Rules and Regulations

Federal Register
Vol. 68, No. 193
Monday, October 6, 2003

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

9 CFR Part 113

[Docket No. 01–067–2]

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

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Final rule.

SUMMARY: We are amending the Virus-Serum-Toxin Act regulations for the determination of moisture content in desiccated biological products to require that such determinations be made using a gravimetric method 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. The gravimetric method has been adopted as an international standard by scientific experts and regulatory authorities in the United States, Canada, Japan, and the European Union. In addition, we are amending 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 will 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.

EFFECTIVE DATE: November 5, 2003.

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) prescribe standard requirements for the preparation and testing of veterinary biological products. Standard requirements consist of test methods, procedures, and criteria that define the standards for purity, safety, potency, and efficacy for a given type of veterinary biologic product. When a standard procedure for testing veterinary biological products is validated and approved by the Animal and Plant Health Inspection Service (APHIS) for general use, it is proposed for codification in the regulations. Section 113.29 of the regulations sets forth the requirement for determination of moisture content in desiccated biological products.

On August 5, 2002, we published in the **Federal Register** (67 FR 50606–50608, Docket No. 01–067–1) a proposal to amend the regulations for determination of moisture content in desiccated biological products to specify that such determinations be made using a gravimetric method, and to require that the maximum percentage of moisture permitted for a satisfactory test must be specified in a filed Outline of Production. The proposed rule was intended to 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.

We solicited comments on our proposed rule for 60 days ending on October 4, 2002. We received two comments by that date, from a veterinary biologics manufacturer and a national trade association representing veterinary biologics manufacturers. Both commenters supported the proposed rule. One commenter did, however, request that we ''clarify the exceptions to the use of the proposed method.'' The commenter recommended that if we intend to handle such instances via outline exemptions, then that should be stated. Additionally, the commenter asked that we indicate whether one valid reason for an exemption would be that a firm does not have the equipment necessary to conduct the test.

In this final rule, we are adopting the gravimetric method as the standard procedure for determining moisture content. As a Standard Requirement test, the gravimetric method should be used whenever the test for moisture content is performed. However, we note that exemptions to the use of the gravimetric method, like exemptions to any test prescribed in the various standard requirements found in part 113, may be granted for any valid reason in accordance with § 113.4, ''Exemptions to tests.'' Exemption requests are evaluated on a product-by-product basis, and in our review of such requests, we focus on the methods, equipment, and procedures that would be used in place of those prescribed in the Standard Requirement. It is the validity of the alternative methods and procedures that serves as the basis for the granting of an exemption.

Therefore, for the reasons given in the proposed rule and in this document, we are adopting the proposed rule as a final rule, without change.

Executive Order 12866 and Regulatory Flexibility Act

This 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 amending 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 gravimetric method that determines residual moisture by measuring the percentage of weight a product loses during a product drying cycle. In addition, this rule provides that the maximum percentage of moisture permitted for a satisfactory test must be specified in a filed Outline of Production. The effect of this action will be to provide a standardized method for the determination of moisture content in desiccated biological products that has been adopted internationally and ensure that such moisture determinations are uniform and reproducible.

This rule will 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.

We do not expect that this rule will impose any additional testing or economic burden on these manufacturers because manufacturers currently test their products for moisture content by methods specified in their filed Outline of Production and the reagents and equipment necessary to perform the gravimetric test for moisture content that will be required under this rule are expected to be comparable in cost.

Under these circumstances, the Administrator of the Animal and Plant Health Inspection Service has determined that this action will not 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 final rule has been reviewed under Executive Order 12988, Civil Justice Reform. It is not intended to have retroactive effect. This rule will 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 final 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 are amending 9 CFR part 113 as follows:

PART 113—[AMENDED]

■ 1. The authority citation for part 113 continues to read as follows:

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

■ 2. Section 113.29 is 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 November 5, 2004 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:

$(B - C)/(B - A) \times (100)$ = 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) is amended by adding a new paragraph (e)(3) to read 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 is amended by revising paragraph (e) to read 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 September 2003.

Kevin Shea,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 03–25251 Filed 10–3–03; 8:45 am]

BILLING CODE 3410–34–P