Animal and Plant Health Inspection Service

Veterinary Services

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Conditional Licenses

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Notes:

Conditional Licenses

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.

Table of Contents

1. Purpose and Scope

Conditional licenses, authorized under title 9, *Code of Federal Regulations* (9 CFR), part 102.6, are used to meet an emergency condition, limited market, local situation, or other special circumstance.

The data required for conditional licensure are reduced from that needed for full licensure in that there needs only to be a "reasonable expectation" of efficacy as defined by the agency, and a fully validated potency test may not be not required. Conditionally licensed products must meet the same safety and purity requirements as fully licensed products.

Conditional licenses are effective for a finite time period, usually 1 year. They may be renewed at the discretion of the Center for Veterinary Biologics (CVB). Guidance documents related to conditional licenses include:

- Veterinary Services Memorandum (VSM) 800.75 Reissuance of Product Licenses for Products Under Conditional Licenses
- VSM 800.85 Avian Influenza Vaccines
- VSM 800.213 Guidelines for Obtaining a Conditional Veterinary Biologics License for Production Platform Derived, Recombinant, Non-replicating, Nonviable Constructs

2. Eligibility for a Conditional License

By regulation, we issue conditional licenses to meet an emergency condition, limited market, local situation, or other special circumstance. Ensure that products proposed for conditional licensure fit the following guidelines:

2.1 Conditional licenses may be issued for the first product for a new antigen, provided that the firm can demonstrate that there is an urgent need for a product.

2.2 Conditional licenses are not issued for products containing new antigens if they are in combination with antigens found in fully licensed products.

2.3 Conditional licenses may be issued to more than one establishment for similar products, but as soon as any of the establishments is issued a full license for the product, no additional conditional licenses will generally be issued. [redacted]

2.4 Conditional licenses may, under certain circumstances, be issued for "old" antigens in a product labeled for a new animal species. For example, if all available products are unsafe in a given animal species, a product specially made for that species may be granted conditional licensure.

2.5 Production Platform based antigens may have abbreviated licensing requirements based on antigenic shift or drift, unusual culture requirements which are difficult to

reproduce *in vitro* or traditional manufacturing procedures are problematic and/or cultivation of the live agent poses human and/or animal health hazards. This does not preclude the need for the firm to demonstrate an urgent need for the product they are proposing for a conditional license.

3. Conditional Licenses are not issued for:

3.1 Permits for Distribution and Sale (imported products) are not issued on a conditional basis. Such products must meet the requirements for a regular permit.

3.2 New antigens in combination with fully licensed products.

3.3 An additional establishment after a full license has been granted for a similar product

4. Data Required to Support Conditional Licensure

4.1 The firm must demonstrate that there is an urgent need in the field for such a product. Firms may submit articles from scientific and trade journals or letters from recognized experts to demonstrate need. Urgent need must be demonstrated regardless of the type of product to be considered for conditional licensure.

4.2 The product must have a "reasonable expectation" of efficacy. This may be demonstrated by a limited-scale trial or other methods that have perceived clinical relevance (for example measuring neutralizing antibody in a serology assay). The data should come from use of the actual product and not another related product (e.g., autogenous serials containing the same antigen, but not the same seed). The type and quantity of data required varies with the individual product.

4.3 The product must meet the same requirements for safety and purity as do fully licensed products. Platform products are exempt from field safety and inactivation kinetics requirements, after this work has been accepted for the first product using the platform. All Master Seeds and Cells must be fully characterized.

4.4 Because efficacy is not fully established and potency must be linked to efficacy, a fully validated potency test is not required for conditionally licensed products. There should, however, be some type of testing to ensure batching consistency (e.g., pre-inactivation titer). This testing should be described in Section V.C. of the Outline of Production. Wording should indicate "Batching consistency for conditional licensure: Each serial will contain….." or wording to that effect. This testing should be reported on APHIS Form 2008.

4.5 Because efficacy is not fully established, conditionally licensed products should not have label claims, such as "aids in the prevention of." The claim should be similar to

what we will use for single-tier labeling: For vaccination against <agent or disease>.

5. Restrictions Associated with a Conditional License

A conditional license contains multiple restrictions. The following section lists the preferred wording for each restriction and its practical implication.

5.1 *Reissuance of this license shall be considered in accordance with 9 CFR 102.6. The licensee shall demonstrate acceptable progress toward completion of host animal efficacy and potency test studies in accordance with acceptable protocols filed with the Center for Veterinary Biologics prior to reissuance.* (LSRTIS license restriction #48)

5.2 *This license shall terminate <specify date or length of time> from the date of issuance.* (LSRTIS license restriction #56)

Unlike regular (full) licenses, conditional licenses are issued for a finite time period, usually one year for traditional products. Niche products (for example cancer therapy products, or immunomodulators) that take a considerable amount of time to generate enough field data for full licensure may be issued a two year conditional license. As per VSM 800.213, production platform products may be issued a two year conditional license. Circumstances may sometimes dictate that a conditional license may be less than one year. When conditional licenses expire, they may be renewed or allowed to expire (terminate). See VS Memorandum 800.75 for additional detail.

If a firm wishes to renew a conditional license, they should make a request in writing prior to the expiration date of the license. They should submit a progress report to demonstrate a good-faith effort toward obtaining full licensure. The report may summarize efficacy data, potency test development, etc. The reviewer makes a recommendation to the CVB Director regarding the acceptability of the progress report to justify license renewal.

It is our policy that conditional licensure is a transitory, not a permanent, state, but the amount of time that a product remains conditionally licensed may vary considerably. There is no statutory limit on the number of times that a conditional license may be renewed.

If there are multiple conditional licenses for a given product, when the first full license is issued for the product, the remaining conditional licenses are typically allowed to expire. (Depending on the expiration date of each license, however, individual licensees may continue releasing product up to an additional year under a conditional license.) We also grant some latitude to firms that are nearing full licensure for their products; conditional licenses may be renewed, even if a full license exists, if the firm needs a few extra months to complete licensing requirements. Continued conditional licensure also may be allowed if the product still conditionally licensed is sufficiently different from the one that became fully licensed (e.g., recommended for different species, protects against

different disease syndrome). This decision is left to the discretion of the reviewer, with concurrence by the CVB Director.

5.3 *Distribution in each State is limited to authorized recipients designated by proper State officials – under such additional conditions as these authorities may require.* (LSRTIS license restriction #43)

This means that the firm must get permission each year to market the product in each state. Some states will forward a copy of their letter of permission to us for our files.

5.4 *Export distribution shall be limited to authorized recipients designated by proper animal health regulatory officials – under such additional conditions as these authorities may require*. (LSRTIS license restriction #46)

This gives additional assurance that foreign regulatory authorities understand the conditional nature of the license and have the opportunity to restrict/control distribution in their country as they see fit. Labels for export for conditionally licensed products should not be approved unless the required conditional license disclaimers (LSRTIS license restrictions #49 and #50) appear on the labels.

5.5 *The following statement shall appear on all labels: This product license is conditional. Efficacy and potency test studies in progress.* (LSRTIS license restriction #49)

The label must disclose that the license is conditional. The exact wording may vary slightly, depending on the data that still need to be submitted.

5.6 *Trade names shall not be used with this product*. (LSRTIS license restriction #50)

The label should contain only a true name and no trade names while the product is conditionally licensed.

Additional restrictions may be added, as appropriate, on a case-by-case basis. See the Chapter on License Restrictions for details.

6. Office Procedure for Renewing a Conditional License

Reviewers recommending a conditional license forward the Mail Log record with the firm's request for renewal to the Program Assistant:

- Use License Pkg-Initiate activity
- Ensure the current license restrictions remain appropriate – arrange for update in LSRTIS, if necessary.
- Provide justification why the conditional license should be reviewed – may be done by adding an explanation in the Synopsis of Reviewer Response, by informationally linking

relevant Mail Log items, or writing up a justification and attaching to the Mail Log as Other CVB Working Papers.