



September 21, 2012

CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 12-18

**United States
Department of
Agriculture**

Animal and Plant
Health Inspection
Service

Veterinary Services

Center for Veterinary
Biologics

1920 Dayton Avenue
PO Box 844
Ames, IA 50010

(515) 337- 6100

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

FROM: Richard E. Hill, Jr. /s/ *Richard E. Hill, Jr.*
Director
Center for Veterinary Biologics

SUBJECT: Potential Forms to Facilitate Requests to Submit Samples of Master Seeds,
Master Cells, and Product Serials for Confirmatory Testing

I. PURPOSE

The purpose of this Notice is to solicit input from interested parties regarding two forms to request authorization to submit samples for confirmatory testing by the Center for Veterinary Biologics (CVB) Laboratory. The first form is intended for Master Seeds and Cells; the second is for submitting product serials (whether to support initial licensure, or a post-license change to the Outline of Production).

II. BACKGROUND

The CVB is currently evaluating methods to increase efficiency while maintaining quality. One potential method is to develop forms that will facilitate requests to ship samples of Master Seeds, Master Cells, precensuring serials, and validation serials to support Outline changes for licensed products to the CVB Laboratory for confirmatory testing. The single-page form serves as a cover application to which supporting documentation may be attached. It also contains a checklist to assist in assembling a complete submission. The bottom of the form contains space for the CVB to authorize sample shipment.

The use of the forms, although voluntary, should reduce a firm's time in creating a request. Since the forms contain prompts for all required supporting documentation, they should reduce the number of resubmissions. The forms will also decrease the time needed for the CVB to prepare a regulatory response.

III. ACTION

The CVB is soliciting input from industry regarding the content and usability of the attached draft forms. We also welcome stakeholder opinion regarding the potential use

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of standard forms for other common submissions. Please submit comments by October 15, 2012, to the CVB at the address shown in the left margin above or to CVB@aphis.usda.gov.

IV. IMPLEMENTATION/ APPLICABILITY

If the CVB receives favorable feedback, these forms will be forwarded to the Office of Management and Budget (OMB) for approval under the Paperwork Reduction Act of 1995. Upon OMB approval, the forms will be available on the Veterinary Biologics portion of the APHIS website.

ARCHIVED

According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a valid OMB control number. **This form is currently being considered for submission to the OMB.** The time required to complete this information collection is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

OMB Approval Pending
DRAFT

This application may be submitted to request authorization to ship biological samples for confirmatory testing by APHIS.

INSTRUCTIONS: See reverse side.

| | | |
|--|---|---|
| U.S. DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE VETERINARY SERVICES, CENTER FOR VETERINARY BIOLOGICS (CVB) 1920 DAYTON AVE. AMES, IA 50010 APPLICATION FOR AUTHORIZATION TO SHIP MASTER SEED OR CELL SAMPLES FOR CONFIRMATORY TESTING BY APHIS | | 1. NAME AND FULL MAILING ADDRESS OF APPLICANT |
| 2. U.S. VET. EST. NO. | 3. APPLICATION TYPE: <input type="checkbox"/> NEW <input type="checkbox"/> AMENDMENT TO SUBMISSION DATED _____ AND/OR PRIOR CVB MAIL LOG NO _____ | |

| 4. ITEM(S) TO BE SHIPPED (USE SEPARATE FORM FOR EACH SEED OR CELL) | | | | CVB USE ONLY |
|--|------------|---|---|--------------------------------|
| A. COMPLETE IDENTIFICATION OF SEED/CELL, EXACTLY AS IT APPEARS ON CONTAINERS (INCLUDING LOT NO.) | B. PASSAGE | C. HOW TO BE SHIPPED | D. BIOTECH- DERIVED | E. QUANTITY REQUESTED BY APHIS |
| BASELINE PASSAGE | X | <input type="checkbox"/> DRY ICE <input type="checkbox"/> LIQUID NITROGEN <input type="checkbox"/> OTHER (describe) | <input type="checkbox"/> YES <input type="checkbox"/> NO | |
| HIGH PASSAGE (CELLS AND BIOTECHNOLOGY-DERIVED SEEDS ONLY) | X+ _____ | | | |
| PARENTAL CONSTRUCT (BIOTECHNOLOGY-DERIVED ONLY) | | | | |

| CHECKLIST OF SUPPORTING MATERIAL | | | |
|--|--|--------------------------------|--|
| ITEM | DESCRIPTION (SEE INSTRUCTIONS ON REVERSE SIDE FOR ADDITIONAL GUIDANCE) | A. WITH THIS APPLICATION ("X") | B. DATE AND/OR CVB MAIL LOG ID OF PRIOR SUBMISSION |
| 5. MASTER SEED OR CELL REPORT | HISTORY, PREPARATION, AND TESTING OF SEED OR CELL | | |
| 6. ASSAY PROTOCOLS | STEPWISE PROCEDURES FOR NON-CODIFIED ASSAYS USED TO TEST SEED/CELL | | |
| 7. SUMMARY OF INFORMATION FORMAT | FOR BIOTECHNOLOGY-DERIVED OR IMPORTED SEEDS/CELLS | | |
| 8. ELECTRONIC FILES CONTAINING GENETIC SEQUENCE DATA | BIOTECHNOLOGY-DERIVED SEEDS/CELLS OR AS REQUESTED BY APHIS | | |
| 9. OTHER | | | |
| 10. BY DEFAULT, ALL CVB COMMUNICATIONS ARE DIRECTED TO THE APHIS LIAISON FOR THE ESTABLISHMENT. IF YOU WISH TO DESIGNATE A LABORATORY CONTACT TO HANDLE COMMUNICATIONS FOR THIS SEED/CELL, LIST THIS INDIVIDUAL BELOW. | | | |
| A. CONTACT NAME | B. PHONE | C. EMAIL | |

11. OTHER COMMENTS

I agree to ship samples in accordance with applicable USDA and hazardous shipping regulations and to provide any reagents requested by the CVB. I agree to provide the CVB with an anticipated shipping date, ideally 2 weeks beforehand. Once shipped, I will provide tracking information.

| | | |
|---|----------------------------|--------------------|
| 12. PRINTED NAME AND TITLE OF APPLICANT | 13. SIGNATURE OF APPLICANT | 14. DATE SUBMITTED |
|---|----------------------------|--------------------|

FOR CENTER FOR VETERINARY BIOLOGICS USE ONLY

The applicant is authorized to ship the above Seed/Cell to the CVB, with any Exceptions that may be attached (i.e., if there is a check in the box in item 19). The CVB Laboratory Coordinator (item 17) will contact the APHIS liaison or, if applicable, the designated Contact (item 10) to discuss needed reagents. Ship the requested quantity of samples and reagents under cover of APHIS Form 2020, noting the test authorization and, if applicable, institutional biosafety committee numbers in the Remarks section. Ship to the CVB address listed above, addressed to the attention of the CVB Laboratory Coordinator.

| | | |
|--|--|--|
| 15. TEST AUTHORIZATION NO | 16. INSTITUTIONAL BIOSAFETY COMMITTEE NO (genetically modified Seed/Cell only) | |
| 17. CENTER FOR VETERINARY BIOLOGICS LABORATORY COORDINATOR | 18. COORDINATOR'S EMAIL | |

| | | |
|--|-------------------|----------------------|
| 19. APPLICATION APPROVED BY (Signature) <input type="checkbox"/> CVB EXCEPTIONS ATTACHED | 20. DATE APPROVED | 21. CVB MAIL LOG NO. |
|--|-------------------|----------------------|

INSTRUCTIONS FOR COMPLETING APHIS FORM 2070:

Submit one copy of the form. Enclose two copies of each supporting document, except for electronic files. If additional space is needed, attach additional sheets and refer to Item No.

If APHIS's Center for Veterinary Biologics (CVB) approves the request, the CVB will complete items 4E and 14-21 and return the form to the applicant.

1. NAME AND FULL MAILING ADDRESS OF APPLICANT

Enter the establishment name and complete mailing address (street, city, state, ZIP) of the applicant. The processed form will be returned to this address.

2. U.S. VETERINARY ESTABLISHMENT NUMBER

Enter the veterinary biologics establishment number assigned by APHIS.

3. APPLICATION TYPE

Indicate whether this is a new request or an amendment to a prior authorization. If it is an amendment, enter the submission date and, if known, the CVB mail log number of the prior submission. The CVB mail log number appears in Item 21 of processed forms.

4. ITEMS TO BE SHIPPED

Applicants should prepare to ship a baseline passage (x) of conventional Master Seeds. Master Cells and biotechnology-derived Master Seeds require a baseline passage and the highest passage to be used in production (typically X+20 for cells and X+5 for Seeds). Parental constructs also may be required for Seeds with defined gene insertions or deletions.

A. **Complete Identification:** Enter the complete identification of the Seed/Cell, including lot number, exactly as it appears on Seed/Cell container labels. If the identifier on the container contains only acronyms or abbreviations and does not clearly state the agent or cell type, add this information in parentheses at the end.

B. **Passage:** All baseline passages are considered passage X. Specify the passage beyond X for the high passage item.

C. **How to be shipped:** Specify whether the samples will be shipped to the CVB on dry ice, liquid nitrogen, or some other defined environmental condition.

E. **Biotech-derived:** Indicate whether the Seed/Cell is derived from biotechnological methods.

D. **Quantity Requested by APHIS:** This item will be completed by the CVB upon review of the application. The amount will typically be in accordance with 9CFR 113.3(c)(1 through 4), unless extra samples are needed for testing specific to an individual Seed or Cell.

CHECKLIST OF SUPPORTING MATERIAL

The checklist includes items that must be satisfactorily reviewed by the CVB prior to authorizing shipment of Seed/Cell samples for confirmatory testing. If supporting information is attached to, or provided concurrently with, the application, place an X in column A of the corresponding item. If the information was provided previously, it is permissible to cite the submission date and/or CVB Mail Log Number of the prior submission in lieu of providing another copy.

5. MASTER SEED OR CELL REPORT

This is a comprehensive report detailing the history, preparation, and testing of the Master Seed/Cell candidate. See Veterinary Services Memorandum 800.109 for guidance on preparing this report. All Master Seed/Cell testing required by 9CFR, as well as any other testing conducted, should be included in this report. The CVB typically does not accept samples for confirmatory testing until the applicant has satisfactorily completed required testing.

6. ASSAY PROTOCOLS

Applicants frequently use custom testing protocols to demonstrate specific characteristics of an individual Master Seed or Cell. Applicants need to provide stepwise instructions for any assays that are not codified. The protocols should have sufficient detail to allow the CVB to replicate the assay.

7. SUMMARY INFORMATION FORMAT

The Summary Information Format (SIF) is a standardized document that assists in risk evaluations for biotechnology-derived and imported Seeds and Cells. There are several categories, depending on the nature of the Seed and the product in which it will be used. Templates are available at http://www.aphis.usda.gov/animal_health/vet_biologics/vb_sifs.shtml. For Category I, submit the complete SIF. For Category II, Sections I and II should be complete; Section III may be preliminary. For the Importation SIF, Sections I and II should be complete.

8. ELECTRONIC FILES CONTAINING GENETIC SEQUENCE DATA

Genetic sequence data should be provided electronically for Seeds/Cells that have specific gene modifications (insertions/deletions). The CVB may request sequence data on conventional Seeds as well if product labeling or promotional materials will describe a Seed to a high degree of specificity.

9. OTHER

The CVB may request other data to support an application to submit samples for confirmatory testing. Any such requirements will be communicated by the CVB licensing reviewer for the applicant.

10. APPLICANT'S LABORATORY CONTACT

By default, the CVB communicates through the APHIS liaison for the applicant establishment. The applicant, however, may designate a Laboratory Contact to

serve as the point of contact for all communications regarding the testing of this Seed/Cell. Provide the contact's name, phone number, and email address. If all communications should go through the APHIS liaison, enter NA (not applicable).

11. OTHER COMMENTS

Enter any other pertinent information here.

12. PRINTED NAME AND TITLE OF APPLICANT

The APHIS primary or alternate liaison for the establishment should serve as the applicant.

13. SIGNATURE OF APPLICANT

Self-explanatory

14. DATE SUBMITTED

This date should correspond to the date the application is mailed. This will be the submission date cited in all return correspondence.

THE FOLLOWING ITEMS ARE FOR CENTER FOR VETERINARY BIOLOGICS USE ONLY

15. TEST AUTHORIZATION NO

The CVB will issue a Test Authorization Number for the Seed/Cell. Include this number in the Remarks section of the APHIS Form 2020 that accompanies the samples, as well as any other communications regarding the testing.

16. INSTITUTIONAL BIOSAFETY COMMITTEE NO

The CVB follows the guidelines of the National Institutes of Health (NIH) when working with biotechnology-derived samples. An Institutional Biosafety Committee (IBC) reviews all testing proposals prior to biotechnology-derived sample submission. The IBC issues a number to all approved proposals. If a number is provided, include it in the Remarks section of the APHIS Form 2020 that accompanies sample shipment.

17-18. CENTER FOR VETERINARY BIOLOGICS LABORATORY COORDINATOR AND PHONE NUMBER

The CVB designates a Laboratory Coordinator for each Seed/Cell. This contact serves as the laboratory point of contact for interactions with the applicant and the CVB licensing reviewer.

19. APPLICATION APPROVED BY

Signature of CVB official approving the application. If APHIS identifies any exceptions or special circumstances regarding the authorization to ship samples, they will be noted on an attached document. If the application is not approved, the form will not bear a signature in this item and reasons for denial will be attached. If APHIS attaches documents to the return form, a check will appear in the box in this item.

20. DATE APPROVED

Self-explanatory. Shipment of Seed/Cells or reagents should not occur prior to this date.

21. CVB MAIL LOG NUMBER

The application is assigned a unique tracking number when received by the CVB. For improved efficiency, cite this number in future communications regarding this application.

According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a valid OMB control number. **This form is currently being considered for submission to the OMB.** The time required to complete this information collection is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

OMB Approval Pending
DRAFT

This application may be submitted to request authorization to ship biological product samples for confirmatory testing by APHIS. **INSTRUCTIONS: See reverse side.**

| | | |
|---|---|---|
| U.S. DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE VETERINARY SERVICES, CENTER FOR VETERINARY BIOLOGICS (CVB) APPLICATION FOR AUTHORIZATION TO SHIP BIOLOGICAL PRODUCT SAMPLES FOR CONFIRMATORY TESTING BY APHIS | | 1. NAME AND FULL MAILING ADDRESS OF APPLICANT |
| 2. U.S. VET. EST. NO. | 3. APPLICATION TYPE: <input type="checkbox"/> NEW <input type="checkbox"/> AMENDMENT TO SUBMISSION DATED _____ AND/OR PRIOR CVB MAIL LOG NO _____ | |

4. PURPOSE: PRE-LICENSE POST-LICENSE OUTLINE CHANGE OTHER (describe) _____

5. ITEM(S) TO BE SHIPPED (CHECK HERE IF ADDITIONAL ITEM INFORMATION IS APPENDED)

| A. TRUE NAME OF PRODUCT | B. PRODUCT CODE | C. SERIAL NUMBER |
|-------------------------|-----------------|------------------|
| | | |
| | | |
| | | |

CHECKLIST FOR SUPPORTING MATERIAL FOR CONFIRMATORY TESTING

| ITEM | DESCRIPTION (SEE INSTRUCTIONS ON REVERSE FOR DETAILS) | A. WITH THIS APPLICATION ("X") | B. DATE AND/OR CVB MAIL LOG NO OF PRIOR SUBMISSION |
|---|--|--------------------------------|--|
| 6. ITEMIZATION OF SERIAL RELEASE TESTING, VALIDITY CRITERIA, REQUIREMENTS FOR RELEASE | SECTION V OF OUTLINE OF PRODUCTION (9CFR 114.9) IN FINAL FORMAT | | |
| 7. STEPWISE PROTOCOLS FOR EACH ASSAY IN SECTION V OF OUTLINE OF PRODUCTION | <input type="checkbox"/> OUTLINE OF PRODUCTION (9CFR 114.9) <input type="checkbox"/> SPECIAL OUTLINE | | |
| 8. ASSAY VALIDATION REPORT(S) | TO BE SUBMITTED <i>PRIOR</i> TO REQUESTING AUTHORIZATION TO SUBMIT SAMPLES | | |
| 9. DILUTION OF PRESERVATIVE STUDY | 9CFR 113.25(d) | | |
| 10. RESULTS OF TESTING CONDUCTED BY APPLICANT | APHIS FORM 2008 | | |
| 11. OTHER | | | |

12. BY DEFAULT, ALL CVB COMMUNICATIONS ARE DIRECTED TO THE APHIS LIAISON FOR THE ESTABLISHMENT. IF YOU WISH TO DESIGNATE A LABORATORY CONTACT TO HANDLE COMMUNICATIONS FOR THIS CONFIRMATORY TESTING, LIST THIS INDIVIDUAL BELOW.

| | | |
|-----------------|----------|----------|
| A. CONTACT NAME | B. PHONE | C. EMAIL |
|-----------------|----------|----------|

I agree to ship this product in accordance with 9CFR 113.3, under cover of APHIS Form 2020, and to provide any test reagents requested by the CVB. I agree to provide the CVB with an anticipated shipping date for reagents. Once shipped, I will provide tracking information.

13. OTHER COMMENTS

| | | |
|---|----------------------------|--------------------|
| 14. PRINTED NAME AND TITLE OF APPLICANT | 15. SIGNATURE OF APPLICANT | 16. DATE SUBMITTED |
|---|----------------------------|--------------------|

FOR CENTER FOR VETERINARY BIOLOGICS USE ONLY

The applicant is authorized to ship the above product(s) to the CVB, with any Exceptions that may be attached (i.e., if there is a check in the box in item 20). The CVB Laboratory Coordinator (item 18) will contact the APHIS liaison or, if applicable, the designated Contact (item 12) to discuss needed reagents. Ship the requested quantity of samples and/or reagents under cover of APHIS Form 2020, noting the test authorization in the Remarks section. Ship to the CVB address listed above, addressed to the attention of the CVB Laboratory Coordinator.

17. TEST AUTHORIZATION NO

| | |
|--|-------------------------|
| 18. CENTER FOR VETERINARY BIOLOGICS LABORATORY COORDINATOR | 19. COORDINATOR'S EMAIL |
| 20. APPLICATION APPROVED BY (Signature) <input type="checkbox"/> CVB EXCEPTIONS ATTACHED | 21. DATE APPROVED |
| | 22. CVB MAIL LOG NO. |

DRAFT ONLY

INSTRUCTIONS FOR COMPLETING APHIS FORM 2072:

Submit one copy of the form. Enclose two copies of each supporting document, except for electronic files. If additional space is needed, attach additional sheets and refer to Item No.

If APHIS's Center for Veterinary Biologics (CVB) approves the request, the CVB will complete items 4E and 14-21 and return the form to the applicant.

1. NAME AND FULL MAILING ADDRESS OF APPLICANT

Enter the establishment name and complete mailing address (street, city, state, ZIP) of the applicant. The processed form will be returned to this address.

2. U.S. VETERINARY ESTABLISHMENT NUMBER

Enter the veterinary biologics establishment number assigned by APHIS.

3. APPLICATION TYPE

Indicate whether this is a new request or an amendment to a prior authorization. If it is an amendment, enter the submission date and, if known, the CVB mail log number of the prior submission. The CVB mail log number appears in Item 21 of processed forms.

4. PURPOSE

Indicate whether the confirmatory testing is for a prelicense product or a licensed product with a proposed change in manufacture (Outline of Production change). If testing is being conducted for another purpose, please describe.

5. ITEMS TO BE SHIPPED

Applicants should submit samples in accordance with 9CFR 113.3. Indicate the True Name, USDA Product Code, and serial number of the product(s) to be shipped. It is permissible to enter more than one serial number on a single line.

CHECKLIST OF SUPPORTING MATERIAL

The checklist includes items that must be satisfactorily reviewed by the CVB prior to authorizing submission of product samples for confirmatory testing. If supporting information is attached to, or provided concurrently with, the application, place an X in column A of the corresponding item. If the information was provided previously, it is permissible to cite the submission date and/or CVB Mail Log Number of the prior submission in lieu of providing another copy.

6. Itemization of Serial Release Testing: Section V of the Outline of Production (9CFR 114.9) should be in its expected final format with regard to tests conducted, validity criteria, and requirements for a satisfactory serial.

7. Stepwise Protocols for tests: Stepwise assay protocols, with sufficient detail for the CVB laboratory to replicate the assay, should be provided either in Section V of the Outline of Production or Special Outlines.

8. Assay validation reports: All non-codified assays must be validated for use in serial release testing. Please submit validation reports *prior to* submitting an application to ship product samples. Assays must be validated before the CVB conducts confirmatory testing.

9. Dilution of preservative study: Testing per 9CFR 113.25(d) must be conducted to determine the appropriate volume of diluent for sterility and purity testing (9CFR 113.26 or 113.27).

10. Results of Testing Conducted by the Applicant: All Section V testing must be conducted by, or under the oversight of, the applicant prior to requesting confirmatory testing. Submit all results on APHIS Form 2008. See Veterinary Services Memorandum 800.53 for additional guidance on completing APHIS Form 2008.

11. Other: The CVB may request other data to support an application to submit samples for confirmatory testing. Any such requirements will be communicated by the CVB licensing reviewer for the applicant.

12. APPLICANT'S LABORATORY CONTACT

By default, the CVB communicates through the APHIS liaison for the applicant establishment. The applicant, however, may designate a Laboratory Contact to serve as the point of contact for all communications regarding the testing of this product. Provide the contact's name, phone number, and email address. If all communications should go through the APHIS liaison, enter NA (not applicable).

13. OTHER COMMENTS

Enter any other pertinent information here.

14. PRINTED NAME AND TITLE OF APPLICANT

The APHIS primary or alternate liaison for the establishment should serve as the applicant.

15. SIGNATURE OF APPLICANT

Self-explanatory

16. DATE SUBMITTED

This date should correspond to the date the application is mailed. This will be the submission date cited in all return correspondence.

THE FOLLOWING ITEMS ARE FOR CENTER FOR VETERINARY BIOLOGICS USE ONLY**17. TEST AUTHORIZATION NO**

The CVB will issue a Test Authorization Number for the Product(s). Include this number in the Remarks section of the APHIS Form 2020 that accompanies the samples, as well as any other communications regarding the testing.

18-19. CENTER FOR VETERINARY BIOLOGICS LABORATORY COORDINATOR AND PHONE NUMBER

The CVB designates a Laboratory Coordinator for confirmatory testing. This contact serves as the laboratory point of contact for interactions with the applicant and the CVB licensing reviewer.

20. APPLICATION APPROVED BY

Signature of CVB official approving the application. If APHIS identifies any exceptions or special circumstances regarding the authorization to ship samples, they will be noted on an attached document. If the application is not approved, the form will not bear a signature in this item and reasons for denial will be attached. If APHIS attaches documents to the return form, a check will appear in the box in this item.

21. DATE APPROVED

Self-explanatory. Shipment of product should not occur prior to this date.

22. CVB MAIL LOG NUMBER

The application is assigned a unique tracking number when received by the CVB. For improved efficiency, cite this number in future communications regarding this application.