assigned OMB control number is 0579–0015.

List of Subjects in 9 CFR Part 94

Animal diseases, Imports, Livestock, Meat and meat products, Milk, Poultry and poultry products, Reporting and recordkeeping requirements.

Accordingly, 9 CFR part 94 is amended as follows:

PART 94—RINDERPEST, FOOT-AND-MOUTH DISEASE, FOWL PEST (FOWL PLAGUE), VELOGENIC VISCEROTROPIC NEWCASTLE DISEASE, AFRICAN SWINE FEVER, HOG CHOLERA, AND BOVINE SPONGIFORM ENCEPHALOPATHY: PROHIBITED AND RESTRICTED IMPORTATIONS

1. The authority citation for part 94 continues to read as follows:

Authority: 7 U.S.C. 147a, 150ee, 161, 162, and 450; 19 U.S.C. 1306; 21 U.S.C. 111, 114a, 134a, 134b, 134c, 134f, 136, and 136a; 31 U.S.C. 9701; 42 U.S.C. 4331 and 4332; 7 CFR 2.22, 2.80, and 371.2(d).

§ 94.1 [Amended]

2. In § 94.1, paragraph (a)(2) is amended by adding the words ''Czech Republic,'' immediately after the words ''Costa Rica,'' and by adding the word ''Italy,'' immediately after the word ''Ireland,''.

§ 94.11 [Amended]

3. In § 94.11, the first sentence in paragraph (a) is amended by adding the words ''Czech Republic,'' immediately after the word ''Chile,'' and by adding the word ''Italy,'' immediately after the word ''Hungary,''.

Done in Washington, DC, this 30th day of September 1996.

A. Strating,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 96–25503 Filed 10–3–96; 8:45 am]

BILLING CODE 3410–34–P

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9 CFR Part 113

[Docket No. 92–124–2]

Viruses, Serums, Toxins, and Analogous Products; Antibody Products

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Final rule.

SUMMARY: This rule amends the regulations by revising the designation for a group of standard requirements from ''Blood Origin Products'' to ''Antibody Products;'' revising five of the six existing standard requirements in the group; removing the sixth; and adding a new standard requirement for products intended for the treatment of failure of passive transfer. These amendments are necessary in order to update the standard requirements for veterinary biological products and to provide for their regulation in a manner that is more consistent with current scientific knowledge and understanding.

EFFECTIVE DATE: November 4, 1996

FOR FURTHER INFORMATION CONTACT: Dr. David A. Espeseth, Deputy Director, Veterinary Biologics, BBEP, APHIS, 4700 River Road Unit 148, Riverdale, MD 20737–1237, (301) 734–8245.

SUPPLEMENTARY INFORMATION:

Background

In accordance with the regulations in 9 CFR part 113 (hereinafter referred to as ''the regulations''), standard requirements are prescribed for the preparation of veterinary biological products. A standard requirement consists of specifications, procedures, and test methods that define the standards of purity, safety, potency, and efficacy for a veterinary biological product. Where a standard requirement for a product does not exist, production procedures and specifications for purity, safety, and potency of a biological product are provided in an Outline of Production filed with the Animal and Plant Health Inspection Service (APHIS). For consistency of review and uniformity of standards, standard requirements are codified in the regulations.

In recent years, the number of license applications received by APHIS for antibody products has increased substantially. Historically, the antibody source material for most of these products has been blood. Increasingly, however, the Agency is being presented with products for licensure that are derived from other sources such as colostrum, milk, and eggs. Standard requirements for many of these products are not codified in the regulations, and many of the products are not adequately addressed by the general requirements for blood origin products in § 113.450.

On July 23, 1993, we published in the Federal Register (58 FR 39462–39467, Docket No. 92–124–1) a proposed rule that would update the regulations to provide more consistent licensing standards and more appropriate product-indication statements that, in turn, should provide greater guidance to manufacturers and lead to more reliable products.

We solicited comments concerning our proposal for 60 days ending September 21, 1993. We received twelve sets of comments by that date. They were from eight manufacturers of veterinary biological products, three consultants, and a national trade association.

One commenter asked what the impact of the rule would be on a product that is currently licensed by APHIS as a veterinary biological but for which no biologic-type claim (i.e., a claim that a product functions through an immunologic mechanism to diagnose, prevent, or alleviate animal disease) is made, overtly or by implication. The commenter noted that the proposed regulations do not seem to specifically address this category of product. In response to the commenter, APHIS notes that these type of products were licensed at the request of producers for use in the nonspecific treatment of anemia, hemorrhage, or shock that may follow injury to horses. The regulations referred to such products as ''normal serum.'' This regulation does not specifically address normal serum because it is not a product which is required to be licensed. Therefore, no new licenses shall be issued for normal serum, which is not intended to affect the immune mechanism. APHIS will work with the producers of any such product that may be currently licensed to resolve any questions involving these type of products. No change to the regulations is made in response to this comment.

One commenter criticized the proposed nomenclature for products intended for the treatment of failure of passive transfer (FPT) proposed in § 113.450(b)(3). The commenter asserted that to refer to these products as ''IgG'' is misleading because such products may contain ''many other protective factors.'' In response to the commenter, APHIS believes the nomenclature proposed for products for the treatment of FPT is appropriate for this category of biological product. The reason for this is that FPT is most commonly defined as a below normal level of circulating, maternally derived immunoglobulin G (IgG) in the neonate, the awareness that IgG is measured in the establishment of product efficacy and potency, and the understanding that the ''other protective factors'' (i.e., substances other than immunoglobulins) cited are at best very poorly characterized. No change to the regulations is made in response to this comment.

Three commenters suggested other changes to proposed § 113.450(c). Two of the commenters stated that the proposed regulations precluded the use of slaughterhouse blood as an antibody

source and opined that the proposed restriction is unwarranted. APHIS believes that, unless slaughtered animals are from a herd that is maintained at a licensed establishment, physically examined, and tested to ensure freedom from infectious disease, their blood is unacceptable as a source of antibody. In this respect, the proposed regulations differ little from the current regulations. Assurance of the health of donor animals is necessary to reduce the risk of product contamination from infectious agents. No change to the regulations is made in response to these comments.

The other commenter addressed the provision in proposed § 113.450(c) that would exempt cattle from Grade A dairies supplying lacteal secretions for the manufacture of a veterinary antibody product from being maintained at a licensed establishment. The commenter recommended that the exemption be broadened to include cattle from Grade B dairies. In response to the commenter, APHIS notes that while Grade A dairies are required to conform to the provisions of the Food and Drug Administration's Grade ''A'' Pasteurized Milk Ordinance, the regulations that apply to dairies supplying Manufacturing Grade milk are less uniform and usually less stringent. In addition, monitoring of ''Grade B'' dairies is significantly less rigorous. Exempting Grade A dairies in § 113.450(c) strikes an appropriate balance between assuring pure, safe, and efficacious products and recognizing that maintenance of a dairy herd of sufficient size at a licensed establishment would be an economic burden. No change to the regulations is made in response to this comment.

Three commenters provided remarks concerning proposed § 113.450(e). One commenter felt that the specified radiation dose should be reduced from 3.0 megarads to at least 2.5 megarads to be more consistent with published information in this area. APHIS agrees with this comment. In addition, we believe the rules should allow a narrow range in the level of radiation, since it is often difficult to assure that an exact radiation dose will be delivered. In response to this comment, the regulations in §§ 113.450(e)(1), 113.450(e)(2), and 113.450(e)(3) are revised to indicate that the level of ionizing radiation to which applicable source material must be subjected shall be at least 2.5 megarads, and that a maximum radiation dosage is to be specified in the Outline of Production, based on data for that product.

The second commenter stated that the proposed treatment methods for the inactivation of extraneous agents would be too limited and that other methods of treatment should be considered by the Agency. In response to the commenter, APHIS agrees that other procedures may be as or more effective than those proposed. We agree that other procedures may be more appropriate for some source materials and that greater flexibility is needed. We are therefore amending the introductory paragraph of proposed § 113.450(e) to allow the use of another procedure, provided it is demonstrated to be at least as effective by data acceptable to APHIS and the procedure chosen is described in the filed Outline of Production for the product. Data submitted should demonstrate the alternative procedure is at least as effective against a battery of potential contaminating pathogenic microorganisms as the thermal- and irradiation-treatment methods specified.

The third commenter asserted that treatment of certain source materials is unnecessary because of the manner in which the materials are obtained. The commenter added that for certain materials, the proposed irradiation regimen would be acceptable (i.e., it would not render the materials unsuitable for use in production) only if the materials were manipulated in special, costly ways prior to treatment. In response to the commenter, the proposed regulations are the same as the current regulations in requiring treatment of source materials. APHIS believes that treatment that is demonstrated to be effective in eliminating viable pathogenic microorganisms is an essential component of an established protocol to ensure that an antibody product poses minimal risk for transmitting a potential pathogen. Regarding the claim that irradiation is unsuitable for certain substances, APHIS believes that ionizing radiation at the levels prescribed may impact the physical character of some source materials. Many of these materials, however, may be successfully heat treated. Because some source materials may not be amenable to either heating or exposure to ionizing radiation, APHIS believes flexibility should be provided in the regulations to permit the use of other procedures, provided that they can be shown to be as effective as the proposed methods for the intended purpose. As explained above, we have amended § 113.450(e) to provide such flexibility.

One commenter expressed opposition to the regulations in proposed § 113.450(h)(2) that require that any retest for purity of dried products for oral administration be conducted within 21 days of the original test. The commenter stated that ''valid circumstances may arise that prevent a test from being restarted within the 21 day time frame.'' In response to the commenter, we believe that some time limit must be prescribed, that it would be improper to allow a very long period of time to elapse before retesting, and that the proposed period would, in almost all situations, prove acceptable to the manufacturer. If we are presented with legitimate ''valid circumstances'' by a manufacturer, an extension of the time period for retest could be considered under the provisions of § 113.4. No change to the regulations is made in response to this comment.

Ten commenters expressed opinions concerning proposed § 113.499, which refers to products for the treatment of FPT. Eight of the commenters felt it was inappropriate to restrict the recommendation of a product to use only in neonates of the same species as that of antibody origin. It appears that five of the commenters misinterpreted the regulations, incorrectly interpreting them to mean that the restriction extended to all antibody products, not just to products intended for the treatment of FPT. In response to the three commenters who correctly interpreted the restriction to apply only to products intended for the treatment of FTP, APHIS believes its position is appropriate. An acceptable FPT product is one that, at the recommended dose, raises the serum IgG concentration of maternal-IgG-deficient neonates by a specified minimum amount. This increase in serum IgG concentration might be expected to confer a significant degree of protection against a broad spectrum of potential pathogens. With few exceptions, however, true broad-spectrum protection by FPT products has not been demonstrated. Furthermore, the potency test for such products, conducted to ensure that a dose of product has at least a minimum quantity of IgG, does not measure the ability of the product to protect against or alleviate disease. Upon considering factors such as antibody functionality, antibody half-life, and the spectrum of antibody activity, the Agency believes that the meaningful clinical efficacy of heterologous (i.e., derived from a different species) FPT products is simply too uncertain to warrant their licensure. No change to the regulations is made in response to these comments.

One commenter stated that the proposed requirement that parenterally administered products for the treatment of FPT should be recommended for use only in animals 120 hours of age or less would be too restrictive. In response to the commenter, APHIS notes that some

manufacturers of parenterally-administered FPT products have recommended that the products be used in animals of virtually any age, even though FPT is limited to neonatal animals. We believed that the inclusion in the proposed regulations of a prohibition against recommending such products for use in older animals would aid in preventing misuse of the product. However, we agree that the proposed rule may have been too restrictive in this regard. Therefore, in response to the comment, APHIS has revised the regulations in § 113.499 to specify that parenterally administered products for the treatment of FPT be recommended for use only in neonatal animals.

Two commenters expressed concern with the regulations in proposed § 113.499(a) pertaining to the establishment of an IgG Reference Product. One commenter stated that ''IgG Reference Product'' and ''IgG Species Standard'' should be more clearly defined and that requiring the establishment of an IgG Reference Product was inappropriate. The commenter described an alternative method for establishing product efficacy and ensuring adequate potency of production serials that was not entirely clear. In response to the commenter, we have amended the regulations to define more completely ''IgG Reference Product'' and ''IgG Species Standard''. In further response to the commenter, we believe that, based on the high degree of variability between radial immunodiffusion (RID) kits for IgG, an IgG Reference Product must be qualified (i.e., shown through efficacy testing to be an acceptable potency test reference).

The other commenter stated that the proposed requirement that dose size be based on body weight should be eliminated. The commenter asserted that because FPT products are usually marketed in a single dose size for all animals for which they are intended, and labels for veterinary biologics are required to state that the entire contents of a container must be used when first opened, portions of containers will often have to be discarded. The commenter also believed that the preparation of an IgG Species Standard would be improper because a standard appropriate for one species would not be appropriate for another. In response to the commenter, we acknowledge that historically, recommended dosages of FPT products have not been linked to body weight and that consumers have come to expect this. As a result, we are amending the regulations to indicate that an IgG Reference Product may be established with a single-dose size for all animals, as long as the animals used are at or near the maximum weight for neonates of the species. Regarding the IgG Species Standard, it is not APHIS' intent to have a single standard for all species. Different standards would be prepared for calves, foals, pigs, and so on.

In addition to the comments received, APHIS is making the following changes to the regulations for clarity. APHIS notes that the test media specified in proposed §§ 113.450(h)(2)(i) and 113.450(h)(2)(ii) are quite selective. It is possible, however, that an occasional noncoliform or nonSalmonella growth may appear on one or more test plates. To allow for this possibility, the regulations under these sections are revised to change the term ''growth'' to ''characteristic growth'' to indicate that the purity test is intended to screen for the growth of specified bacteria.

APHIS also notes that some antibody source materials—for example, whey from cheese making operations—may contain high levels of innocuous bacteria, and that biological products made from these materials may contain so many bacteria per dose that rehydrated product would have to be further diluted to do a meaningful total bacterial count as proposed in § 113.450(h)(2)(iv). To allow for this, the regulations are revised to provide for an appropriate dilution of the rehydrated sample prior to its addition to the test plates.

APHIS further notes that the regulations in §§ 113.499(a) and 113.499(c) may not make it clear whether one IgG measurement is to be obtained from each of five radial immunodiffusion (RID) plates or if five IgG measurements may be obtained from just one, or possibly two, RID plates. In addition, APHIS believes that five IgG measurements of each of the paired serum samples to qualify an IgG Reference Product is unnecessary. The regulations are revised to specify that ''five IgG measurements'' be made (§ 113.499(a)(6) and (c)) and to replace the proposed five replicate tests with one concurrent test for paired serum samples (§ 113.499(a)(5)).

In addition, APHIS notes that because the RID assay is semiquantitative, five IgG measurements of two samples instead of one, as proposed, should be made for retests for potency of serials of FPT products. The regulations are revised in § 113.499(c) to specify that two samples of a serial be included in a retest instead of one. This is consistent with retest requirements for other product types.

Therefore, based on the rationale set forth in the proposed rule and in this document, we are adopting the provisions of the proposed rule as a final rule, with the changes discussed in this document. The agency will review, on a case-by-case basis, within one year after the effective date of this rule, products that may be affected by this rule to ensure that such products come into conformance by the end of the review period.

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.

The amendments to the regulations should, in most instances, either have no significant economic impact or have a positive economic impact. For example, manufacturers will not be restricted to pasteurization for the treatment of source materials. Where this final rule may have a negative economic impact on manufacturing, such impact should be minimal. A negative impact may arise because this rule prohibits recommendations for cross-species use of FPT products. Notification, however, that such a prohibition was being considered was given by APHIS over 7 years ago.

Sections 113.450 through 113.455 are amended to reflect current scientific understanding and to establish uniform standards for antibody products made from substances other than blood. One such amendment is the provision for use of other procedures for eliminating potential contaminating microorganisms. The Agency believes the amendment is important because the Agency intends to require that all antibody products be subjected to an appropriate procedure for inactivation of potential contaminating microorganisms or another procedure demonstrated to be equally effective in eliminating viable pathogenic microorganisms. Currently, equine plasma products are exempted from heat treatment by approval of Outlines of Production. At the time this exemption was given, no other products were available for treatment of FPT in foals and it was believed that plasma-based products were not amenable to heat treatment. Certain equine FPT products that are now licensed are subjected to a treatment step in their manufacture. The Agency believes that no special benefit associated with the biologic-type claim has been demonstrated for plasma-based products to offset the added risk associated with no procedure for elimination. The amendment will give the manufacturers

of antibody products derived from equine plasma the option to use other procedures for such products provided they are demonstrated to be equally effective as heat or irradiation treatment by data acceptable to APHIS.

Section 113.499 is added to provide standards for products for the treatment of failure of passive transfer. The addition of the provision in this section that restricts the use of such products to the same species as that of antibody origin will economically impact the one manufacturer of an FPT product currently approved for cross-species use. The firm was notified over 7 years ago of our intent to establish such regulations that would restrict the recommendations for use of its product. The Agency believes the firm has been given adequate notice to provide compelling efficacy and potency data or prepare for the removal of the cross-species recommendation from labeling and advertising. Given the length of time from notification, we believe the loss of the recommendation should result in minimal economic loss to the producer.

The addition of § 113.499 may initially increase the cost to some FPT product manufacturers as necessary label changes are made and IgG Reference Products are qualified. This is not unexpected when a standard requirement is codified. No negative economic impact beyond that initially incurred is anticipated. Firms will be given one year from the effective date of this rule to come into compliance with it.

We do not expect any increase in cost to the other biologics manufacturers affected by this rule.

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.)

Paperwork Reduction Act

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

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 would not preempt any State or local laws, regulations, or policies, unless they present an irreconcilable conflict with this rule. There are no administrative procedures that must be exhausted prior to a judicial challenge to the provisions of this rule.

Regulatory Reform

This action is part of the President's Regulatory Reform Initiative, which, among other things, directs agencies to remove obsolete and unnecessary regulations and to find less burdensome ways to achieve regulatory goals.

List of Subjects in 9 CFR Part 113

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

Accordingly, 9 CFR part 113 is amended as follows:

PART 113—STANDARD REQUIREMENTS

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 371.2(d).

2. The undesignated center heading preceding § 113.450 is revised to read ''ANTIBODY PRODUCTS''.

3. Section 113.450 is revised to read as follows:

§ 113.450 General requirements for antibody products.

Unless otherwise prescribed in a Standard Requirement or in a filed Outline of Production, all antibody products shall meet the applicable requirements of this section.

(a) *Terminology.* The following terms in the regulations and standards concerning antibody products shall mean:

Antibody. An immunoglobulin molecule, having a precise glycoprotein structure, produced by certain cells of the B lymphocyte lineage in response to antigenic stimulation, and functioning to specifically bind and influence the antigens that induced its synthesis.

IgG (Immunoglobulin G). One of the several recognized classes of structurally related glycoproteins whose representatives include all known antibodies.

Monoclonal. Produced by, or derived from, the offspring of a single common progenitor cell.

Failure of passive transfer. A condition of neonates characterized by an abnormally low concentration of circulating maternal IgG.

(b) *Nomenclature.* Antibody products shall be named as follows:

(1) *Virus-specific products.* The true name of a virus-specific product shall: include the term ''antibody,'' specify the disease for which the product is intended, and indicate the type of animal that supplied the component antibodies. If the antibodies are monoclonal, the term ''monoclonal'' shall be used. Example: ''Duck Virus Hepatitis Antibody, Duck Origin.''

(2) *Bacterium-specific products.* The true name of a bacterium-specific product shall: include the term ''antibody'' if the component antibodies are directed against a nontoxin antigen or the term ''antitoxin'' if the component antibodies are directed against toxin, specify the organism against which the product is intended, and indicate the type of animal that supplied the component antibodies. If the antibodies are monoclonal, the term ''monoclonal'' shall be used. Example: ''Escherichia Coli Monoclonal Antibody, Murine Origin.''

(3) *Failure of passive transfer products.* The true name of a product for treatment of failure of passive transfer shall include the term ''IgG'' and indicate the type of animal that supplied the component IgG. Example: ''Bovine IgG.''

(4) *Combination products.* The true name of a product for treatment of failure of passive transfer as well as for the prevention and/or alleviation of a specific viral or bacterial disease shall be named according to the nomenclature prescribed above for virus-specific or bacterium-specific products.

(c) *Animals.* All animals used in the production of antibody products shall be healthy. Their health status shall be determined by physical examination by, or under the direct supervision of, a licensed veterinarian and by tests for infectious diseases. Such animals shall be maintained at licensed establishments: *Provided,* That cows maintained at Grade A dairies (or the equivalent) that are not injected with antigens for the purpose of stimulating the production of specific antibodies and that are used only for the purpose of supplying lacteal secretions are exempt from being maintained at a licensed establishment.

(1) No animal shall be used while showing clinical signs of disease. The presence of minor localized injuries or lesions (contusions, lacerations, burns, etc.) without body temperature elevation and without significant pain

and distress shall not be construed as clinical evidence of disease.

(2) Before first use and on a regular basis, all animals used in the manufacture of antibody products shall be individually subjected to applicable tests for infectious diseases. Records of all test results shall be maintained. An animal which tests positive for an infectious disease shall not be used in the manufacture of antibody products. Retests shall be conducted as deemed necessary by the Administrator.

(i) Before first use, horses shall be tested as follows for:

(A) Equine infectious anemia (EIA) at a laboratory approved by APHIS.

(B) Piroplasmosis, dourine, and glanders at the National Veterinary Services Laboratories.

(C) Brucellosis at a laboratory approved by APHIS. Horses with standard agglutination titers of 1:50 or less can be used for production. Horses with standard agglutination titers equal to or greater than 1:100 may be tested by the Rivanol or card tests. Reactors to these supplemental tests shall not be used for production. Nonreactors to the supplemental tests shall be retested after 30 days. If the supplemental tests are negative and the agglutination titer has not increased, the animal may be used for production. Otherwise, the animal is unsatisfactory for this purpose.

(ii) Horses shall be retested annually for EIA and, if housed or pastured with any other species, shall be retested annually for brucellosis.

(iii) Before first use, cattle shall be tested as follows for:

(A) Tuberculosis by an accredited veterinarian: *Provided,* That cattle at Grade A dairies supplying only lacteal secretions need only be tested for tuberculosis in accordance with applicable Milk Ordinances or similar laws or regulations.

(B) Brucellosis at a laboratory approved by APHIS. Cattle with standard agglutination titers of 1:50 or less can be used for production. Cattle with standard agglutination titers equal to or greater than 1:100 may be tested by the Rivanol or card tests. Reactors to these supplemental tests shall not be used for production. Nonreactors to the supplemental tests shall be retested after 30 days. If the supplemental tests are negative and the agglutination titer has not increased, the animal may be used for production; otherwise, the animal is unsatisfactory for this purpose. Cattle at Grade A dairies supplying only lacteal secretions need not be tested individually for brucellosis if a portion of their secretions contribute to the herd milk pool tested as required by the brucellosis ring test. An animal of a herd testing positive by this test shall not be used in production.

(iv) Cattle shall be retested annually for both tuberculosis and brucellosis. Cattle at Grade A dairies supplying only lacteal secretions need only be tested for tuberculosis in accordance with applicable Milk Ordinances or similar laws or regulations. Cattle at Grade A dairies supplying only lacteal secretions need not be tested individually for brucellosis if a portion of their secretions contribute to the herd milk pool tested as required by the brucellosis ring test. An animal of a herd testing positive by this test shall not be used in production.

(v) For other species, appropriate tests and the frequency with which they are applied shall be specified in the filed Outline of Production for the product.

(vi) If a positive result is obtained on any prescribed test, the positive animal(s) shall be removed from the herd and the remaining animals retested. Production shall not be renewed until a negative herd test is obtained not less than 28 days following removal of the positive animal(s).

(vii) Negative animals shall be maintained separate and apart from untested or positive animals of any species. Production animals shall not be used for any other purpose, such as testing, work, or recreation.

(d) *Collection procedures.* Blood, lacteal secretions, and egg material shall be collected as described in the filed Outline of Production for the product.

(e) *Ingredient handling and processing.* Blood derivatives (serum, plasma, etc.), lacteal secretions, and egg material used in the production of antibody products shall be subjected to an appropriate procedure for the inactivation of potential contaminating microorganisms. The procedure shall be one of those described below and specified in the filed Outline of Production for the product: *Provided,* That another procedure may be substituted if demonstrated to be at least as effective by data acceptable to APHIS and specified in the filed Outline of Production for the product. These data are expected to come from a study comparing the effectiveness of the established and substitute procedures against a satisfactory battery of potential contaminating microorganisms.

(1) Blood derivatives of equine origin shall be heated at 58.0–59.0° C for 60 minutes, and blood derivatives of bovine, porcine, or other origin shall be heated at 58.0–59.0° C for 30 minutes. In lieu of heat treatment, blood derivatives of any origin may be treated with at least 2.5 megarads of ionizing radiation, with a maximum radiation dosage specified in the filed Outline of Production for the product.

(2) Lacteal secretions shall be heated as described in paragraph (e)(1) of this section, or shall be pasteurized at either 72° C for 15 seconds or 89° C for 1 second using appropriate equipment. In lieu of the heat treatment regimens prescribed, lacteal secretions may be treated with at least 2.5 megarads of ionizing radiation, with a maximum radiation dosage specified in the Outline of Production for the product.

(3) Egg material shall be heated at 58.0–59.0° C for 30 minutes, or treated with at least 2.5 megarads of ionizing radiation, with a maximum radiation dosage specified in the filed Outline of Production for the product.

(4) Blood derivatives, lacteal secretions, and egg material shall not contain preservatives at the time of heat treatment, and immediately after heat treatment shall be cooled to 7° C or lower.

(5) Licensees shall keep detailed records as to each batch treated and each serial of product prepared for marketing. Recording charts shall bear full information concerning the material treated and tests made of the equipment used for treatment.

(f) *Preservatives.* Liquid antibody products, except those immediately frozen following preparation and maintained in a frozen state until time of use, shall contain at least one preservative from the following list, within the range of concentration set forth:

(1) Phenol 0.25 to 0.55 percent, or

(2) Cresol 0.10 to 0.30 percent, and/or

(3) Thimerosal 0.01 to 0.03 percent, or

(4) Other preservative(s) specified in the filed Outline of Production for the product.

(g) *Antigens for hyperimmunization.* If animals are hyperimmunized to generate antibodies for a product for the prevention and/or alleviation of a specific infectious disease, and a USDA-licensed veterinary biological product is not employed for this purpose, the following shall apply:

(1) For each antigen, a Master Seed shall be established.

(i) Bacterial Master Seeds shall be tested for purity and identity as prescribed for live bacterial vaccines in § 113.64.

(ii) Viral Master Seeds shall be tested for purity and identity as prescribed for live virus vaccines in § 113.300.

(2) The maximum allowable passage level of the hyperimmunizing antigen shall be the passage level of the antigen used to generate product shown to be

efficacious and shall not exceed 10 passages from the Master Seed.

(h) *Purity tests.* Final container samples of each serial and each subserial shall be tested for viable bacteria and fungi as follows:

(1) Dried products for parenteral administration and liquid products shall be tested as prescribed in § 113.26.

(2) For dried products for oral administration, 10 final container samples shall be reconstituted with sterile water at the volume recommended on the label and tested for the following contaminants:

(i) *Coliforms.* One milliliter of each rehydrated sample shall be pipetted into a 100 × 15 mm petri dish and 10–15 ml of violet red bile agar at 45–50° C added. The plate shall be manipulated to coat its entirety with the agar-sample mixture and allowed to stand until the mixture solidifies. The plate shall then be incubated at 35° C for 24 hours. A positive control plate and a negative control plate shall be prepared at the same time and in the same manner as the plates containing samples of the serial. All plates shall be examined at the end of the incubation period. If characteristic growth is observed on the negative control plate, or no characteristic growth is observed on the positive control plate, the test shall be considered inconclusive and may be repeated. If characteristic growth is observed on any of the 10 plates containing samples of the serial, one retest to rule out faulty technique may be conducted on samples from 20 final containers. If characteristic growth is observed on any of the retest plates, or if a retest is not initiated within 21 days of the completion of the original test, the serial or subserial is unsatisfactory.

(ii) *Salmonellae.* One milliliter of each rehydrated sample shall be pipetted into a 100 × 15 mm petri dish and 10–15 ml of brilliant green agar at 45–50° C added. The dish shall be manipulated to coat its entirety with the agar-sample mixture and allowed to stand until the mixture solidifies. The plate shall then be incubated at 35° C for 24 hours. A positive control plate and a negative control plate shall be prepared at the same time and in the same manner as the plates containing samples of the serial. All plates shall be examined at the end of the incubation period. If characteristic growth is observed on the negative control plate, or no characteristic growth is observed on the positive control plate, the test shall be considered inconclusive and may be repeated. If characteristic growth is observed on any of the 10 plates containing samples of the serial, one retest to rule out faulty technique may be conducted on samples from 20 final containers. If characteristic growth is observed on any of the retest plates, or if a retest is not initiated within 21 days of the completion of the original test, the serial or subserial is unsatisfactory.

(iii) *Fungi.* One milliliter of each rehydrated sample shall be pipetted into a 100 × 15 mm petri dish and 10–15 ml of appropriately acidified potato dextrose agar at 45–50° C added. The plate shall be manipulated to coat its entirety with the agar-sample mixture and allowed to stand until the mixture solidifies. The plate shall then be incubated at 20–25° C for 5 days. A positive control plate and a negative control plate shall be prepared at the same time and in the same manner as the plates containing samples of the serial. All plates shall be examined at the end of the incubation period. If growth is observed on the negative control plate, or no growth is observed on the positive control plate, the test shall be considered inconclusive and may be repeated. If growth is observed on any of the 10 plates containing samples of the serial, one retest to rule out faulty technique may be conducted on samples from 20 final containers. If growth is observed on any of the retest plates, or if a retest is not initiated within 21 days of the completion of the original test, the serial or subserial is unsatisfactory.

(iv) *Total bacterial count.* One milliliter of each rehydrated sample, undiluted or diluted as prescribed in the Outline of Production, shall be pipetted into a 100 × 15 mm petri dish and 10–15 ml of tryptone glucose extract agar at 45–50° C added. The plate shall be manipulated to coat its entirety with the agar-sample mixture and allowed to stand until the mixture solidifies. The plate shall then be incubated at 35° C for 48 hours. A positive control plate and a negative control plate shall be prepared at the same time and in the same manner as the plates containing samples of the serial. All plates shall be examined at the end of the incubation period. If growth is observed on the negative control plate, or no growth is observed on the positive control plate, the test shall be considered inconclusive and may be repeated. If the average number of bacterial colonies on the 10 plates containing samples of the serial exceeds that specified in the filed Outline of Production for the product, one retest to rule out faulty technique may be conducted on samples from 20 final containers. If the average number of bacterial colonies on the retest plates exceeds that specified in the filed Outline of Production for the product, or if a retest is not initiated within 21 days of the completion of the original test, the serial or subserial is unsatisfactory.

(i) *Safety tests.* Bulk or final container samples of each serial shall be tested as prescribed in § 113.33(b). Dried product shall be reconstituted as indicated on the label and 0.5 ml injected per mouse.

4. In § 113.451, paragraphs (b) and (c) are removed, paragraph (d) is redesignated paragraph (b), and the introductory text of the section is revised to read as follows:

§ 113.451 Tetanus Antitoxin.

Tetanus Antitoxin is a specific antibody product containing antibodies directed against the toxin of *Clostridium tetani.* Each serial shall meet the applicable general requirements provided in § 113.450 and paragraph (a) of this section, and be tested for potency as provided in paragraph (b) of this section. Any serial found unsatisfactory by a prescribed test shall not be released.

* * * * *

5. In § 113.452, the section heading, introductory text of the section, and paragraph (a) are revised; paragraph (b) is removed; paragraph (c) is redesignated as new paragraph (b); and newly redesignated paragraph (b) introductory text, paragraphs (b)(1) and (b)(3) are revised to read as follows:

§ 113.452 Erysipelothrix Rhusiopathiae Antibody.

Erysipelothrix Rhusiopathiae Antibody is a specific antibody product containing antibodies directed against one or more somatic antigens of *Erysipelothrix rhusiopathiae.* Each serial shall be tested as provided in this section. Any serial found unsatisfactory by a prescribed test shall not be released.

(a) Each serial shall meet the applicable general requirements provided in § 113.450.

(b) *Potency test.* Bulk or final container samples of completed product from each serial shall be tested using the two-stage test provided in this section.

(1) In the first stage, each of 40 Swiss mice, each weighing 16 to 20 grams, shall be injected subcutaneously with 0.1 ml of product (dried product shall be rehydrated according to label directions). Twenty-four hours postinjection, the injected mice and 10 additional mice designated controls shall be challenged subcutaneously with the same culture of *Erysipelothrix rhusiopathiae.*

* * * * *

(3) The mice injected with product shall be observed for 10 days postchallenge and all deaths recorded.

The second stage shall be required when 7–10 of the mice injected with product die in the first stage. The second stage shall be conducted in a manner identical to the first stage.

* * * * *

§ 113.453 [Removed and Reserved]

6. Section 113.453 is removed and reserved.

7. In § 113.454, the introductory text of the section and paragraph (a) are revised; paragraph (b) is removed; paragraph (c) is redesignated as new paragraph (b); and the introductory text of newly designated paragraph (b) is revised to read as follows:

§ 113.454 Clostridium Perfringens Type C Antitoxin.

Clostridium Perfringens Type C Antitoxin is a specific antibody product containing antibodies directed against the toxin of *Clostridium perfringens* Type C. Each serial shall be tested as provided in this section. Any serial found unsatisfactory by a prescribed test shall not be released.

(a) Each serial shall meet the applicable general requirements provided in § 113.450.

(b) *Potency test.* Bulk or final container samples of completed product from each serial shall be tested using the toxin-neutralization test for Beta Antitoxin provided in this section. Dried products shall be rehydrated according to label directions.

* * * * *

8. In § 113.455, the introductory text of the section and paragraph (a) are revised; paragraph (b) is removed; paragraph (c) is redesignated as new paragraph (b); and the introductory text of newly redesignated paragraph (b) is revised to read as follows:

§ 113.455 Clostridium Perfringens Type D Antitoxin.

Clostridium Perfringens Type D Antitoxin is a specific antibody product containing antibodies directed against the toxin of *Clostridium perfringens* Type D. Each serial shall be tested as provided in this section. Any serial found unsatisfactory by a prescribed test shall not be released.

(a) Each serial shall meet the applicable general requirements provided in § 113.450.

(b) *Potency test.* Bulk or final container samples of completed product from each serial shall be tested using the toxin-neutralization test for Epsilon Antitoxin provided in this section. Dried products shall be rehydrated according to label directions.

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§§ 113.456 through 113.498 [Added and Reserved]

9. New §§ 113.456 through 113.498 are added and reserved.

10. New § 113.499 is added to read as follows:

§ 113.499 Products for treatment of failure of passive transfer.

A product for the treatment of failure of passive transfer (FPT) shall contain a specified minimum quantity of IgG per dose and shall be recommended for use only in neonates of the same species as that of antibody origin. A product for oral administration shall not be recommended for use in animals more than 24 hours of age, while one for parenteral administration shall only be recommended for use in neonatal animals. Each serial shall meet the applicable general requirements provided in § 113.450 and be tested for potency as provided in this section. Any serial found unsatisfactory by a prescribed test shall not be released.

(a) *Qualification of an IgG Reference Product.* An IgG Reference Product (reference) shall be a serial of product that is manufactured according to the filed Outline of Production, properly qualified, and used to assess the potency of subsequent product serials, as described in paragraph (c) below. The reference shall be qualified as follows:

(1) At least 20 newborn, colostrum-deprived animals of the species for which the product is recommended shall be randomly selected.

(2) Blood samples shall be taken from each animal.

(3) Each animal shall be administered one dose of reference by the recommended route and shall be observed for 24 hours.

(i) Any adverse reactions shall be recorded.

(ii) The dosage of reference administered to each animal shall be in accordance with label directions. Label directions may indicate a single dosage regardless of weight, in which case the animals in the study shall be at or near the maximum weight for neonates of the species.

(4) After 24 hours, blood samples shall be taken from each animal.

(5) Pretreatment and post treatment serum IgG concentrations shall be concurrently determined for each animal using a radial immunodiffusion (RID) method acceptable to APHIS and described in the filed Outline of Production for the product.

(6) Concurrently, using the same method, five IgG measurements shall be made on an IgG Species Standard supplied or approved by APHIS. The IgG Species Standard shall be a preparation that contains IgG specific for the species in question at a concentration acceptable to APHIS.

(7) For an IgG Reference Product to be satisfactory, all animals used to qualify the reference must remain free of unfavorable product-related reactions and at least 90 percent of the paired serum samples must reflect an increase in IgG concentration (posttreatment minus pretreatment concentration) equal to or greater than the IgG concentration of the IgG Species Standard.

(b) *Antibody functionality.* Prior to licensure, the prospective licensee shall perform a neutralization study, or another type of study acceptable to APHIS, to demonstrate functionality of product antibody.

(c) *Potency.* Bulk or final container samples of completed product from each serial shall be tested for IgG content as provided in this paragraph. Samples of the test serial and of an IgG Reference Product established in accordance with paragraph (a) of this section shall be concurrently tested for IgG content by the RID method referred to in paragraph (a)(5) of this section. Five IgG measurements shall be made on each. If the IgG level per dose of the test serial does not meet or exceed that of the reference, one complete retest, involving five IgG measurements on both the reference and two samples of the test serial, may be conducted. If, upon retest, the average IgG level per dose of the two samples of the test serial does not meet or exceed that of the reference, or if a retest is not conducted, the serial is unsatisfactory.

Done in Washington, DC, this 30th day of September 1996.

A. Strating,

Acting Administrator, Animal and Plant Health Inspection Service.

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DEPARTMENT OF THE TREASURY

Office of the Comptroller of the Currency

12 CFR Part 2

[Docket No. 96–22]

RIN 1557–AB49

Sales of Credit Life Insurance

AGENCY: Office of the Comptroller of the Currency, Treasury.

ACTION: Final rule.

SUMMARY: The Office of the Comptroller of the Currency (OCC) is revising its