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 Part 113

[Docket No. 01–067–1]

Viruses, Serums, Toxins, and Analogous Products; Determination of Moisture Content in Desiccated Biological Products

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Proposed rule.

SUMMARY: We are proposing to amend the Virus-Serum-Toxin Act regulations for the determination of moisture content in desiccated biological products to specify that such determinations be made using the harmonized gravimetric method adopted by the International Cooperation on Harmonization of Technical Requirements for the Registration of Veterinary Medicinal Products that expresses moisture content as the percentage of weight a product loses during a drying cycle, and to require that the maximum percentage of moisture permitted for a satisfactory test must be specified in a filed Outline of Production. We are proposing this change in order to replace the variety of tests for moisture determination that are currently described by manufacturers in Outlines of Production filed with the Animal and Plant Health Inspection Service with a test recognized as an international standard by scientific experts and regulatory authorities in the United States, Japan, and the European Union. In addition, we are proposing to amend sections of the regulations pertaining to general requirements for live bacterial vaccines and general requirements for live virus vaccines to specify the gravimetric method when testing for moisture content. These actions would update the regulations by providing a uniform method of determining moisture content in desiccated products and ensure the stability of that product during its dating period.

DATES: We will consider all comments that we receive on or before October 4, 2002.

ADDRESSES: You may submit comments by postal mail/commercial delivery or by e-mail. If you use postal mail/commercial delivery, please send four copies of your comment (an original and three copies) to: Docket No. 01–067–1, Regulatory Analysis and Development, PPD, APHIS, Station 3C71, 4700 River Road Unit 118, Riverdale, MD 20737–1238. Please state that your comment refers to Docket No. 01–067–1. If you use e-mail, address your comment to regulations@aphis.usda.gov. Your comment must be contained in the body of your message; do not send attached files. Please include your name and address in your message and ''Docket No. 01–067–1'' on the subject line.

You may read any comments that we receive on this docket in our reading room. The reading room 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) 690–2817 before coming.

APHIS documents published in the **Federal Register**, and related information, including the names of organizations and individuals who have commented on APHIS dockets, are available on the Internet at http://www.aphis.usda.gov/ppd/rad/webrepor.html.

FOR FURTHER INFORMATION CONTACT: Dr. Albert P. Morgan, Chief of Operational Support, Licensing and Policy Development, Center for Veterinary Biologics, VS, APHIS, 4700 River Road Unit 148, Riverdale, MD, 20737–1231; (301) 734–8245.

SUPPLEMENTARY INFORMATION:

Background

The Virus-Serum-Toxin Act regulations in 9 CFR part 113 (referred to below as the regulations) contain requirements for the preparation and testing of certain veterinary biological products. Section 113.29 of the regulations sets forth the requirement for determination of moisture content in desiccated biological products.

In this document, we are proposing to amend the regulations regarding the determination of moisture content in desiccated biological products. Residual moisture in desiccated biological products is related to the stability of these products during their dating period. Under the current regulations in § 113.29, a uniform method for determining residual moisture is not prescribed. Rather, biologics manufacturers establish an acceptable range for moisture for each of their products and test for moisture content using approved procedures specified in a filed Outline of Production. This allows biologics manufacturers to utilize test procedures that may be unique to specific products.

Three common methods are generally recognized for use in determining residual moisture:

- The titrimetric method, also known as the Karl Fischer method, which involves titration of the water content of a sample and comparison with a standard curve that has been created by titrating different volumes of water;
- The azeotropic method, which measures change in the composition (weight) of a mixture after it is boiled under a given pressure; and
- The gravimetric method, which expresses residual moisture as a percentage of weight a product loses during a drying cycle.

Although the gravimetric method or some variation thereof is used by most of the veterinary biologics manufacturers licensed by the U.S. Department of Agriculture (USDA) to test for residual moisture, the other methods may also be used if they are prescribed as a required test by regulatory authorities in other countries that receive these products as exports. Some manufacturers may be using two or more test methods in order to satisfy the regulatory requirements of other countries.

Currently, each manufacturer describes its own test for moisture content in its filed Outline of Production. Because of the variety of assay procedures specified in Outlines of Production and the conditions that exist in the different laboratories performing the procedures, even a subtle difference in conditions or technique can cause large variations in measured moisture content and raise questions concerning the stability of the

product. When performing moisture determinations, control of all critical factors that may affect an assay is important. The validity of the assay and the quality of the product during its dating period are greatly dependent on control of all factors critical to the assay. The use of a uniform method for determining the moisture content would allow for the control of all the critical factors that are part of the assay.

Therefore, in an attempt to harmonize residual moisture testing in countries with similar regulatory requirements, the International Cooperation on Harmonization of Technical Requirements for the Registration of Veterinary Medicinal Products (VICH) is recommending that regulatory authorities cooperating in the VICH initiative adopt a harmonized procedure for determining residual moisture that is based on the gravimetric method. (VICH is a unique project that brings together regulatory authorities of the United States, European Union, and Japan and representatives from the animal health industry in the three regions to harmonize technical requirements for veterinary products as a means of reducing the differences in technical requirements for veterinary drugs and biologics among regulatory agencies in different countries.) The agreement by VICH to recommend adoption of a harmonized gravimetric procedure was preceded by collaborative and comparative testing by regulatory agencies and representatives of the veterinary biologics industry to validate the method.[1] The harmonized procedure has been adopted in this proposed rule.

We are proposing to implement the recommendation of the VICH by amending the regulations in § 113.29 concerning determination of moisture content in desiccated biological products. We are proposing to require that final container samples of completed desiccated biological products be tested for residual moisture using the harmonized gravimetric method. We also are proposing to require that the maximum allowable moisture content for each product must be specified in the Outline of Production approved for filing by the Animal and Plant Health Inspection Service (APHIS). The majority of USDA-licensed biologics manufacturers currently specify a gravimetric method for determining residual moisture in their Outlines of Production. However, manufacturers are allowed to customize the assay procedure to accommodate conditions that are most suitable to a particular product. Therefore, while most manufacturers express moisture content as a percentage of weight a product loses during a drying cycle, the methods used to determine the percentage of weight loss are not uniform and, therefore, not easily duplicated or confirmed by other laboratories. This proposed rule would establish a uniform test method applicable to all products that are tested for moisture content.

The residual moisture assay proposed in this document would apply to final container samples of completed product for all desiccated vaccines. It was selected because it is a familiar, commonly used procedure that does not require special equipment or reagents, and should yield reproducible results in all laboratories. However, manufacturers would be allowed an exemption under § 113.4 of the regulations to use other test methods based on specific requirements or characteristics of the test material.

Determination of Moisture Content in Desiccated Biological Products

We are proposing to amend the regulations to specify that the requirements in § 113.29 pertain to using a VICH harmonized gravimetric method to determine the moisture content of desiccated biological products. The basis for this proposed amendment is the collaborative and comparative study performed by APHIS, other VICH members, and the animal health industry to validate the gravimetric method and earn its recognition as a VICH-recommended, harmonized procedure. In addition, we propose to amend the regulations in §§ 113.64 and 113.300 to specify the gravimetric method as the applicable procedure for determining moisture content.

Materials and Equipment

The proposed change to the regulations in § 113.29 would require the use of a heat-regulated vacuum oven with air-drying device attached to the inlet valve, a balance with a rated precision of ± 0.1 mg, and other commonly used and readily available laboratory equipment.

Compliance

Veterinary biologics manufacturers that determine moisture content in desiccated biological products by a method other than the gravimetric method that would be required by this proposed rule would be allowed 1 year after the effective date of the final rule to come into compliance or to request an exemption under § 113.4 of the regulations.

Executive Order 12866 and Regulatory Flexibility Act

This proposed rule has been reviewed under Executive Order 12866. The 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.

We are proposing to amend the Virus-Serum-Toxin Act regulations for determination of moisture content in desiccated biological products to require that such moisture determinations be made using a VICH harmonized gravimetric method that determines residual moisture by measuring the percentage of weight a product loses during a product drying cycle. In addition, we are proposing to specify the gravimetric method as the applicable test for moisture content for live bacterial and live viral vaccines. The effect of this action would be to provide a standardized method for the determination of moisture content in desiccated biological products and ensure that such moisture determinations are uniform and reproducible.

This proposed rule would affect all licensed manufacturers of veterinary biologics that test desiccated vaccines for moisture content. Currently, there are approximately 135 veterinary biologics establishments, including permittees. According to the standards of the Small Business Administration, most veterinary biologics establishments would be classified as small entities.

This proposed rule should not impose any additional testing or economic burden on these manufacturers because the regulations currently require manufacturers to specify an assay procedure for moisture content in their filed Outline of Production, and most manufacturers currently specify the gravimetric method, or some variation thereof, as the test procedure that they are using. In addition, manufacturers would have the ability to request an exemption to use other test methods based on specific requirements or characteristics of the test material.

Under these circumstances, the Administrator of the Animal and Plant Health Inspection Service has determined that this action would not

[1] We published a notice in the **Federal Register** on January 24, 2001 (65 FR 7614–7615, Docket No. 00–123–1), regarding the draft guideline ''Testing of Residual Moisture'' developed by VICH. The notice included information on how a copy of the draft guideline could be obtained from APHIS. The VICH harmonized gravimetric method can be viewed on the Internet at http://vich.eudra.org/htm/guidelines.htm#t3.

have a significant economic impact on a substantial number of small entities.

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 7 CFR part 3015, subpart V.)

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, unless they present an irreconcilable conflict with this rule. The Virus-Serum-Toxin Act does not provide administrative procedures which must be exhausted prior to a judicial challenge to the provisions of this rule.

Paperwork Reduction Act

This proposed rule contains no new information or recordkeeping requirements under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq*.).

List of Subjects in 9 CFR Part 113

Animal biologics, Exports, Imports, Reporting, and recordkeeping requirements.

Accordingly, we propose to amend 9 CFR part 113 as follows:

1. The authority citation for part 113 would continue to read as follows:

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

2. Section 113.29 would be revised to read as follows:

§ 113.29 Determination of moisture content in desiccated biological products.

Methods provided in this section must be used when a determination of moisture content in desiccated biological products is prescribed in an applicable Standard Requirement or in the filed Outline of Production for the product. Firms currently using methods other than those provided in this section for determining the moisture content in desiccated biological products have until [Insert date 1 year from effective date of the final rule] to update their Outlines of Production to be in compliance with this requirement.

(a) Final container samples of completed product shall be tested. The weight loss of the sample due to drying in a vacuum oven shall be determined. All procedures should be performed in an environment with a relative humidity less than 45 percent. The equipment necessary to perform the test is as follows:

(1) Cylindrical weighing bottles with airtight glass stoppers.

(2) Vacuum oven equipped with validated thermometer and thermostat. A suitable air-drying device should be attached to the inlet valve.

(3) Balance, accurate to 0.1 mg (rated precision ± 0.01mg).

(4) Desiccator jar equipped with phosphorous pentoxide, silica gel, or equivalent.

(5) Desiccated vaccine in original sealed vial. Sample and control should be kept at room temperature in their original airtight containers until use.

(b) Test procedure:

(1) Thoroughly cleaned and labeled sample-weighing bottles with stoppers should be allowed to dry at 60 ± 3 °C under vacuum at less than 2.5 kPa.

(i) Transfer hot bottles and stoppers into the desiccator and allow to cool to room temperature.

(ii) After bottles have cooled, insert stoppers and weigh and record the weights of the bottles as ''A.''

(iii) Return weighing bottles to the desiccator.

(2) Remove the sample container seal.

(i) Using a spatula, break up the sample plug and transfer the required amount of sample to the previously tared weighing bottle.

(ii) Insert the stopper and weigh and record the weights of the weighing bottles as ''B.''

(3) Place the weighing bottle with the stopper at an angle in the vacuum oven. Set the vacuum to < 2.5 kPa and the temperature to 60 ± 3 °C.

(4) After a minimum of 3 hours of drying time, turn off the vacuum pump and allow dry air to bleed into the oven until the pressure inside the oven is equalized with the prevailing atmospheric pressure.

(5) While the bottle is still warm, replace the stopper in its normal position and transfer the weighing bottle to the desiccator .

(i) Allow a minimum of 2 hours for the weighing bottle to cool to room temperature or for its weight to reach equilibrium.

(ii) Weigh, and record the weight as ''C.''

(6) Calculate the percentage of moisture in the original sample as follows:

(B–C)/(B–A) × (100) = Percentage of residual moisture, where:

A = tare weight of weighing bottle

B–A = weight of sample before drying

B—C = weight of sample after drying

(7) The results are considered satisfactory if the percentage of residual moisture is less than or equal to the manufacturer's specification.

3. In § 113.64, paragraph (e) would be amended by adding a new paragraph (e)(3) as follows:

§ 113.64 General requirements for live bacterial vaccines.

* * * * *

(e) * * *

(3) Final container samples of completed product from each serial and subserial must be tested for moisture content in accordance with the test provided in § 113.29.

4. Section 113.300 would be amended by revising paragraph (e) as follows:

§ 113.300 General requirements for live virus vaccines.

* * * * *

(e) *Moisture content.* (1) The maximum moisture content in desiccated vaccines must be stated in the filed Outline of Production.

(2) Final container samples of completed product from each serial or subserial must be tested for moisture content in accordance with the test prescribed in § 113.29.

Done in Washington, DC, this 30th day of July 2002.

Peter Fernandez,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 02–19669 Filed 8–2–02; 8:45 am]

BILLING CODE 3410–34–P

COMMODITY FUTURES TRADING COMMISSION

17 CFR Part 15

RIN 3038–AB91

Reporting Levels for Large Trader Reports; TRAKRS

AGENCY: Commodity Futures Trading Commission.

ACTION: Proposed rules.

SUMMARY: The Commodity Futures Trading Commission (Commission or CFTC) is proposing to amend its regulations to establish a reporting level for TRAKRS futures contracts to be traded on the Chicago Mercantile Exchange (CME). The reporting level being proposed is 25,000 contracts.

DATES: Comments must be received by September 4, 2002.

ADDRESSES: Comments should be sent to the Commodity Futures Trading Commission, Three Lafayette Centre, 1155 21st Street, NW., Washington, DC 20581, attention: Office of the Secretariat. Comments may be sent by