Proposed Rules

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This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

9 CFR Parts 101 and 116

[Docket No. APHIS–2014–0063]

RIN 0579–AE11

VSTA Records and Reports Specific to International Standards for Pharmacovigilance

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Proposed rule; withdrawal and reproposal.

SUMMARY: We are proposing to amend the Virus-Serum-Toxin Act regulations concerning records and reports. This change would require veterinary biologics licensees and permittees to record and submit reports concerning adverse events associated with the use of biological products they produce or distribute. The information that must be included in the adverse event reports submitted to the Animal and Plant Health Inspection Service would be provided in separate guidance documents. This proposed rule replaces a previously published proposed rule, which we are withdrawing as part of this document.

DATES: We will consider all comments that we receive on or before November 3, 2015.

ADDRESSES: You may submit comments by either of the following methods:

- Federal eRulemaking Portal: Go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2014-0063*.
- Postal Mail/Commercial Delivery: Send your comment to Docket No. APHIS–2014–0063, Regulatory Analysis and Development, PPD, APHIS, Station 3A–03.8, 4700 River Road Unit 118, Riverdale, MD 20737–1238.

Supporting documents and any comments we receive on this docket may be viewed at *http://www.regulations.gov/#!docketDetail;D=APHIS-2014-0063* or in our reading Room, which is located in Room 1141 of the USDA South Building, 14th Street and Independence Avenue SW., Washington, DC. Normal reading room hours are 8 a.m. to 4:30 p.m., Monday through Friday, except holidays. To be sure someone is there to help you, please call (202) 799–7039 before coming.

FOR FURTHER INFORMATION CONTACT: Dr. Donna L. Malloy, Section Leader, Operational Support, Center for Veterinary Biologics Policy, Evaluation, and Licensing, VS, APHIS, 4700 River Road Unit 148, Riverdale, MD 20737–1231; (301) 851–3426.

SUPPLEMENTARY INFORMATION:

Background

The Virus-Serum-Toxin Act regulations in 9 CFR part 116 (referred to below as the regulations) contain requirements for maintaining detailed records of information necessary to give a complete accounting of all the activities within a veterinary biologics establishment. These records include records and reports for unfavorable or unintended events that occur in animals after the use of a biological product.

Specifically, the regulations in § 116.1, paragraph (a) state that such reports must include, but are not limited to, the items enumerated in the regulations, including inventory and disposition records, (§ 116.2), information concerning product development and preparation and market suspension and recalls (§ 116.5), animal records (§ 116.6), and test records (§ 116.7).

In § 116.5, paragraph (b) states that if at any time there are indications that raise questions regarding the purity, safety, potency, or efficacy of a product, or if it appears that there may be a problem regarding the preparation, testing, or distribution of a product, the licensee, permittee, or foreign manufacturer must immediately notify the Animal and Plant Health Inspection Service (APHIS) concerning the circumstances and the action taken, if any.

However, the regulations in § 116.1 do not explicitly require licensees and permittees to maintain records of adverse events associated with the use of veterinary biologics, nor do the regulations in § 116.5 provide specific guidance in determining whether an adverse event should be considered an indication that raises questions regarding the purity, safety, potency, efficacy, preparation, testing, or distribution (PSPEPTD) of such product. Consequently, each veterinary biologics manufacturer makes an independent determination concerning (1) whether an adverse event report raises PSPEPTD questions and (2) when and in what manner such report of the adverse event will be provided to APHIS.

To limit the harm to animals posed by unsatisfactory veterinary biologics, APHIS must rely on adverse event reports provided by veterinary biologics licensees and permittees. However, without any explicit guidance as to the form those reports should take, licensees and permittees are using nonstandardized methods to record and submit reports regarding adverse events to APHIS. Similarly, without explicit reporting requirements concerning adverse events, reports that may signal problems concerning the use of veterinary biological products are not all being submitted to APHIS in a timely manner.

The changes we are proposing are also consistent with guidelines set out by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). VICH is a unique project conducted under the World Organization for Animal Health, that brings together the regulatory authorities of the European Union, Japan, and the United States and representatives from the animal health industry in the three regions. Regulatory authorities and industry experts from Australia, Canada, and New Zealand participate as observers.

The purpose of VICH is to harmonize technical requirements for veterinary medicinal products (both pharmaceuticals and biologics). As a VICH member, APHIS provides expertise on veterinary biological products and participates in efforts to enhance harmonization. Both APHIS and the animal health industry are committed to seek scientifically based harmonized technical requirements for the development and use of veterinary biological products. VICH Guideline GL42 specifically addresses data

elements for submission of adverse event reports.[1]

By amending our regulations based on VICH pharmacovigilance guidelines we would be integrating into our regulations internationally accepted practices that would enhance the safety and efficacy of veterinary biologics in the United States. Furthermore, our consistency with these international guidelines would enhance the ability of the U.S. biologics industry to export their products.

We have previously undertaken rulemaking to address the problems described above and to bring our reporting and recordkeeping requirements into closer alignment with the VICH guidelines. Specifically, on August 17, 2005, we published in the **Federal Register** (70 FR 48325–48329, Docket No. 00–071–2) a proposed rule [2] to amend the regulations concerning records and reports to require veterinary biologics licensees and permittees to record and submit reports to APHIS concerning adverse events associated with the use of veterinary biological products that they produce or distribute. The proposed rule would have required veterinary biologics licensees and permittees to report to APHIS the number of doses of each licensed product that they distribute. The proposed rule also would have amended the regulations in 9 CFR part 101 to provide definitions for the terms *adverse event* and *adverse event report.*

We solicited comments on our proposal for 60 days ending on October 17, 2005. We received seven comments by that date. The comments were from industry associations, manufacturers of veterinary biologics, and a software company that specializes in pharmacovigilance. Four of these commenters expressed conceptual support for the proposed rule, but were concerned that parts of the proposed regulations were overly broad or ambiguous and would increase the regulatory burden on the industry and possibly compromise confidential business information. One commenter was skeptical of the need for the rule. The remaining commenters neither supported nor opposed the rule but instead either asked for clarification or suggested wording that they believed would provide greater clarity.

In response to these comments, we believe it is necessary to clarify those provisions that could be subject to multiple interpretations and to provide more specifics concerning the information that should be included in adverse event reports associated with the use of veterinary biologics that are submitted to the Agency. Therefore, we are withdrawing the August 17, 2005, proposed rule and are replacing it with the proposed changes described in this document. The proposed recordkeeping and reporting requirements regarding adverse events that would apply to each licensee, permittee, and foreign establishment that prepares and distributes biological products are described below.

Definitions

The regulations in 9 CFR part 101 contain definitions of terms used in the regulations concerning veterinary biologics. The proposed changes to part 116 of the regulations would make it necessary for us to add definitions for two terms used in the proposed regulations to § 101.2. We would define *adverse event* as ''any observation in animals, whether or not the cause of the event is known, that is unfavorable and unintended, and that occurs after any use (as indicated on the label or any off-label use) of a biological product, including events related to a suspected lack of expected efficacy. For products intended to diagnose disease, adverse events refer to a failure in product performance that hinders an expected discovery of the correct diagnosis.'' We would define *adverse event report* as ''any communication concerning the occurrence of an adverse event from an identifiable first-hand reporter which includes at least the following information: An identifiable reporter; an identifiable animal; an identifiable biologic product; and one or more adverse events.''

Adverse Event Records

We are proposing to add a new § 116.9 to provide requirements for adverse event records and reports. First, we would require that licensees and permittees maintain a detailed record for every adverse event report the licensee or permittee receives that is associated with the use of biological products they produce or distribute. APHIS will provide guidance on the information to be included in the reports on our Web site, based on the recommendations in the VICH Guideline GL42, which addresses data elements for submission of adverse event reports. We will release guidance documents as a final rule is being implemented, and we will make the documents available on our Web site in draft form for public comment.

Second, we would require that licensees and permittees compile a report of all adverse events reports they receive and submit that report to the APHIS at regular intervals. Specifically, we would require that these reports be submitted immediately if at any time there are indications that raise questions regarding the purity, safety, potency, or efficacy of a product, or if it appears that there may be a problem regarding the preparation, testing, or distribution of a product. If the licensee or permittee determines the adverse event report to be product-related, serious, and unexpected, the report would have to be submitted to APHIS within 15 business days of the date the report was first received. All other adverse event reports would have to be submitted within 90 calendar days of the date the report was first received.

Completion of Records

The regulations in §§ 116.1(a)(3) and 116.8 provide that all records (other than disposition records) required under part 116 shall be completed by the licensee, permittee, or foreign manufacturer before any portion of a serial of any product may be marketed in the United States or exported. We are proposing to amend those provisions to also allow adverse event records to be excluded from the list of records that must be completed before a product may be marketed or exported. Like disposition records, adverse event records could not be expected to have been completed prior to the marketing or exportation of a product.

If this proposed rule is adopted as a final rule, there would be an 18-month implementation period to allow licensees and permittees sufficient time to bring their recordkeeping and reporting into compliance with the new reporting and recordkeeping requirements.

Miscellaneous

We would also make several minor, nonsubstantive changes to the regulations to improve their clarity.

Executive Order 12866 and Regulatory Flexibility Act

This proposed rule has been determined to be not significant for the purposes of Executive Order 12866 and, therefore, has not been reviewed by the Office of Management and Budget.

In accordance with 5 U.S.C. 603, we have performed an initial regulatory flexibility analysis, which is summarized below, regarding the economic effects of this rule on small entities. The full analysis may be viewed on the Regulations.gov Web site

[1] The VICH pharmacovigilance guidelines can be accessed at *http://www.vichsec.org/guidelines/pharmacovigilance.html.*

[2] To view the proposed rule and the comments we received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2005-0071.*

(see **ADDRESSES** above for instructions for accessing Regulations.gov) or obtained from the person listed under **FOR FURTHER INFORMATION CONTACT**.

The proposed rule would affect all of the approximately 314 U.S. veterinary biologics manufacturers, including permittees. All the affected entities would have to take at least some additional action—even if that additional action involved sending a negative affirmation report to APHIS annually.

The Small Business Administration (SBA) standard for establishments primarily engaged in manufacturing vaccines, toxoids, blood fractions, and culture media of plant or animal origin (NAICS 325414) is 500 employees or fewer. It is reasonable to assume that most are small in size, under the SBA standards. This assumption is based on composite data for providers of the same and similar services in the United States. In 2012, there were 314 U.S. establishments in NAICS 325414 [3] with a total employment of 40,411. The average number of employees per firm in 2012 was 128. Similarly, in 2012, there were 235 U.S. establishments in NAICS 325413, a classification comprised of establishments primarily engaged in manufacturing in-vitro diagnostic substances, including biological substances. The average number of employees per firm in 2012 was 108.[4]

The proposed rule has the potential to benefit animals and their owners, to the extent that it allows APHIS to act quickly to limit the harm to animals posed by unsatisfactory veterinary biologics. For animal owners, the monetary benefits are difficult to estimate, because they would depend on several factors that are currently unknown—the significance, or gravity, of the harm that would be avoided with the rule in effect, and the number, and value, of animals that would avoid harm with the rule in effect. For some animal owners, especially those with large numbers of high value animals, the potential monetary benefits could be significant. This proposed rule clarifies reporting requirements. Manufacturer costs to comply with the proposed rule are expected be minimal in most cases. By revising our regulations based on VICH pharmacovigilance guidelines we will be applying an international standard to the industry which will enhance the safety and efficacy of veterinary biologics in the United States. Furthermore, our compliance with this international standard will enhance the ability of the biologics industry to export their products.

[3] *http://thedataweb.rm.census.gov/TheDataWeb_HotReport2/econsnapshot/2012/snapshot.hrml?NAICS=325414.*

[4] *http://thedataweb.rm.census.gov/TheDataWeb_HotReport2/econsnapshot/2012/snapshot.hrml?NAICS=325413.*

Executive Order 12372

This program/activity is listed in the Catalog of Federal Domestic Assistance under No. 10.025 and is subject to Executive Order 12372, which requires intergovernmental consultation with State and local officials. (See 2 CFR chapter IV.)

Executive Order 12988

This proposed rule has been reviewed under Executive Order 12988, Civil Justice Reform. It is not intended to have retroactive effect. This rule would not preempt any State or local laws, regulations, or policies where they are necessary to address local disease conditions or eradication programs. However, where safety, efficacy, purity, and potency of biological products are concerned, it is the Agency's intent to occupy the field. This includes, but is not limited to, the regulation of labeling. Under the Act, Congress clearly intended that there be national uniformity in the regulation of these products. There are no administrative proceedings which must be exhausted prior to a judicial challenge to the regulations under this rule.

Executive Order 13175

This rule does not significantly or uniquely affect the communities of Indian tribal governments. The rule does not impose any mandate on tribal governments or impose any duties on these entities. Thus, no further action is required under Executive Order 13175.

Paperwork Reduction Act

In accordance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*), the information collection or recordkeeping requirements included in this proposed rule have been submitted for approval to the Office of Management and Budget (OMB). Please send written comments to the Office of Information and Regulatory Affairs, OMB, Attention: Desk Officer for APHIS, Washington, DC 20503. Please state that your comments refer to Docket No. APHIS–2014–0063. Please send a copy of your comments to: (1) APHIS, using one of the methods described under **ADDRESSES** at the beginning of this document, and (2) Clearance Officer, OCIO, USDA, Room 404–W, 14th Street and Independence Avenue SW., Washington, DC 20250.

This proposed rule would require veterinary biologics licensees and permittees to record and submit reports to APHIS concerning adverse events associated with the use of biological products they produce or distribute. APHIS would provide guidance as to the information to be included in these reports. The reports would also be required to be maintained for a specified amount of time.

We are soliciting comments from the public (as well as affected agencies) concerning our proposed information collection and recordkeeping requirements. These comments will help us:

(1) Evaluate whether the proposed information collection is necessary for the proper performance of our agency's functions, including whether the information will have practical utility;

(2) Evaluate the accuracy of our estimate of the burden of the proposed information collection, including the validity of the methodology and assumptions used;

(3) Enhance the quality, utility, and clarity of the information to be collected; and

(4) Minimize the burden of the information collection on those who are to respond (such as through the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology; *e.g.,* permitting electronic submission of responses).

Estimate of burden: Public reporting burden for this collection of information is estimated to average 0.33 hours per response.

Respondents: U.S. importers and exporters of veterinary biological products, shippers of veterinary biological products, State veterinary authorities, and operators of establishments that produce or test veterinary biological products or that engage in product research and development.

Estimated annual number of respondents: 9,999.

Estimated annual number of responses per respondent: 1.59.

Estimated annual number of responses: 15,996.

Estimated total annual burden on respondents: 5,280 hours. (Due to averaging, the total annual burden hours may not equal the product of the annual number of responses multiplied by the reporting burden per response.)

Copies of this information collection can be obtained from Ms. Kimberly Hardy, APHIS' Information Collection Coordinator, at (301) 851–2727.

E-Government Act Compliance

The Animal and Plant Health Inspection Service is committed to

compliance with the E-Government Act to promote the use of the Internet and other information technologies, to provide increased opportunities for citizen access to Government information and services, and for other purposes. For information pertinent to E-Government Act compliance related to this proposed rule, please contact Ms. Kimberly Hardy, APHIS' Information Collection Coordinator, at (301) 851–2727.

Lists of Subjects

9 CFR Part 101

Animal biologics.

9 CFR Part 116

Animal biologics, Reporting and recordkeeping requirements.

Accordingly, we propose to amend 9 CFR parts 101 and 116 as follows:

PART 101—DEFINITIONS

■ 1. The authority citation for part 101 continues to read as follows:

Authority: 21 U.S.C. 151–159; 7 CFR 2.22, 2.80, and 371.4.

■ 2. Section 101.2 is amended by adding definitions for *adverse event* and *adverse event report* in alphabetical order to read as follows:

§ 101.2 Administrative terminology.

* * * * *

Adverse event. Any observation in animals, whether or not the cause of the event is known, that is unfavorable and unintended, and that occurs after any use (as indicated on the label or any off-label use) of a biological product, including events related to a suspected lack of expected efficacy. For products intended to diagnose disease, adverse events refer to a failure in product performance that hinders an expected discovery of the correct diagnosis.

Adverse event report. Any communication concerning the occurrence of an adverse event from an identifiable first-hand reporter which includes the following information:

(1) An identifiable reporter;

(2) An identifiable animal;

(3) An identifiable biologic product; and

(4) One or more adverse events.

* * * * *

PART 116—RECORDS AND REPORTS

■ 3. The authority citation for part 116 continues to read as follows:

Authority: 21 U.S.C. 151–159; 7 CFR 2.22, 2.80, and 371.4.

■ 4. In § 116.1, paragraph (a)(3) is revised to read as follows:

§ 116.1 Applicability and general considerations.

(a) * * *

(3) Records (other than disposition records and adverse event records) required by this part must be completed by the licensee, permittee, or foreign manufacturer, as the case may be, before any portion of a serial of any product may be marketed in the United States or exported.

* * * * *

■ 5. Section 116.8 is revised to read as follows:

§ 116.8 Completion and retention of records.

All records (other than disposition records and adverse event records) required by this part must be completed by the licensee, permittee, or foreign manufacturer before any portion of a serial of any product may be marketed in the United States or exported. All records must be retained at the licensed or foreign establishment or permittee's place of business for a period of 2 years after the expiration date of a product or longer as may be required by the Administrator.

■ 6. Section 116.9 is added to read as follows:

§ 116.9 Recording and reporting adverse events.

(a) Licensees and permittees must maintain a detailed record for every adverse event report the licensee or permittee receives for any biological product it produces or distributes. These records shall be maintained for a period of 3 years after the date the adverse event report is received. The adverse event report form and guidance on how to complete it, including guidance specific to the various information blocks on the form, is available on the APHIS Web site at [ADDRESS TO BE ADDED IN FINAL RULE] or by writing to APHIS at [POSTAL ADDRESS TO BE ADDED IN FINAL RULE].

(b) A report of all adverse events reports received by a licensee or permittee must be compiled and submitted to the Animal and Plant Health Inspection Service. The frequency of report submission is as follows:

(1) Immediate notification is required if at any time there are indications that raise questions regarding the purity, safety, potency, or efficacy of a product, or if it appears that there may be a problem regarding the preparation, testing, or distribution of a product.

(2) Adverse event reports determined by the licensee or permittee to be product-related, serious, and unexpected must be reported within 15 business days of the date the report was first received.

(3) All other adverse event reports must be reported within 90 calendar days of the date the report was first received.

Done in Washington, DC, this 31st day of August 2015.

Kevin Shea,

Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 2015–21997 Filed 9–3–15; 8:45 am]

BILLING CODE 3410–34–P

NUCLEAR REGULATORY COMMISSION

10 CFR Part 73

[NRC–2015–0179]

RIN 3150–AJ64

Cyber Security at Fuel Cycle Facilities

AGENCY: Nuclear Regulatory Commission.

ACTION: Draft regulatory basis; request for comment.

SUMMARY: The U.S. Nuclear Regulatory Commission (NRC) is requesting comments on a draft regulatory basis to support a rulemaking that would amend its regulations by adopting new cyber security requirements for certain nuclear fuel cycle facility (FCF) licensees in order to address safety and security consequences of concern. Potentially affected licensees include certain FCFs authorized to possess Category I, II, or III quantities of special nuclear material and uranium hexafluoride conversion and deconversion facilities.

DATES: Submit comments by October 5, 2015. Comments received after this date will be considered if it is practical to do so, but the NRC is only able to ensure consideration of comments received on or before this date.

ADDRESSES: You may submit comments by any of the following methods (unless this document describes a different method for submitting comments on a specific subject):

• *Federal Rulemaking Web site:* Go to *http://www.regulations.gov* and search for Docket ID NRC–2015–0179. Address questions about NRC dockets to Carol Gallagher; telephone: 301–415–3463; email: *Carol.Gallagher@nrc.gov.* For technical questions, contact the individual listed in the **FOR FURTHER INFORMATION CONTACT** section of this document.

• *Email comments to: Rulemaking.Comments@nrc.gov.* If you