United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

Washington, DC 20250

November 7, 2006

VETERINARY SERVICES MEMORANDUM NO. 800.53

SUBJECT: Release of Biological Products

TO: VS Management Team
Biologics Licensees and Permittees
Directors, Center for Veterinary Biologics

I. PURPOSE

The purpose of this memorandum is to establish policy and procedures to comply with Title 9, Code of Federal Regulations, Parts 113 and 116, Sections 113.3, 113.6 and 116.7, for the release of biological products to licensees and permittees. A licensee or permitte shall withhold products from the market until a determination by APHIS has been made. For the purpose of this memorandum, the term "release" is the process used by APHIS in this determination.

II. CANCELLATION

Veterinary Services Memorandum No. 800.53, dated August 7, 1985, is hereby rescinded.

III. PROCEDURES FOR SHIPMENT AND RECEIPT OF BIOLOGICS SAMPLES (APHIS Form 20-20)

A. APHIS Form 2020 dated "JUL 90" and previous editions are acceptable for submission. Licensees or permittees must complete a form for each shipment of samples. A separate form must be used for each sample type indicated in Block 4. For more information refer to Veterinary Biologics Memorandum 800.59.

B. Receipt of samples will be acknowledged by APHIS with entries in Blocks 9 and 17 to 19, and a copy will be returned to the licensee or permittee.

IV. PROCEDURES FOR SUBMISSION OF VETERINARY BIOLOGICS PRODUCTION AND TEST REPORT (APHIS Form 2008 and APHIS Form 2008A)

A. The APHIS Form 2008 dated "DEC 88" or a substitute previously approved by APHIS may be used. Previous editions of VS Form 14-8 are obsolete and may not be used. Computer generated APHIS Forms 2008 and 2008a (Continuation for Veterinary Biologics Production and Test Report) forms have been reviewed

by the Center for Veterinary biologics (CVB) and, if appropriate, have been approved by the CVB, Inspection and Compliance (CVB-IC), as an acceptable substitute since 1985. Forms not previously approved by CVB should be submitted for review and approval prior to use. The use of APHIS Forms 2008 and 2008a posted on the CVB web site (www.aphis.usda.gov/vs/cvb/html/forms.htm) is acceptable.

B. When signed by an authorized representative of APHIS, the APHIS Form 2008 is the exclusive disposition document for marketing decisions. A released product, by definition, is a finished product released for marketing after all requirements have been satisfactorily complied with. If release is not granted or is subject to restrictions, an explanation is shown. Other documents may be attached for information.

C. When completed product samples in bulk form have been submitted to APHIS, an APHIS Form 2008 showing the firm's test results on bulk samples must be submitted and clearly marked as a "**BULK**" submission. This release of bulk material does not exempt a licensee or permittee from submitting an APHIS Form 2008 for the release of finished product.

D. Licensees and permittees must complete a form for each serial or subserial prepared.

1. *Serials prepared for marketing* – An original APHIS Form 2008 and one copy is to be submitted to the CVB-IC, USDA-APHIS-VS, Suite 104, 510 South 17th Street, Ames, IA 50010.

2. *Serials prepared for prelicensing evaluation or Outline of Production revisions* - An original APHIS Form 2008 and 2 copies should be sent to the appropriate Staff Reviewer, CVB-Policy, Evaluation and Licensing (CVB-PEL), USDA-APHIS-VS, at the address listed in D. 1 above.

E. Complete the APHIS Form 2008 as follows:

1. *Block 1* - Enter the page number. For subsequent pages, use APHIS Form 2008A or an acceptable equivalent.

2. *Block 2* - Enter the license or permit number [9 CFR, Parts 102 and 104, Sections 102.4(c) and 104.7(a)].

3. *Block 3* - Enter the name and mailing address of the licensee or permittee.

4. *Block 4* - Enter the date the final containers were filled. Enter N/A (not applicable) for bulk submissions.

5. *Block 5* - Enter the Veterinary Biologics product code number from the current product license or permit. [9 CFR, Parts 101 and 102, Sections 101.3(k) and 102.5(b)(3)].

6. *Block 6* - Enter the expiration date to be used on the final container labels. Compute the expiration date in accordance with the Outline of Production [9 CFR, Parts 101 and 114, Sections 101.4(f) and 114.13].

7. *Block 7* - Enter the serial or subserial number [9 CFR, Part 101, Sections 101.3(h) and (i) and 101.4(e)]. Serial and subserial numbers are limited to no more than 12 alpha-numeric characters.

8. *Block 8* - Enter the true name of the veterinary biological product as stated on the current product license or permit [9 CFR Part 101, Section 101.4(d)]. For bulk samples, specify **"BULK"** after the true name. Include the identification of the component organisms and the host animal species for which the product is intended for autogenous biologics.

9. *Block 9* - Enter all tests conducted to support release of the serial or subserial as listed in Section V of the Outline of Production, including no-tests and inconclusive tests. If the space in Block 9 is not adequate, use APHIS Form 2008a or an acceptable equivalent to report additional test results.

    a. Block 9A - Enter the test reference, also known as the test code, provided by the CVB. If the test reference is not available, enter the paragraph identification from the filed Outline of Production in which the specific test is described.
    b. Block 9B & 9C - Enter the started and concluded dates for the test. For animal potency tests, the dates entered in 9B and 9C should be all-inclusive for the complete test, including vaccination, challenge, and/or serological testing dates.
    c. Block 9D - Enter all test results, including the validity and control requirements for each test needed to determine the test conclusion.
    d. Block 9E - Insert the letter code as noted on the APHIS Form 2008 that corresponds to the test conclusion. Explain in Block 11 Remarks, the basis for a "No Test" or "Inconclusive" entry.

        (1) A *satisfactory* (S) test designation is a final conclusion given to a valid test with results which meet the release criteria stated in the filed Outline of Production or 9 CFR Standard Requirement.
        (2) An *unsatisfactory* (U) test designation is a final conclusion given to a valid test with results which do not meet the release criteria stated in the filed Outline of Production or 9 CFR Standard Requirement.
        (3) An *inconclusive* (I) test designation is an intermediate designation used for a test with a sequential design established in the filed Outline of Production or Standard Requirement. If the filed Outline of Production or Standard Requirement allows a valid test that is not satisfactory (equivocal or unsatisfactory first stage test) to be further tested, the first segment of the test is designated inconclusive (I). If a test designated inconclusive is not further tested, the conclusion of unsatisfactory is the final conclusion.
        (4) A *no test* (NT) test designation is an intermediate designation used when a deficiency in the test system has rendered a test unsuitable for drawing a valid

final conclusion. The deficiency can be a failure to meet the test's internal validity requirements which have been established in the filed Outline of Production or a standard operating procedure, or an uncontrollable occurrence such as a power outage of an incubator. This designation cannot be used to evaluate a biological product. A further process is then required to determine a final test conclusion of satisfactory or unsatisfactory based on the filed Outline of Production or 9 CFR.

10. *Block 10* - Enter the inventory of product containers or quantities to which testing and disposition apply. For serials or subserials designated as "Eligible for Release", this quantity is the entire inventory of product prepared for marketing. For serials or subserials designated as "Destroyed by Firm" or "Other- not to be marketed", indicate at least an estimated quantity. For imported material, enter the entire inventory of a completed serial prepared for marketing.

    a. Block 10A - Enter the number of containers, using a separate line for each size of container. Counts should be as accurate as possible. If it is determined after submission that there is an inventory deviation of greater than 3% from what was reported, an amended APHIS Form 2008 or acceptable equivalent should be submitted with a corrected inventory.
    b. Block 10B - Indicate the quantity in each container or kit (doses, ml, or units). Enter doses for vaccines and bacterins. For product with more than one dose size, enter the maximum number of doses that could be marketed. Enter number of tests, not plates, for diagnostic test kits. Products "For Further Manufacture" (FFM) which are not shipped in final container should indicate the volume in milliliters or liters. Specify which unit of measure is being used for each entry.
    c. Block 10C - Enter the total quantity (10A x 10B) for each line of inventory.
    d. Total columns A and C and enter the respective totals.

11. *Block 11* - Place any pertinent remarks in this block.

    a. Enter information explaining the reason a test conclusion was considered a "No Test" or "Inconclusive" as noted in Block 9E.
    b. Serials of finished product which contain material from FFM serials, must indicate the establishment number, product code, and serial number of all FFM serials contained in the finished product serial.
    c. The amount of imported product shipped for marketing in the US should be noted. An authorized sampler at the permittee's quarantine facility must certify the amount and condition of inventory received per shipment of product imported for sale and distribution. Include the date the product was received at the permittee's quarantine facility.
    d. Indicate whether the submission is in support of prelicensing or a revision to the Outline of Production.

e. If Section V of the filed Outline of Production states that potency test sera shall be submitted to APHIS, indicate the date of submission. (e.g., "Potency test sera submitted to CVB-PEL laboratory on 01 Jan 2000").
f. Reference bulk results previously submitted.

12. *Block 12* - Mark the applicable disposition block.

a. "Destroyed" is a certification of actual destruction, not the intent to destroy. Indicate the date of destruction. If destruction is for a reason other than unsatisfactory tests, state the reason in Block 11.
b. "To be Reprocessed and Retested" is a request that must be approved in accordance with 9 CFR 114.18 and VS Memorandum 800.62.
c. Use "Other" for reports of corrected inventory counts, supplemental information, etc. with an appropriate explanation provided in Block 12. Additional remarks may be recorded in Block 11.

13. *Block 13* - The APHIS Form 2008 or acceptable equivalent must have the original signature of a person whose authorization has been previously filed with APHIS in accordance with 9 CFR 114.7(a) and VS Memorandum 800.63.

14. *Block 14* - Enter the title for the person whose signature appears in Block 13.

15. *Block 15* - Enter the date the APHIS Form 2008 was signed.

F. Preparation of APHIS Form 2008A or acceptable equivalent. - All instructions given for APHIS Form 2008 apply to APHIS Form 2008A or acceptable substitute. Block 5 of APHIS Form 2008A is not applicable and need not be completed.

V. PROCEDURE FOR MARKET DETERMINATION BY APHIS

A. The APHIS Form 2008 or acceptable equivalent will be reviewed for compliance with release requirements. When exceptions are noted, the licensee or permittee will be notified of the necessary corrections or additions. An APHIS Form 2044, Audit and Correction Transmittal, may be used for this purpose.

B. Market Serials Not Selected for Testing.

1. Disposition by APHIS will be granted or withheld by completion of Blocks 16 through 19 on the APHIS Form 2008 or acceptable equivalent.

C. Market Serials Selected for Testing.

1. CVB-PEL Laboratory, within 14 calendar days after receipt of test samples, may select serials. Diagnostic test kits may be selected for testing within 3 calendar days of receipt of samples. Exceptions to the initiation of tests within 14 or more days

after the receipt of serial or test samples may be made under special circumstances. Licensees will be notified in writing whenever such exceptions are made.

2. CVB-PEL Laboratory will notify the CVB-IC that a particular serial has been selected and provide the approximate test completion date. CVB-IC will inform the manufacturer of the approximate test completion date.

3. Disposition by APHIS will be granted or withheld by completion of Blocks 16 through 19 on the APHIS Form 2008 or acceptable equivalent.

D. Serials for Prelicensing or Outline of Production Revision or Evaluation - If an APHIS Form 2008, or acceptable equivalent, is submitted in support of licensure or Outline of Production revisions, note the purpose clearly in Block 11. Upon review by CVB-PEL, the original copy of the form will be forwarded to CVB-IC. Except for the 14-day limit on the initiation of confirmatory tests by the CVB-PEL Laboratory, procedures will then be the same as for market serials. Prelicense submissions will be held by APHIS pending issuance of the product license.

E. Distribution - APHIS will retain the completed original APHIS Form 2008 or acceptable equivalent. One completed copy of the APHIS Form 2008 or acceptable equivalent, with additional documentation, as applicable, will be sent to the licensee or permittee.

VI. CENTER FOR VETERINARY BIOLOGICS-LABORATORY TEST REPORTS

A. Preparation and Processing.

1. *Serials for Marketing* - CVB-PEL Laboratory will report test results to CVB-IC on each serial or subserial tested by the CVB-PEL. Supplementary reports will be appended if additional data and explanatory comments, beyond those included on a standard report, are warranted.

2. *Serials Involved in Prelicensing Evaluation or Outline of Production Revisions* - CVB-PEL Laboratory will report test results to CVB-PEL with supplementary reports, if indicated. CVB-PEL will make recommendations to CVB-IC on the final APHIS disposition.

B. Distribution - The completed test report will be sent by CVB-IC to the licensee or permittee. APHIS will retain copies, as appropriate.

VII. EXCEPTIONS

A. First Serial Autogenous Biologics

1. Refer to VS Memorandum 800.69.

2. If the disposition of the serial is "Destroyed By Firm" (DBF), the date of final disposition and the reason the serial was destroyed should be included in the "Remarks" column.

3. Use of the APHIS Form 2008 is not required.

B. Allergenic Extracts (reference Veterinary Services Biologics Notice dated June 13, 1984)

1. The licensee will submit a summary report quarterly for product labeled for veterinary use, including the total volume released for each product licensed.

2. The summary report shall be submitted no later than the 21st day of January, April, July and October.

3. Test results for specific serials shall be made available to CVB upon request.

/s/ John R. Clifford

John R. Clifford
Deputy Administrator
Veterinary Services