



VS MEMORANDUM 800.53

Serial Release of Licensed Biological Products

1. Purpose and Background

This memorandum conveys policy and procedures to comply with title 9, *Code of Federal Regulations* (9 CFR), parts 113 and 116, sections [113.3](#), [113.6](#), and [116.7](#). The Animal and Plant Health Inspection Service (APHIS) prohibits a licensee or permittee from marketing a serial of licensed/permitted product until they receive notification, from APHIS, of the APHIS disposition authorizing or prohibiting the market release or shipment of that product serial.

This memorandum represents the Agency's position on this topic. It does not create or confer any rights for or on any person and does not bind the U.S. Department of Agriculture (USDA) or the public. The information it contains may be made available to the public. While this document provides guidance for users outside VS, VS employees may not deviate from the directions provided herein without appropriate justification and supervisory concurrence.

Pursuant to the Congressional Review Act (5 U.S.C. § 801 et seq.), the Office of Information and Regulatory Affairs designated this rule as a non-major rule, as defined by 5 U.S.C. § 804(2).

2. Document Status

- A. Issue date: 07/15/2020
- B. This document replaces Veterinary Services Memorandum 800.53 dated October 25, 2016, which is cancelled.

3. Reason for Reissuance

CVB is updating this document to harmonize procedures for serials intended for immediate marketing, prelicense evaluation, and technology transfers, as well as supporting changes to the Outline of Production. It also clarifies that CVB prefers electronic submission via the National Centers for Animal Health (NCAH) Portal for documents supporting release of biological products, serials submitted for prelicense evaluation, and technology transfer requests.



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4. Authority and References

A. Authorities (*Code of Federal Regulations (CFR)*):

- [7 CFR 371.4](#)
- [9 CFR part 101](#)
- [9 CFR part 102](#)
- [9 CFR part 113](#)
- [9 CFR part 114](#)
- [9 CFR part 116](#)

B. References:

- [VS Memorandum 800.59](#); Biological Product Samples
- [VS Memorandum 800.62](#); Relabeling, Rebottling, and Reprocessing Veterinary Biological Products
- [VS Memorandum 800.63](#); Personnel at Licensed Establishments
- [VS Memorandum 800.69](#); Guidelines for Autogenous Biologics
- [VS Memorandum 800.101](#); U.S. Veterinary Biological Product Permits for Distribution and Sale
- [VS Memorandum 800.214](#); Prescription Platform Product Biologics

C. Definitions:

- 1) **Released Product** - A finished product released for marketing after all requirements are satisfactorily met.
- 2) **Serial Release** – The CVB evaluation process of a serial resulting in a final APHIS disposition.
- 3) **APHIS Disposition** – The final decision by CVB authorizing or prohibiting a licensee or permittee to begin marketing a serial.
- 4) **NCAH Portal** - Secure web-based electronic submission portal between registered biologics licensees and permittees and CVB. CVB considers NCAH Portal submissions an acceptable equivalent to hard-copy APHIS Form 2008 and APHIS Form 2020 submissions.
- 5) **Authorized firm representative** - Personnel responsible for any phase of development, manufacture, or distribution of a veterinary biological product, and who have access to submit official correspondence to CVB.

5. Audience

VS employees and members of the biologics industry.



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6. Guidance

A. Procedures for Shipment and Receipt of Biologics Samples (APHIS Form 2020)

- 1) CVB encourages licensees and permittees to send an APHIS Form 2020 (Form 2020) from an authorized firm representative through the NCAH Portal. Form 2020s on the Biologics Forms page within the CVB website and previous editions are also acceptable for submission as hard copies. Licensees or permittees must either generate a packing slip through the NCAH Portal or prepare a Form 2020 for each shipment of samples. Use a separate Form for each sample type indicated in block 4 (Purpose). If CVB requests additional samples, the licensee/permittee must use a separate Packing Slip or Form 2020 and mark "RESUBMISSION" in block 4. For more information, refer to VS Memorandum [800.59](#) or the instructions on the CVB website for submitting an APHIS Form 2020.
 - a. Only employees with the "Sampler, authorized" role and USDA Level 2 eAuthentication can submit the information to CVB through the NCAH Portal.
 - b. Alternatively, an Authorized Firm Representative (authorized government samplers) may submit a paper copy of the Form 2020.
 - c. Send shipments of biological samples, with accompanying packing slip or Form 2020, to the following address:

Center for Veterinary Biologics
NVSL, Laboratory Resources Unit – Sample Processing
1920 Dayton Avenue
Ames, IA 50010
- 2) APHIS acknowledges receipt of samples with entries in blocks 9 and 17 through 19. CVB returns a signed copy of Form 2020, with the assigned sample number notated, to the licensee or permittee if the licensee/permittee submitted a hard-copy Form 2020. Alternatively, CVB provides a response containing the assigned sample number in the NCAH Portal if the licensee/permittee submitted via the NCAH Portal.

B. Procedures for Submission of Veterinary Biologics Production and Test Report (APHIS Form 2008, APHIS Form 2008A, and Acceptable Equivalent)

- 1) CVB encourages licensees and permittees to submit an APHIS Form 2008 (Form 2008) from an authorized firm representative through the NCAH Portal. Alternatively, the authorized firm representative may submit paper copies of Forms 2008 available on



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the Biologics Form page within the CVB website or use an approved substitute. Submit forms not previously approved by CVB for review and approval prior to use.

- a. Only employees with the Liaison, Alternate Liaison, or Serial Release roles and USDA Level 2 eAuthentication may submit the information to CVB through the NCAH Portal. For more information, see VS Memorandum [800.63](#).
- b. Alternatively, authorized firm representatives may submit a paper Form 2008 with an original signature, and one copy, to the following address:

CVB – Inspection and Compliance
USDA-APHIS-VS
1920 Dayton Avenue
P.O. Box 844
Ames, IA 50010

- 2) CVB considers the submission of a Form 2008, 2008A, or equivalent as confirmation by the licensee or permittee that all manufacturing, including that prior to Section V of the approved Outline of Production, complies with the Outline of Production and the applicable regulations.
- 3) When licensees/permittees submit completed product samples in bulk form to APHIS, they must submit a Form 2008, clearly marked as a “BULK” submission, showing the manufacturer’s test results on the bulk samples. Receiving an APHIS disposition allowing the release of bulk material does not exempt a licensee or permittee from submitting a Form 2008 for the release of finished product.
- 4) Licensees and permittees must submit a Form 2008 for each completed serial or subserial prepared. The licensee/permittee must submit all completed Form 2008s, regardless of whether the serial is intended for release immediately or in support of product licensure, to CVB-Inspection and Compliance (CVB-IC).
- 5) Serials (Form 2008) Submissions Requested by CVB-Policy, Evaluation, and Licensing (CVB-PEL)
 - a. Serials Prepared for Prelicensing Evaluation
 1. Serials may be prepared for various reasons during the product licensing process. Typically three serials are prepared for prelicense evaluation that may become eligible for release when the license issuance occurs. Firms should discuss this requirement with their CVB-PEL Reviewer in advance of serial preparation. This section does not apply to preliminary or partial data



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that CVB may request prior to availability of all testing data or to testing of experimental product.

2. For Forms 2008 meeting the above criteria, the firm representative should ensure that "Other" is marked in Block 12 and add the word "Prelicense" in remarks (Section 11). If submitting via the NCAH Portal, the firm representative should indicate the Disposition by Firm to be "Other-Prelicensing". Reviewers in CVB-PEL receive notification when Forms 2008 are submitted for prelicense serials. Cite the Form 2008 submission date in any subsequent related correspondence to CVB-PEL in which a copy of Form 2008 historically would have been included.
 3. CVB-IC still processes serials made for prelicense evaluation that CVB-PEL does not test. Submit samples as "Prelicense", as they are still required.
- b. Serials Supporting Outline of Production Revisions
1. Firms may make changes to the Outline of Production after product licensure. CVB-PEL may not approve certain changes until CVB has satisfactorily tested at least one serial produced and/or tested under the new method(s). Such Outline changes typically include, but are not limited to, changes in Section V testing methods or material changes to manufacture that may impact product quality. Discuss testing requirements with the Reviewer.
 2. When a Reviewer directs a licensee or permittee to provide a serial or serials for confirmatory testing to support a proposed Outline change, the Disposition by Firm on the Form 2008 for the applicable serial should be "Other-Outline Change." As with other Form 2008 submissions, cite any correspondence with the Reviewer by the Mail Log number on the Form 2008.
- c. Serials Supporting Technology Transfer Requests
1. Firms may make changes to the Outline of Production for the location of product production and/or testing. CVB-PEL must accept this change before marketing of the product, for which production and/or testing at the new location applies, may occur. CVB-IC may perform an inspection or request additional documentation to substantiate the facility has the proper equipment and personnel to manufacture the product prior to the release of a serial.



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2. When a Reviewer directs a licensee or permittee to provide a serial or serials for confirmatory testing and/or approval to support a proposed change to the location of serial production and/or testing, the Disposition by Firm on the Form 2008 for the applicable serial should be "Other-Technology Transfer."
- 6) Preparation of a Form 2008 or 2008A
- a. A firm representative must complete the paper Form 2008 as follows (See NCAH Portal User Guide for guidance on corresponding NCAH Portal fields):
 - *Block 1.* Enter the page number. For subsequent pages, use Form 2008A.
 - *Block 2.* Enter the Establishment license or permit number (9 CFR [102.4\(c\)](#) and [104.7\(a\)](#)).
 - *Block 3.* Enter the name and mailing address of the licensee or permittee.
 - *Block 4.* Enter the fill date for the final containers. Enter N/A (not applicable) for bulk submissions.
 - *Block 5.* Enter the Veterinary Biologics Product Code number from the current product license or permit (9 CFR [101.3\(k\)](#) and [102.5\(b\)\(3\)](#)). For prelicense serials, enter the assigned Product Code.
 - *Block 6.* Enter the expiration date on the final container labels. Compute the expiration date in accordance with the Outline of Production (9 CFR [101.4\(f\)](#) and [114.13](#)).
 - *Block 7.* Enter the serial or subserial number (9 CFR, [101.3\(h\)](#) and [\(i\)](#) and [101.4\(e\)](#)). Serial and subserial numbers are limited to no more than 15 alphanumeric characters.
 - *Block 8.* Enter the true name of the veterinary biological product as stated on the current product license or permit (9 CFR [101.4\(d\)](#)).
 - *Block 9.* Enter all tests conducted to support release of the serial or subserial as defined in Section V of the Outline of Production, including No Tests and Inconclusive Tests. If the space in block 9 is not adequate, use a Form 2008A to report additional test results.



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- *Block 9A.* Enter the test reference by entering the paragraph identification from the filed Outline of Production in which the specific test is described (e.g., V.C.2) and, if applicable, 9 CFR reference.
- *Blocks 9B & 9C.* Enter the Started and Concluded dates for each test conducted on bulk or final product. 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.
- *Block 9D.* Enter all test results, including the validity and control requirements as described in the filed Outline of Production.
- *Block 9E.* Insert the letter code as noted on the Form 2008 that corresponds to the test conclusion. Explain in block 11, Remarks, the basis for a "No Test" or "Inconclusive" entry.
 - *A satisfactory (S) test designation.* The firm makes this final conclusion for a valid test with results that meet the release criteria stated in the filed Outline of Production or 9 CFR Standard Requirement (9 CFR [101.5\(l\)\(2\)](#)).
 - *An unsatisfactory (U) test designation.* The firm makes this final conclusion for a valid test with results that do not meet the release criteria stated in the filed Outline of Production or 9 CFR Standard Requirement (9 CFR [101.5\(l\)\(3\)](#)).
 - *An inconclusive (I) test designation.* The firm uses this designation for an initial test when a sequential test design established in the filed Outline of Production or Standard Requirement allows further testing if a valid initial test is not satisfactory. When the initial or any subsequent test is declared inconclusive, the reasons shall be reported in the test records, the result shall not be considered as final, and the test may be repeated as established in the filed Outline of Production or Standard Requirement. If the firm designates a test as inconclusive and the biological product is not further tested, the test designation of unsatisfactory is the final conclusion. (9 CFR [101.5\(l\)\(4\)](#))
 - *A No Test (NT) designation.* The firm uses this designation when a deficiency in the test system has rendered a test unsuitable for drawing a valid conclusion. When the firm declares an initial or any subsequent test is a No Test, report the reasons in the test records.



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CVB shall not consider the results to be final, and firms may repeat the test. If the firm designates a test a No Test and the biological product is not further tested, the test designation of unsatisfactory is the final conclusion (9 CFR [101.5\(l\)\(1\)](#)).

- *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,” indicate at least an estimated quantity. For imported material, enter the entire inventory of a completed serial prepared for marketing.
 - *Block 10A.* Enter the number of containers, using a separate line for each size of container. Entities must maintain accurate accountability of product. If an inventory of product reported on the Form 2008 is inaccurate and falls outside the control limits as determined by the manufacturer, submit an amended Form 2008 with a corrected inventory.
 - *Block 10B.* Indicate the quantity in each container or the number of tests in each 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. Indicate the volume in milliliters (mL) for products “For Further Manufacture” (FFM) not shipped in final container. Specify which unit of measure applies to each entry.
 - *Block 10C.* Enter the total quantity (10A x 10B) for each line of inventory and include the unit of measure for each size (doses, mL, or units).
 - Total columns A and C and enter the respective totals, including the unit of measure for each (doses, mL, or units).
- *Block 11.* Place any pertinent remarks in this block.
 - Enter information explaining the reason a test conclusion indicated a “No Test” or “Inconclusive,” as noted in block 9E.
 - 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.



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- Note the amount of imported product shipped for marketing in the United States. 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 that the product arrived at the permittee's quarantine facility. For more information, refer to VS Memorandum [800.101](#).
 - Indicate whether the submission is in support of prelicensing, a revision to the Outline of Production, or a technology transfer request.
 - Reference test results previously submitted on a Form 2008 for another subserial.
 - Indicate if the submission is for a "Bulk" sample.
 - If the serial is the result of an approved reprocessing or rebottling submission, note the original Product Code and serial number.
 - If the serial is the result of an approved for inventory transfer submission, note the original establishment number, Product Code, and serial number.
 - If the serial has been reprocessed by adding one completed serial of product to another completed serial of product, note both serial numbers.
 - Indicate the identity and expiration date of all reference preparations used for potency testing of serials.
 - For autogenous biologics, include the identification of the component organisms and the host animal species for which the product is intended. See VS Memorandum [800.69](#) for further information on autogenous biologics. For Prescription Platform Products, include the information as indicated in VS Memorandum [800.214](#).
- *Block 12.* Mark the applicable firm disposition block.
 - "Eligible for Release" is a certification by the licensee/permittee that the serial is prepared and tested in accordance with the Outline of Production and is eligible for market release.
 - "Destroyed" is a certification of actual destruction and 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.



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- “To be Reprocessed and Retested” is a request that requires approval in accordance with 9 CFR [114.18](#) and VS Memorandum [800.62](#).
 - Use “Other” for prelicense serials, inventory or expiration date corrections, extensions or shortening of dating, rebottling, transfer requests, serials to support Outline of Production changes, technology transfers, or additional information. Provide an appropriate explanation in block 12. Record additional remarks in block 11. Note that these individual requests have their own Firm Dispositions in the NCAH Portal.
 - *Block 13.* The Form 2008 and 2008A 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](#).
 - *Block 14.* Enter the title for the person whose signature appears in block 13.
 - *Block 15.* Enter the signature date for the Form 2008.
- b. Preparation of Form 2008A. All instructions given for Form 2008 apply to Form 2008A or acceptable substitute. Block 5 of Form 2008A is not applicable; no entry needed.
1. If Section V testing per the Outline of Production is performed by the licensee/permittee after APHIS marketing release, the licensee/permittee must report unsatisfactory testing to CVB-IC in adherence to 9 CFR [116.5](#).
 2. CVB does not require the manufacturer to report satisfactory testing performed after marketing release to CVB-IC unless CVB requests the testing records. However, the manufacturer must maintain the testing records.

C. Procedure for Determination of an APHIS Disposition

CVB uses the serial release process to review test summaries related to the purity, safety, potency, or efficacy of each serial and subsequently provides an APHIS Disposition to the firm. This section applies to product serials manufactured after the license/permit of the product. It also applies to those prelicense serials produced shortly before license issuance that subsequently may become marketable after the license/permit of the product.

- 1) CVB-IC examines the final results of the licensee/permittee on a Form 2008 and evaluates whether a serial meets the criteria with testing requirements within the



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Outline of Production or Standard Requirement(s). CVB notifies the licensee/permittee of the necessary corrections or additions if there are any noted exceptions. CVB-IC may use the Audit and Correction Transmittal for this purpose. Once CVB-IC makes an authorization determination regarding whether the licensee/permittee may market or ship the serial, an authorized representative of CVB-IC signs the Form 2008. This signed form (whether on the Form 2008 or electronically) is the exclusive documentation of CVB's marketing authorization. If CVB-IC does not authorize release or determines it is subject to restrictions, CVB-IC provides an explanation on the APHIS Form 2008. CVB-IC may also provide additional information for action by the licensee/permittee.

- a. *Market Serials Not Selected for Testing.* CVB-IC will document its decision to authorize or prohibit marketing of a serial which the CVB-PEL Laboratory has not tested, by selecting an APHIS Disposition in blocks 16 through 19 on the APHIS Form 2008.
- b. *Market Serials Selected for Testing*
 1. The CVB-PEL Laboratory may select any serial of a licensed product for testing, but it must make a decision whether to test a specific serial within seven (7) full calendar days after receipt and processing of representative samples of that serial from the firm. The CVB-PEL Laboratory has three (3) full calendar days after receipt and processing of a specific diagnostic test kit sample to make a decision whether to test that specific sample.
 2. CVB-IC may select a serial of a licensed product for testing beyond the three (3) or seven (7) calendar day selection period after sample receipt. CVB-IC may notify licensees and permittees whenever such exceptions occur.
- 2) CVB-IC documents its decision to authorize or prohibit the release of a product serial in blocks 16 through 19 on the Form 2008. See Section IX.C and IX.D for the APHIS Dispositions that authorize and prohibit marketing or shipment of a serial.
- 3) Distribution. CVB-IC retains the completed original Form 2008. CVB-IC sends one completed copy of the Form 2008, with additional documentation, as applicable, to the licensee or permittee. Likewise, CVB-IC notifies the licensee or permittee by means of the NCAH Portal.

D. CVB Laboratory Test Reports

- 1) Preparation and Processing



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- a. *Serials for Marketing.* CVB-PEL Laboratory reports test results to CVB-IC on each serial or subserial tested. CVB appends supplementary reports if additional data and explanatory comments, beyond those included on a standard report, are necessary.
 - b. *Serials Involved in Prelicensing Evaluation, Outline of Production Revisions, and Technology Transfer.* CVB-PEL Laboratory reports test results to CVB-PEL with supplementary reports, if indicated. CVB-PEL makes recommendations to CVB-IC on the final APHIS disposition.
- 2) Distribution. CVB-IC sends completed test report(s) to the licensee or permittee. APHIS retains copies, as appropriate.

E. Exceptions

- 1) First Serial Autogenous Biologics
 - a. Refer to VS Memorandum [800.69](#), *Guidelines for Autogenous Biologics*.
 - b. If the disposition of the serial is "Destroyed By Firm" (DBF), the date of final disposition and the reason the firm destroyed the serial should be included in the "Remarks" column.
 - c. The licensee/permittee must make test results for specific serials available to CVB on request.

F. Electronic Notification of Marketing Authorization (Serial Release)

- 1) Electronic same-day notification is sent for final APHIS disposition of serials. This notification process is standard for all Forms 2008 CVB receives, if the licensee/permittee has provided an email address for this purpose. See Attachment 1 for an example of electronic notification.
 - a. A licensee or permittee receives email notification from CVB Serial Release, cvb.serialrelease@usda.gov, for each Form 2008 CVB processes. The email notifications may be any APHIS disposition, including notifications that a serial is not eligible for marketing. The recipient is responsible for review of the APHIS disposition and appropriate action based on the market status of the serial as determined by APHIS.
 - b. The establishment may market the product in accordance with the final disposition designated by APHIS on receipt of the electronic notification.



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- c. There is no U.S. regulatory requirement that the manufacturing site physically have a signed hard-copy of the Form 2008 before shipping an approved serial. The electronic notification is the official notification for marketing purposes.
- 2) The following statement is included on each electronic notification: This electronic notification is equivalent to an APHIS Form 2008 signed by an Authorized APHIS Representative and is appropriate for marketing authorizations.
 - 3) APHIS dispositions authorizing the market release or shipment of serials are as follows:
 - a. Not to be Tested
 - b. Tests Completed Satisfactory
 - c. Shorten Dating Approved
 - d. Other – Release for Further Manufacture
 - e. Other – Serial Released for Market
 - f. Other – Subsequent Shipment Approved (for permitted product)
 - g. Other – Conditional Release Granted
 - h. Prelicense – Test Completed Satisfactory
 - i. Prelicense Serial – Release for Market
 - 4) The following APHIS dispositions prohibiting the market release or shipment of the serial:
 - a. Test Completed UNSATISFACTORY
 - b. Shorten Dating DENIED
 - c. Other – UNSATISFACTORY Based on Firm’s Results
 - d. Other – Serial NOT RELEASED FOR MARKET
 - e. Other – Subsequent Shipment DENIED



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- f. Prelicense – EXPIRED
 - g. Prelicense – Tests completed UNSATISFACTORY
- 5) If a licensee/permittee submits a hard-copy APHIS Form 2008 for processing, the signed hard-copy Form 2008 and related CVB test reports are returned to the licensee/permittee's mailing address. CVB performs these mailings once a week. Use only one route of submission per serial submission.
- 6) CVB uses electronic notification for audit and correction transmittals. Conditions of release (Serial Release Requirements) are included within the electronic notification, if applicable.

G. Implementation/Applicability

Updated policy in this memorandum is effective immediately.



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Attachment 1



U.S. Department of Agriculture
Animal and Plant Health Inspection Services
Veterinary Biologics Marketing Notification

Name, Mailing Address of Licensee or Permittee	License or Permit No.
[REDACTED]	[REDACTED]

True Name of Product	Product Code	Serial Number	Expiration Date
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

APHIS Disposition Date	APHIS Disposition
August 24, 2016	Not to be Tested

Authorized APHIS Representative - William Huls, Biologics Specialist

This electronic notification is equivalent to an APHIS Form 2008 signed by an Authorized APHIS Representative and is appropriate for marketing authorizations. See Veterinary Services Memorandum 800.53, Release of Biological Products for more information.

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