Animal and Plant Health Inspection Service

Veterinary Services

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Final Steps for Licensure

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Notes: *Used to prepare a Licensing Package*

Final Steps for Licensure

Mention of trademark or proprietary product does not constitute a guarantee or warranty of the product by USDA and does not imply its approval to the exclusion of other products that may be suitable.

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1. Purpose and Scope

You finally have a product ready to license/permit. At this point, everybody is anxious to get the license/permit signed and mailed as quickly as possible. This chapter discusses how to prepare the licensing package for review by the Director so that it may be efficiently and quickly routed through the Center for Veterinary Biologics (CVB). In this chapter, a "licensing" package applies to product licenses and product permits. Additional information regarding establishment licenses is found in the Establishments chapter.

2. Reviewer's Responsibility in Preparing a Product Licensing Package

2.1 Complete a licensing checklist to ensure that all documentation is in order. The checklist template is available in MasterControl. Use the checklist for product licensing packages for all products, including vaccines, antisera, immunomodulators, and diagnostic test kits.

The checklist includes additional instructions for items that reviewers need to complete in preparation for licensure. The checklist should be uploaded to the mail log that contains the product license application.

2.2 Products currently being licensed may have paper submissions as well as electronic ones. For various reasons, some firms will never be portal enabled and so their submissions will continue to be paper. Sort all of the paper submissions in chronological order (most recent on top), by date of outgoing CVB correspondence.

- Separate out *all* label submissions and the *current* Outline, and place them on top; these will be processed differently. Ensure the final approved stamped Outline is included. Ensure that labels are approved, the APHIS Form 2015 is signed, and the labels are assigned to the Program Assistant (PA) to prepare for mailing in the mail log (ML).

- Remove any duplicate copies of submissions that may have been placed in the prelicense file. Duplicate copies of submissions should be discarded in a designated CBI trash bin.

- Check that all relevant correspondence prior to 2012 has been uploaded to the ML. If this has not been done, it is the reviewer's responsibility to ensure that the documents are scanned and uploaded to the mail log before the licensing package is moved forward. Items that should be uploaded if not already done:

  - Copies of Master Seed and Master Cell reports and approval letters
  - Backpassage studies and approval letter
  - Residue clearance/slaughter withdrawal period
  - Final efficacy studies
  - Lack of interference studies

- Specificity/sensitivity studies (diagnostic kits only)
- Potency test validation studies
- Potency test reference qualification studies (if separate from efficacy)
- Safety studies
- SIF/Risk analysis approvals
- Suitability studies (diagnostic kits only)
- Prelicense serial test results (CVB results and APHIS Forms 2008)
- Efficacy and safety study summaries (ISS)
- Any other document dealing with a key licensing consideration

2.3 Remove all tags that may be hanging on the edges of submissions. Remove any sticky notes containing unofficial notes. If the sticky note needs to be a part of the permanent record, ensure that it is stapled to a piece of paper that will be pegged in the #1 file.

2.4 Remove the **final** APHIS Forms 2008 (2008) **for prelicense serials** from the package and forward them to CVB-Inspection and Compliance (IC) if this has not already been done. Retain one copy of each forwarded 2008 for the #1 file. This only applies to 2008s received prior to mid-2013, as anything after that should have been forwarded to CVB-IC. Any 2008s received after 2013 should be tagged as "Forward 2007/2008 to IC."

2.4.1 Do **not** forward preliminary 2008s or those used to report results of Master Seed, Master Sequence, or Master Cell testing.

2.4.2 The forwarded 2008s should be filled out in accordance with VS Memorandum 800.53. Review the 2008s before forwarding to IC to ensure the forms are completed appropriately. The following are sometimes not completed on the 2008s submitted to IC for prelicensing serials:

2.4.2.1 Complete Testing as required by Section V of the OP (Block 9)

2.4.2.2 Expiration date as required by Section VI of the OP (Block 6)

2.4.2.3 Inventory prepared should be included (Block 10)

2.4.2.4 Indicate the 2008 is for a prelicensing serial to support licensure (Block 11)

2.4.2.5 Signature in Block 13.

2.5 If the product is the first of its kind and will be conditionally licensed, prepare a CVB Notice. (Notices are not required for subsequent conditional licenses for the same product.) Upload an electronic copy of the draft notice to the mail log for the license transmittal letter. See **CVB-TEM-1016** and Appendix III of this document for templates.

2.6 If the product is the first for a particular antigen, the first product of its kind for a particular species, or has some other novel aspect, provide the summary information needed for the support staff to draft a letter to the American Veterinary Medical Association (AVMA). Upload this summary information electronically to the ML for the license transmittal letter. The AVMA publishes key new product information in the Journal of the American Veterinary Medical Association. The following information is needed. See **Appendix I** for an example.

- Product True Name
- Establishment Name and Number, City and State
- Species and indications for use
- Route of administration
- Brief information regarding efficacy data

2.7 If requested by the Director, prepare a press release for Veterinary Services to issue to the wire services. See **Appendix II** as an example.

2.8 Run a PEL Mail Log search of all active submissions for the product being licensed. Move forward any submissions that are processed at licensure (or were missed earlier) for the appropriate processing or log-out activity. If any submissions were logged in prior to issuance of the Product Code, ensure that they are identified with the Code, and not with "UNASGN".

2.9 Check that all LSRTIS entries are correct and consistent with the final approved Outline of Production.

2.10 Check that there is a cleared ISS for each label claim, if applicable.

2.11 Check that the Product Licensing Plan is complete.

3. Processing Licensing Packages

3.1 Reviewer's responsibilities

- The reviewer is responsible for ensuring that the licensing package is complete. **Incomplete licensing packages will be returned to the reviewer.**
- The reviewer is responsible for the **critical review** of the accuracy of the licensing information and accompanying documents. Do not rely on the support staff to do this for you, it is not their responsibility.

3.2 When the licensing package is ready, place all hard-copy documents in a multi-colored polka-dot folder. In EDIT MAIL LOG ITEM, add the appropriate "Product" tag (Buyout Transfer, Initial, Reissue). **When forwarding in the ML, use the License Pkg-Single Tier Check activity and forward the APHIS Form 2003/2005 to the License Pkg-Single Tier Check** (if the product does not fall under Single Tier, the license package may be forwarded directly to the License Pkg-LSRTIS Check). Do **not** add a "log out without response" tag. The polka-dot folder should be given to the person performing the Single Tier Check (or LSRTIS Check, if applicable).

3.3 Licensing packages go through a series of checks and reviews before they are presented to the Director for signature. The program assistant prepares the license/permit and the correspondence that accompanies it. Your PA and LIE have reviewed the license package. The section leader will review the package and a designated reviewer will perform the final compliance check before it is presented to the Director. The package may be returned to you at any time if discrepancies are found. The Director also may ask questions if the documentation is not clear and complete.

3.4 After the license is signed by the Director, the licensing package is returned to the PA to be mailed.

3.5 The mail log system automatically delivers an e-mail to the CVB IC BCA-OAA, RMA, Sample Processing section head and alternate with the following info:

Establishment #:
Product Code:
License or Permit:
Restrictions: (Y or N)
Prelicense Serials:
Date license was issued:

3.6 Flow chart of pathway in the Mail Log for the APHIS Form 2003 or 2005:

Reviewer has all items completed for licensure
↓
License Pkg-Single Tier Check (can omit if product is not Single Tier)
↓
License Pkg-LSRTIS Check
↓
License Pkg-PA
↓
License Pkg-LIE
↓
Approval-content section leader
↓
License Pkg-Final Compliance Check
↓
License Pkg-Dir Approval

APPENDIX I: Sample Summary to Accompany AVMA Letters

New Veterinary Biological Product

Product Name	Species and Indications for Use	Route of Administration	Remarks
West Nile Virus Vaccine, Killed Virus, (Fort Dodge Laboratories, Inc., Fort Dodge, Iowa, U.S. Vet. Lic. No. 112)	For vaccination of healthy horses as an aid in the prevention of viremia caused by West Nile Virus. Efficacy was demonstrated in horses that received two doses of the vaccine and were challenged one year post-vaccination with West Nile Virus.	IM	USDA Licensed <date>

APPENDIX II: Sample VS Press Release

USDA ISSUES CONDITIONAL LICENSE FOR WEST NILE VIRUS ANTIBODY FOR HORSES

The U.S. Department of Agriculture announced today that it has issued a conditional license to Grand Laboratories, of Larchwood, Iowa, a division of Novartis Corporation, for an equine-origin antibody product intended to aid in the treatment of disease in horses caused by West Nile virus.

USDA's Animal and Plant Health Inspection Service issues conditional licenses for veterinary biologics products to meet an emergency situation, limited market, local situation, or special circumstance. The special circumstance addressed here is the need for a product to aid in the treatment of disease caused by West Nile virus.

Under these regulations, a product that is shown to be pure and safe and demonstrates a reasonable expectation of efficacy may be licensed while data to establish efficacy and potency are still being obtained.

West Nile virus is a mosquito-borne virus that was first detected in the United States in 1999. The virus, which can cause encephalitis, or inflammation of the brain, in animals and in some cases, humans, has been found in Africa, western Asia, the Middle East, and the Mediterranean region of Europe. Most recently it has spread to most regions of the United States.

West Nile virus infection in horses may include both central nervous system and peripheral nervous system signs. Although horses can be infected by the virus, there is no documentation that infected horses can spread the virus to uninfected horses or other animals. In 2002, there were 14,717 reported cases of horses infected with the virus.

The most common signs of West Nile virus infection in U.S. horses have been stumbling or incoordination, weakness of limbs, partial paralysis, muscle twitching and death. Fever has been detected in less than one-quarter of all confirmed cases. Approximately 1/3 of horses that become ill with West Nile Virus die or must be euthanized.

Conditional licenses are generally issued with restrictions and for a limited period of time. At the end of the conditional license period, data obtained in support of the product’s efficacy, potency, and product performance are evaluated to determine if the conditional license should be renewed or if a regular product license may be issued.

In keeping with these regulations, the product described above has been issued a conditional license for one year. The product is restricted to use by a veterinarian in those states where use of the product has been approved by the appropriate state regulatory authorities.

APPENDIX III: Template for CVB Notice for Conditional Licenses

<date>

CENTER FOR VETERINARY BIOLOGICS NOTICE NO. <YR>-##

Subject: Issuance of a Conditional License for <Product True Name>

To: Area Veterinarians in Charge, VS
State Veterinarians
Veterinary Services Management Team
Directors, Center for Veterinary Biologics

The Animal and Plant Health Inspection Service (APHIS) has issued a conditional United States Veterinary Biological Product License to <Establishment Name>, Establishment No. <###>, <City>, <State> for the manufacture and distribution of <Product True Name>.

A veterinary biological product regulated under the Virus-Serum-Toxin Act must be shown to be pure, safe, potent, and efficacious before a veterinary biological product license may be issued. The regulations in 9 CFR part 102 regarding the licensing of biological products provide that a conditional veterinary biological product license may be issued to meet an emergency situation, limited market, local situation, or special circumstance. The special circumstance addressed here is the need for a product to <label claim of product>.

Conditionally licensed products are required to be pure and safe, and have a reasonable expectation of efficacy. The conditional license was issued on the basis that <Establishment Name>, has demonstrated that the product has a reasonable expectation of efficacy. Safety of the product has been established through field safety trials. <Establishment Name> has provided a written commitment to APHIS to complete studies to demonstrate the efficacy of this product and to conduct any other work required for full licensure. APHIS will evaluate their progress later this year. The conditional license will expire one year from the date of the license.

<Director's name>
Director