are affixed to or included with a biological product shall not be removed or altered in any manner.

§ 112.7 Special additional requirements. The label requirements in this section are additional to those prescribed elsewhere in this part.

(a) In the case of biological products containing live Newcastle Disease virus, a caution statement indicating that Newcastle Disease can cause inflammation of the eyelids of humans, and a warning to the user to avoid infecting his eyes shall be included on the enclosure.

(b) In the case of a biological product containing infectious bronchitis virus, all labels shall show the infectious bronchitis virus type or types used in the product. Abbreviation is permitted.

(c) In the case of a biological product containing inactivated rabies virus, carton labels, enclosures, and all but very small final container labels shall include a warning against freezing and the recommendations provided in this paragraph.

(1) That vaccine be administered to animals at 3 months of age or older, with a repeat dose 1 year later.

(2) Subsequent revaccination as determined from the results of duration of immunity studies conducted as prescribed in § 113.209, paragraph (b) or (c), or both.

(d) In the case of a biological product containing modified live rabies virus, the carton labels, enclosures, and all but very small final container labels shall include the recommendations provided in this paragraph.

(1) For low egg-passage (below the 180th egg-passage level) the statement "For Use in Dogs Only! Not For Use in Any Other Animal!"

(2) For other vaccines containing modified live rabies virus, the statement "For Use In (designate animal(s)) Only! Not For Use In Any Other Animal!"

(3) Intramuscular injection at one site in the thigh shall be recommended.

(4) The statement "In event of accidental exposure to the vaccine virus, the possible hazard to human health should be considered and State Public Health Officials should be consulted for specific recommendations" shall be prominently placed on all carton labels and on enclosures, if used.

- (5) That vaccine be administered to animals at 3 months of age or older, with a repeat dose 1 year later.
- (6) Subsequent revaccination as determined from the results of duration of immunity studies conducted as prescribed in § 113.312, paragraph (b) or (c), or both.

New	Old
<p>(e) Labeling for all products for use in mammals must bear an appropriate statement concerning use in pregnant animals.</p> <p>(1) For bovine rhinotracheitis vaccine or bovine virus diarrhea vaccine containing modified live virus, all labeling except small final container labels shall bear the following statement: "Do not use in pregnant cows or in calves nursing pregnant cows.": Provided, That such vaccines which have been shown to be safe for use in pregnant cows may be excepted from this label requirement by the Administrator.</p> <p>(2) For other modified live and inactivated vaccine, labeling shall bear a statement appropriate to the level of safety that has been demonstrated in pregnant animals.</p> <p>(i) Products known to be unsafe in pregnant animals shall include statements such as "Do not use in pregnant animals," or "Unsafe for use in pregnant animals," or an equivalent statement acceptable to APHIS.</p> <p>(ii) Products without safety documentation acceptable to APHIS, but not known to be unsafe, labeling shall include the statement "This product has not been tested in pregnant animals" or an equivalent statement acceptable to APHIS.</p> <p>(3) For modified live vaccines containing agents with potential reproductive effects but having acceptable pregnant animal safety data on file with APHIS, labeling still must bear the following statement concerning residual risk: "Fetal health risks associated with the vaccination of pregnant animals with this vaccine cannot be unequivocally determined during clinical trials conducted for licensure. Appropriate strategies to address the risks associated</p>	<p>(e) In the case of bovine rhinotracheitis vaccine containing modified live virus, all labeling except small final container labels shall bear the following statement: "Do not use in pregnant cows or in calves nursing pregnant cows.": <i>Provided</i>, That such vaccines which have been shown to be safe for use in pregnant cows may be excepted from this label requirement by the Administrator.</p>

<p>with vaccine use in pregnant animals should be discussed with a veterinarian.”</p>	
<p>(f) For biological products recommending annual booster vaccinations, such recommendations must be supported by data acceptable to APHIS. In the absence of data that establish the need for booster vaccination, labeling must bear the following statement: “The need for annual booster vaccinations has not been established for this product; consultation with a veterinarian is recommended.”</p>	<p>(f) Unless otherwise authorized in a filed Outline of Production, labels for inactivated bacterial products shall contain an unqualified recommendation for a repeat dose to accomplish primary immunization to be given at an appropriate time interval: <i>Provided</i>, That, repeat dose recommendations prescribed in paragraphs (f)(1) through (3) of this section are required for products containing the fractions listed.</p> <p>(1) <i>Clostridium haemolyticum</i>. “Repeat the dose every 5 or 6 months in animals subject to reexposure.”</p> <p>(2) <i>Erysipelothrix rhusiopathiae</i>. “Swine: For breeding animals, repeat after 21 days and annually. Turkeys: Repeat dose every 3 months.”</p> <p>(3) <i>Clostridium botulinum Type C</i>. “Revaccinate breeders 1 month before breeding.”</p>

(g) In the case of a liquid product authorized in a filed Outline of Production to be used as a diluent in a combination package, the carton labels and enclosures used for serials which are either not tested for bactericidal or viricidal activity or have been found unsatisfactory by such test shall contain the statement: “CAUTION: DO NOT USE AS DILUENT FOR LIVE VACCINES.”

(h) In the case of wart vaccine, recommendations shall be limited to use in cattle. Indications for use shall be for prophylactic use only, as an aid in the control of viral papillomas (warts). All labels shall include a dosage recommendation of at least 10 ml to be given subcutaneously and the dose repeated in 3 to 5 weeks.

New	Old
<p>(i) All but very small final container labels for feline panleukopenia vaccines shall contain the following recommendations for use:</p> <p>(1) Killed virus vaccines. Vaccinate healthy cats with one dose, except that if the animal is less than 12 weeks of age, a second dose should be given no earlier than 16 weeks of age.</p> <p>(2) Modified live virus vaccines. Vaccinate healthy cats with one dose, except that if the animal is less than 12 weeks of age, a second dose should be given no earlier than 16 weeks of age.</p>	<p>(i) Unless otherwise authorized in an Outline of Production filed subsequent to the effective date of these amendments, all but very small final container labels for Feline Panleukopenia Vaccines shall contain the following recommendations for use:</p> <p>(1) <i>Killed virus vaccines</i>. Vaccinate healthy cats of any age with one dose except that if the animal is less than 12 weeks of age, a second dose should be given at 12 to 16 weeks of age. Annual revaccination with a single dose is recommended.</p> <p>(2) <i>Modified live virus vaccines</i>. Vaccinate healthy cats of any age with one dose except that if the animal is less than 12 weeks of age, a second dose should be given at 12 to 16 weeks of age. Annual revaccination with a single dose is recommended. Do not vaccinate pregnant cats.</p>

(j) In the case of normal serum, antiserum, or antiserum derivatives, the type of preservative used shall be indicated on all labels.

(k) Unless acceptable data has been filed with Animal and Plant Health Inspection Service, to show that development of corneal opacity is not associated with the product, carton labels and enclosures used with biological products containing modified live canine hepatitis virus or modified live canine adenovirus Type 2 shall bear the following statement: "Occasionally, transient corneal opacity may occur following the administration of this product."

New	Old
(l) All labels for autogenous biologics must specify the name of the microorganism(s) or antigen(s) that they contain, and shall bear the following statement: "Potency and efficacy of autogenous biologics have not been established. This product is prepared for use only by or under the direction of a veterinarian or approved specialist."	(l) All labels for autogenous biologics shall bear the following statement: "Potency and efficacy of autogenous biologics have not been established. This product is prepared for use only by or under the direction of a veterinarian or approved specialist."

(m) In the case of biological products containing Marek's disease virus, all labels shall specify the Marek's disease virus serotype(s) used in the product.

New	Old
(n) All labels for conditionally licensed products shall bear the following statement: "This product license is conditional; efficacy and potency have not been fully demonstrated."	Did not exist previously

§ 112.8 For export only. The applicable regulations for packaging and labeling a biological product produced in the United States shall apply to such biological product if exported from the United States except as otherwise provided in this section. Only labels approved as provided in § 112.5 shall be used.

(a) Biological products which have been packaged and labeled for export or which have been exported, shall be subject to the applicable provisions in this paragraph.

(1) After leaving the licensed establishment, a biological product shall not be bottled, repackaged, relabeled, or otherwise altered in any way while in the United States; and

(2) An exported biological product shall not be returned to the United States: *Provided*, That, in the case of a biological product exported in labeled final containers, the Administrator may authorize by permit the importation of a limited number for research and evaluation by the producing licensee; and

(3) An exported biological product which is bottled, rebottled, or altered in any way in a foreign country shall not bear a label which indicates by establishment license number that it has been prepared in the United States.

(b) Desiccated and frozen liquid products, packaged and labeled as for domestic use, may be exported without the diluent required for rehydration or dilution, as the case may be, if the labeling includes adequate instructions for preparing the product for use and the words "For Export Only".

(c) 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": *Provided*, That such products shall not be diverted to domestic use.

(d) Completed inactivated liquid products, antisera, and antitoxins, may be exported in large multiple-dose containers identified with an approved label that contains the words "For Export Only" prominently displayed.

(e) 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.

§ 112.9 Biological products imported for research and evaluation. A biological product imported for research and evaluation under a permit issued in accordance with § 104.4, with the exception of products imported under § 104.4(d), shall be labeled as provided in this section.

(a) The label shall identify the product and the name and address of the manufacturer and shall provide instructions for proper use of the product, including all warnings and cautions needed by the permittee to safely use the product.

(b) Labels on each product to be further distributed in accordance with § 103.3 shall bear the statement "Notice! For Experimental Use Only—Not for Sale!"

(c) The labeling shall contain any other information deemed necessary by the Administrator and specified on the permit.

§ 112.10 Special packaging and labeling. A biological product, which requires special packaging and/or labeling not provided for in this part, shall be packaged and/or labeled in accordance with requirements written into the approved outline for such product.