



Animal and Plant  
Health Inspection  
Service

Veterinary Services

1400 Independence  
Ave, SW

Washington, DC  
20250

**Comments due: March 6, 2017**

**VETERINARY SERVICES MEMORANDUM NO. 800.54 DRAFT DOC 579**

**TO:** Veterinary Services Leadership Team  
Directors, Center for Veterinary Biologics  
Biologics Licensees, Permittees, and Applicants

**FROM:** Jack A. Shere  
Deputy Administrator

**SUBJECT:** Guidelines for the Preparation and Review of Labeling Materials

**I. PURPOSE**

This memorandum provides guidance regarding labeling materials. Most labeling requirements are found in title 9, *Code of Federal Regulations*, part 112 (9 CFR 112). These requirements were updated substantially in 2015 and 2016 by the publication of APHIS Final Rule [2008-0008](#) (Labeling and Packaging Rule) and APHIS Final Rule [2011-0049](#) (Single Label Claim Rule). The guidance in this memorandum emphasizes or interprets aspects of labeling regulations that merit further detail.

**II. REPLACEMENT**

This memorandum replaces Veterinary Services (VS) Memorandum No. 800.54 dated August 31, 1988. It also incorporates guidance previously found in VS Memorandum No. 800.76 and VS Memorandum No. 800.80, both of which are now rescinded.

**III. LABELING ELEMENTS**

**A. True Names**

1. APHIS assigns True Names. Display the True Name on labeling with the exact wording printed on the product license or permit. Exception: Bovine parainfluenza may be presented as either Parainfluenza<sub>3</sub> or Parainfluenza 3.
2. In the case of very small container labels, an abbreviated version of the True Name may be used if the full True Name is provided on accompanying labeling materials. The abbreviated True Name also appears on the product license or permit and must be reproduced exactly on labeling. Click here for a [list of standardized abbreviations](#).
3. Give equal emphasis (e.g., color, size, boldness, capital letters) to each term in the principal part of the True Name.

**B. Trade Names**

1. Except as otherwise provided, associate a Trade Name with a single product.
2. A manufacturer, distributor, or permittee must have exclusive right-by ownership, assignment, exclusive-use license, or other means-to use a Trade Name on a product.
3. A distributor or permittee who owns exclusive right to a Trade Name may transfer the Trade Name to a new manufacturer for use on the labeling of a substantially similar product for such distributor or permittee. APHIS will determine case by case whether a product is “substantially similar.” APHIS may require the new manufacturer to add a postscript to the Trade Name (Trade Name+x), where, in its opinion, the change of manufacturer creates a product that is substantially similar but not identical with respect to a factor posing a potential risk to users.
4. Configure the label so that the True Name is the most conspicuous feature. Do not allow the Trade Name to overshadow the True Name by size, color, or boldness. Place the Trade Name below the True Name.

**C. Functional Names**

Functional Names are used to identify individual diagnostic kit components. This is in contrast to the True Name, assigned to the composite kit.

**D. Establishment and Product Codes**

Regulations require labels to bear the United States Veterinary Biologics Establishment License Number or the United States Veterinary Biological Product Permit Number, as well as the Product Code Number, except where specifically exempted. Permissible abbreviations for these terms are VLN, VPN, and PCN, respectively. The current regulations state that ONLY these formats may be used.

In addition to the preferred formats above, the Center for Veterinary Biologics will continue to accept the following abbreviations found in 9 CFR 112.2(a)(3) prior to the implementation of the Licensing and Packaging Rule:

- U.S. Veterinary License No.
- U.S. Vet License No.
- U.S. Vet Lic No.
- U.S. Veterinary Permit No.
- U.S. Permit No.

Place an acceptable abbreviation next to the numbers; the numbers should not appear alone, without definition. The regulations also specify that the establishment/permit number and product code number (VLN/PCN or VPN/PCN) are to be placed adjacent to each other, in that order, on labeling. This is intended to help the customer locate and recognize this information.

## E. Indications Statements

### 1. Products Within the Scope of the Single Label Claim Rule

#### a. First paragraph:

##### i. Structure effectiveness claims according to the codified format:

“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](http://productdata.aphis.usda.gov).”

##### ii. If the agent can cause more than one distinct disease syndrome, include the syndrome in the claim. Examples include:

“...against *respiratory disease* due to BVD1 and 2”

“...against *persistently infected calves* due to BVD1 and 2”

##### iii. If the duration of immunity, or a specific onset of immunity, has been established, indicate it before the instruction to see [productdata.aphis.usda.gov](http://productdata.aphis.usda.gov).

#### b. Optional second paragraph:

If the product has been proven effective against specific disease signs or sequelae (e.g., mortality, viremia, shedding), state this in a second paragraph.

##### i. Avoid the use of language that could be construed as a [4-tier claim](#).

Example of permissible language: “The vaccine has been shown to be effective against viremia and virus shedding in the feces.”

##### ii. Include only those signs/sequelae that have been specifically approved by APHIS as part of a label claim.

### 2. Conditional Licenses

Structure claims in the following format:

“For the vaccination of <insert animal species> against <insert agent or disease>. This license is conditional. Efficacy and potency studies are in progress. For more information regarding safety data, see [productdata.aphis.usda.gov](http://productdata.aphis.usda.gov).”

#### F. Minimum Age

Labeling for biologics other than diagnostic kits must include the minimum age of animals recommended for product use. This is based on the age of the animals used in the pivotal efficacy and field safety studies. If the age is not consistent between the studies, cite the older age on labeling. In some cases, it may be acceptable to refer also to the younger age study.

Minimum weight may be used in lieu of age for aquaculture products or other products where weight is a more meaningful criterion than age.

#### G. ISO Symbols

APHIS allows specified symbols on container labeling in situations where the use of text is not practical. Permissible symbols are in accordance with ANSI/AAMI/ISO 15223-1:2012 and ASTM D5445-11a (ISO 780).

1. Click here for a [list of permissible symbols](#).
2. When these symbols are used, include an explanatory key on the carton or the product enclosure. For multi-language labels, the explanatory key must include all languages appearing in the labeling.

#### H. Antigen Type/Strain When Not Included in the True Name

1. Some agents have multiple generally recognized types or strains that impact vaccine effectiveness. The True Name frequently specifies only the agent in the vaccine. Examples include, but are not limited to, bovine virus diarrhea vaccine and equine rhinopneumonitis vaccine. In these cases, provide additional detail on the type/strain included in the product elsewhere on the labeling.
2. Disclose the subtypes and strains included in influenza products. For recombinant/reassortant/subunit products, provide the subtype and strain of the parent isolate. Designate the strains according to accepted standards of influenza virus nomenclature (e.g., “A/equine/Miami/63(H3N8)” or “A/swine/Wisconsin/458/98(H1N1)”). Further identify the strains with commonly used, scientifically justified terms such as “A2,” “European,” “American,” “atypical,” or “classical.” If the product does not contain the N subtype gene, disclose this information on the labeling. Also disclose the subtype and strain of the influenza challenge virus used to demonstrate efficacy of the product.

**I. Minimum Potency**

Labeling may include minimum potency specifications but, if included, provide the through-dating specification. If a foreign marketing authority requires release specifications, indicate that the stated specifications are those for serial release.

**J. Storage Temperature**

The regulations in 9 CFR 112.2(a)(4) state that the storage temperature recommendation for biological product will be 2 to 8 °C or 35 to 46 °F, or both. However, if a product is intended for distribution in a fresh (wet) frozen state, labeling may instruct the user to keep the product frozen until use. For freeze-dried colostrum products that may be held at room temperature, designate an upper temperature limit no greater than 24 °C or 75 °F.

**K. Revaccination Statement**

The regulation in 9CFR 112.7(f) states that when there are no data to support a revaccination interval, the following statement must be included on labeling: “The need for annual booster vaccinations has not been established for this product; consultation with a veterinarian is recommended.” Closely worded alternative statements also may be acceptable; consult your CVB reviewer. An acceptable version for legacy products is:

“Historically, annual revaccination with this product has been recommended. The need for annual booster vaccination has not been established for this product. For advice on re-vaccination frequency, contact your veterinarian or the manufacturer.”

**IV. LABEL TYPES**

**A. Container Labels**

1. Current regulations specify the information that must appear on final container labels. Certain allowances are made for small labels where space is limited, provided that omitted information appears elsewhere on carton labels or enclosures.
  - a. For biologics other than diagnostic test kit components, include the following elements, at a minimum, on small container labels:
    - i. Complete or abbreviated True Name;
    - ii. Serial number;
    - iii. Expiration date;
    - iv. Location of full labeling information;
    - v. Storage temperature;
    - vi. Establishment or permittee and product code identification; and

- vii. Statement to inactivate unused contents if the product contains viable agents.
    - b. For small final containers of diagnostic test kit components, include the following minimum information on small container labels:
      - i. Complete or abbreviated True Name of the kit\*;
      - ii. Functional and/or chemical name and lot number of the component;
      - iii. Establishment number or permittee;
      - iv. Product code of kit\*; and
      - v. Storage temperature.
- \*Small containers of non-critical (interchangeable) kit components do not require the True Name or product code.
- 2. Labeling used for component containers of a combination package does not require the product code of the individually licensed component. On the container label, refer the user to the carton for the product code.
  - 3. Beyond the indications statement described in section III.E above, do not include supporting studies or other promotional statements about product effectiveness on the container label of products subject to the Single Label Claim rule. The following statements, however, are permissible on the container:
    - a. Product-specific warnings (e.g., may cause transient swelling) or other restrictions on use (e.g., only for use in seropositive herds).
    - b. Whether it can be used in breeding and/or pregnant animals (or other special animal category).
    - c. A general disclaimer that the product may not work as intended in ill, malnourished, or immunosuppressed animals.
    - d. A general description of disease an agent causes.

## B. Carton Labels

This section applies to boxes in which product containers are marketed and also to “tray covers” that display underneath the surface of clear “clamshell” boxes.

- 1. Current regulations specify the information that must appear on a carton, particularly if it is not included on the container. Place required elements on the outside of the carton, where they can be viewed without opening the carton.

2. Cartons also may bear non-required information, provided that APHIS determines it is not false or misleading. Place non-required information on the outside or the inner surface of the carton, except as specified in section IV.B.3.
3. For products subject to the Single Label Claim Rule, place optional study data, or other information regarding product use, only on the inner surface of the carton. In such situations, the inner surface of the carton is analogous to an enclosure and is subject to the guidance for enclosures in section IV.C.

### C. Enclosures

Label enclosures (aka circulars, inserts, leaflets) are used to disseminate a wide variety of information about a product.

1. For all products subject to the Single Label Claim Rule, prominently place the following statement at the top of every enclosure, regardless of enclosure content:

**“See [productdata.aphis.usda.gov](https://productdata.aphis.usda.gov) for a summary of the studies approved by the USDA for licensing this product. This package insert may also contain additional information developed by the licensee.”**

2. Study summaries appearing on [productdata.aphis.usda.gov](https://productdata.aphis.usda.gov) may be reprinted on enclosures (or the inner surface of a carton), if desired. Ensure the reproduction is exact and without embellishment. Do not make any other remarks about these studies.
3. Additional data, not used in direct support of product licensure, may be printed on enclosures with APHIS approval.
  - a. This policy is not intended to provide a forum for product comparisons or to generate a marketing advantage. An acceptable example of additional information: Data showing no loss in vaccine titer X hours after reconstitution.
  - b. Submit full study reports for any data to be included on regulated labeling. APHIS reviews such studies for potentially false or misleading information prior to approving labels bearing the information.
4. When describing additional information on labeling, use plain language:
  - a. Avoid subjective descriptors, such as the data “clearly” demonstrate a “robust” effect.
  - b. Avoid terminology that could be construed as promoting [historical 4-tier label claims](#).

- c. Avoid complex statistical analyses, such as p-values, prevented fractions, or confidence intervals.
- d. Avoid summarizing data to the point where conclusions could be misleading.
- e. Do not state that the data are “on file” with APHIS, as this implies full regulatory review and endorsement.

#### D. Experimental Labels

Experimental labels are required for product shipped under 9 CFR 103.3. See VS Memorandum No. 800.67 for additional information on experimental labels.

#### E. Distributor Labels

1. Arrange the names and addresses of the manufacturer and distributor on distributor labels in a manner that gives equal or greater emphasis to the manufacturer compared with the distributor.
  - a. Position the complete names and addresses of the manufacturer and distributor side by side with the manufacturer on the left. Alternatively, stack the information with the manufacturer on top.
  - b. If only one name and address can fit on the front label panel, place the manufacturer on the front panel and the distributor on the back panel.
  - c. Give equal or greater emphasis to the manufacturer in all other aspects of the label. Examples include, but are not limited to, logo, size, shape, coloring, shading, font, print boldness, text arrangement, and print quality.
2. If a distributor logo is used, ensure that the label, when considered in its entirety, does not create the impression that the distributor is the manufacturer.

#### F. Export-Only Labels

Many countries accept labeling that does not meet all current USDA regulations. Considerable regulatory flexibility is extended for differences that do not impact the claimed use or administration of the product or do not make false and misleading statements. Licensees may continue to use non-expired export-only labeling currently approved for use by the CVB as long as it continues to be acceptable to the importing authority. There is no requirement to convert such labeling to meet the Single Label Claim or Packaging and Labeling rules.

New labeling proposed for export-only use, if it does not meet all USDA regulations, will be considered for CVB approval based on documentation of approval by the importing country's registration authority. Exceptions to current labeling regulations will be

considered if the foreign approval allows such differences. Export-only labeling should, however, bear the U.S. Establishment Number unless the labeling qualifies as a Special Label for Export, per VS Memorandum 800.208, or the importing country specifically prohibits the inclusion of the U.S. Establishment Number.

## V. IMPLEMENTATION/APPLICABILITY

### A. Applicability

The Single Label Claim rule applies to vaccines, bacterins, toxoids, and immunomodulators. The Labeling and Packaging rule applies to all products. Exceptions to both rules may be made for Export-Only labeling (see Section IV.F).

### B. Implementation

The Single Label Claim rule was effective September 8, 2015, with a 4-year implementation period. The Labeling and Packaging rule became effective October 31, 2016, with immediate implementation. The implementation of the Single Label Claim rule was delayed until the Label and Packaging rule was published so that the number of individual label revisions could be minimized. Thus implementation of the Single Label Claim rule extends through October 31, 2020. Approximately 25% of labeling should be updated each year, from 2017 through 2020.

1. If labels approved prior to November 2016 do not need to be replaced, or if they only require codified “minor” changes (9CFR 112.5(d)), changes related to the labeling/packaging rule may be delayed until the product is scheduled for conversion to single label claim language, according to the 4-year schedule. This is to prevent doing two major revisions to labeling when two would not otherwise be needed. Single label claim language may not be added to labels until supporting efficacy and safety study summaries have been filed with the CVB to be posted on [productdata.aphis.usda.gov](http://productdata.aphis.usda.gov).

Licensees and permittees will be allowed a similar 4-year schedule to convert labeling for products outside the scope of the Single Label Claim rule, provided that existing labeling does not require change (or only codified minor change) prior to the scheduled conversion date.

2. If labels approved prior to November 2016 require replacement for reasons other than codified minor changes, the CVB expects replacement labels to be compliant with the Labeling and Packaging rule, even if labeling for the product is not yet scheduled for conversion to comply with the Single Label Claim rule. In this case, the labeling will require at least two revisions anyway, so there is no reason to delay making changes due to the Label and Packaging rule.

The CVB expects labeling for products not within the scope of the Single Label Claim rule to be compliant with the Labeling and Packaging rule whenever replacement labels are submitted for reasons other than codified minor changes, provided that all labeling is converted within the 4-year implementation period.

3. Labeling not in full compliance with both rules will be processed with temporary approval, with a default expiration date of October 31, 2020. The CVB reserves the right to reduce the dating for special circumstances or for licensees/permittees who are not making acceptable progress toward yearly conversion goals.

DRAFT