prior to moving interstate by attaching to the left ear a metal tag bearing a serial number and the inscription ''U.S. Reactor,'' or a metal tag bearing a serial number designated by the State animal health official for identifying brucellosis reactors, and must be:

(1) ''B'' branded (as defined in § 78.1); or

(2) Accompanied directly to slaughter by an APHIS or State representative; or

(3) Moved in vehicles closed with official seals applied and removed by an APHIS representative, State representative, accredited veterinarian, or an individual authorized for this purpose by an APHIS representative. The official seal numbers must be recorded on the accompanying permit.

* * * * *

Done in Washington, DC, this 11th day of May 1995.

Lonnie J. King,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 95–12150 Filed 5–16–95; 8:45 am]

BILLING CODE 3410–34–P

9 CFR Parts 101 and 113

[Docket No. 94–051–1]

RIN 0579–AA66

Viruses, Serums, Toxins, and Analogous Products; In Vitro Tests for Serial Release

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Proposed rule.

SUMMARY: We are proposing to amend the regulations regarding the use of in vitro potency tests in place of animal tests for immunogenicity to: change the title of the section; prescribe requirements for in vitro immunoassays used to determine the relative antigen content of inactivated biological products; require that such immunoassays be parallel line assays based upon unexpired reference preparations; require that in vitro tests for relative antigen content be converted to parallel line assays within 2 years; specify procedures and requirements for qualifying or requalifying reference preparations for inactivated products; and add certain definitions to the regulations.

The effect of the amendment would be to standardize the methods used to determine the relative potency of inactivated biological products.

DATES: Consideration will be given only to comments received on or before August 15, 1995.

ADDRESSES: Please send an original and three copies of your comments to Docket No. 94–051–1, Regulatory Analysis and Development, PPD, APHIS, Suite 3C03, 4700 River Road Unit 118, Riverdale, MD 20737–1238. Please state that your comments refer to Docket No. 94–051–1. Comments received may be inspected at USDA, room 1141, South Building, 14th Street and Independence Avenue SW., Washington, DC, between 8 a.m. and 4:30 p.m., Monday through Friday, except holidays. Persons wishing to inspect comments are requested to call ahead (202) 690–2817 to facilitate entry into the comment reading room.

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

The regulations pertaining to the testing of biologics provide that no biological product shall be released (for sale) prior to the completion of tests prescribed to establish the product to be pure, safe, potent, and efficacious (9 CFR 113.5). Efficacy refers to the specific ability of the product to effect the result for which it is offered when used as recommended by the manufacturer. Studies conducted to establish efficacy include immunogenicity tests in host animals using product manufactured according to specific requirements which include specifications for antigen content and/or animal potency. These requirements apply to every serial of product which is produced. Therefore, if a product has been tested for immunogenicity in animals and shown to have the desired effect, it follows that subsequent serials (batches) of the product manufactured to the same specifications should also have the same effect.

Once immunogenicity is established in relation to a specific minimum antigen content in a product, it should no longer be necessary to test every subsequent serial for potency in animals if an evaluation can be made with reasonable certainty of the relative antigen content by testing the serial or subserial in an acceptable in vitro test system. Therefore, when properly qualified and validated, in vitro immunoassays that determine relative antigen content of the product can serve as acceptable substitutes for potency tests that otherwise would need to be performed in animals.

The regulations in 9 CFR 113.8 pertain to the use of in vitro tests in place of animal tests for determining the potency of veterinary biological products. Currently, the in vitro tests prescribed in § 113.8 which include determining the $\log_{10}$ virus titer and performing live bacterial counts are only applicable to veterinary biologicals which contain live microorganisms. The changes and test procedures prescribed in this proposal would make § 113.8 applicable to both live and inactivated products by prescribing validity requirements for in vitro test systems used, in place of animal tests, to test for the potency of inactivated products.

We are proposing to amend the title of § 113.8 to read: ''In vitro potency tests for serial release.'' This change is intended to clarify the fact that the in vitro procedures described in § 113.8 are applicable to in vitro tests used to release serials or subserials of veterinary biological products after the prescribed animal protection studies required for licensing have been completed. In the case of inactivated products, the proposal specifies that in vitro immunoassays (test systems) which compare the relative antigen content (relative potency) of a test serial to a reference preparation must be parallel line assays using an unexpired reference preparation whose potency has been correlated directly or indirectly to immunogenicity in host animals.

In addition, the proposal would require: confirming the accuracy of the protective dose established for live products 3 years after the initiation of the host animal immunogenicity study; and confirming the immunogenicity of reference preparations used in immunoassays for inactivated biological products prior to their expiration. The expiration date for a reference would be equal to the dating of the product or as supported by data acceptable to APHIS.

APHIS is proposing these amendments because current requirements for many of the immunoassays being used to release serials or subserials of product do not have uniform validity criteria and do not include a provision to confirm periodically the immunogenicity of the reference used in such immunoassays. The proposed amendment would standardize the requirements for in vitro potency tests for relative antigen content and update and improve the reliability of such tests that are currently included in filed outlines of production. The proposed amendment does not specify a particular immunoassay provided that it is a parallel line assay using an unexpired reference preparation. While there is not a generally accepted ''best'' immunoassay, there is general agreement that an acceptable

immunoassay must demonstrate linearity, specificity, and reproducibility; and that the reference must be capable of eliciting a protective immune response in animals for as long as it serves as the reference.

APHIS has selected the parallel line assay because it demonstrates linearity, specificity, and reproducibility, and also compares the ''similarity'' of the responses elicited by the test and reference preparations in the immunoassay. APHIS feels that the ''similarity'' feature is critical to the acceptance of any in vitro immunoassay purporting to measure relative antigenic content. We realize that the proposed amendment would necessitate the revalidation of immunoassays currently contained in some filed outlines of production and propose to implement the requirements as set out below.

Firms with filed outlines of production for licensed products with in vitro potency tests that are immunoassays that are not parallel line assays would be allowed 2 years after the effective date of the final rule to come into compliance with the proposed amendments. In the interim, immunoassays, utilizing unexpired references, contained in previously approved outlines of production would continue to be allowed for serial release of previously licensed fractions but would not be acceptable for fractions not previously licensed to the firm. Firms with filed outlines of production for licensed product with in vitro potency tests for relative antigen content would be required to use unexpired references. References that have expired or that are about to expire would need to be requalified or have the dating period extended in accordance with protocols and time schedules acceptable to APHIS.

APHIS has determined that immunoassays that are not based on a parallel line assay using an unexpired reference may not provide reliable relative potency data in all instances. Such instances include the determination of relative potency based on a reference preparation that may have expired or the extrapolation of data based upon standard curves that may not be proportional between serial and reference. These amendments are being proposed in order to provide greater assurance that a serial of product provides adequate potency in all instances.

We are also adding to the regulations in § 101.5 definitions of the term ''immunogenicity'', and the terms ''master reference'', ''working reference'', and ''qualifying serial'' as they apply to reference preparations used in in vitro immunoassays.

Licensees, researchers, and scientists at the National Veterinary Services Laboratories, U.S. Department of Agriculture, have cooperated in the development of this proposed rule. We are therefore proposing to amend §§ 101.5 and 113.8 as set forth below.

Executive Order 12866 and Regulatory Flexibility Act

This proposed rule has been reviewed under Executive Order 12866. The rule has been determined to be no significant for purposes of Executive Order 12866, and therefore, has not been reviewed by the Office of Management and Budget.

This proposed amendment, if adopted, would allow any valid in vitro immunoassay to be used in determining the relative antigen content of an inactivated veterinary biological product, provided that it satisfies the parallel line criteria and that it is conducted using an unexpired reference preparation that has been tested, directly or indirectly, for immunogenicity in a manner acceptable to APHIS. This amendment would affect all licensed manufacturers of veterinary biologicals utilizing in vitro relative potency immunoassays for determining the potency of inactivated products. This proposal, however, does not impose any additional economic burden since the testing of product for potency is already required under § 113.5 of the regulations and outlines of production are routinely amended and updated. Section 113.5 specifies that no biological product shall be released prior to the completion of tests prescribed in a filed outline of production or standard requirement to establish that the product is pure, safe, potent, and efficacious. In the absence of a standard requirement prescribing a specific potency test for inactivated products, the firms develop a potency test suitable for their product, and designate such tests in the outline of production that is filed with APHIS. Currently, firms are using host animal tests, laboratory animal tests, and a variety of in vitro immunoassays as potency tests for inactivated products. This proposed rule does not restrict the firm's discretion to choose the most appropriate test for its product. The proposed rule would only prescribe validity requirements for in vitro immunoassays for relative potency. The overall effect of this proposed amendment would be to standardize in vitro immunoassays that are used to determine the potency of inactivated veterinary biological products.

Under these circumstances, the Administrator of the Animal and Plant Health Inspection Service has determined that this action would 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 12778

This proposed rule has been reviewed under Executive Order 12778, Civil Justice Reform. If this proposed rule is adopted: (1) All State and local laws and regulations that are in conflict with this rule will be preempted; (2) no retroactive effect will be given to this rule; and (3) administrative proceedings will not be required before parties may file suit in court challenging this rule.

Paperwork Reduction Act

In accordance with the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 *et seq.*), the information collection or recordkeeping requirements included in this proposed rule have been approved by the Office of Management and Budget (OMB), and there are no new requirements. The assigned OMB control number is 0579–0013.

List of Subjects

9 CFR Part 101

Animal biologics.

9 CFR Part 113

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

Accordingly, 9 CFR parts 101 and 113 would be amended as follows:

PART 101—DEFINITIONS

1. The authority citation for part 101 would continue to read as follows:

Authority: 21 U.S.C. 151–159; 7 CFR 2.17, 2.51, and 371.2(d).

2. Section 101.5 would be amended by adding new paragraphs (o), (p), (q), and (r) to read as follows:

§ 101.5 Testing terminology.

* * * * *

(o) *Master Reference.* A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity. The Master Reference may be used as the working reference in in vitro tests for relative potency. The Master Reference

may also be used to establish the relative potency of a serial of product used in requalification studies and to establish the relative potency of working references. A Master Reference may be:

(1) A completed serial of vaccine or bacterin prepared in accordance with a field Outline of Production;

(2) A purified preparation of the protective immunogen or antigen; or

(3) A nonadjuvanted harvested culture of microorganisms.

(p) *Working Reference.* A Working Reference is the reference preparation that is used in the in vitro test for the release of serials of product. Working References may be:

(1) Master References; or

(2) Serials of product that have been prepared and qualified, in a manner acceptable to APHIS, for use as reference preparations.

(q) *Qualifying Serial.* (1) A serial of biological product used to test for immunogenicity when the Master or Working Reference is a purified antigen or nonadjuvanted harvest material. Qualifying serials shall be produced in accordance with the filed Outline of Production, tested for immunogenicity in host animals in accordance with protocols acceptable to Animal and Plant Health Inspection Service, and have a geometric mean relative potency, when compared to the Master Reference, of not greater than 1.0 as established by independent parallel line assays with 5 or more replicates.

(2) Qualifying serials used to requalify or extend the dating period of a Master Reference in a repeat immunogenicity test shall satisfy all criteria prescribed above and, it addition, shall have been prepared within 6 months of requalifying testing, i.e., the initiation of the repeat immunogenicity test.

(r) *Immunogenicity.* The ability of a biological product to elicit an immune response in animals as determined by test methods or procedures acceptable to the Animal and Plant Health Inspection Service.

PART 113—STANDARD REQUIREMENTS

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

Authority: 21 U.S.C. 151–159; 7 CFR 2.17, 2.51, and 371.2(d).

4. Section 113.8 would be amended as follows:

a. The section heading would be revised to read as set forth below.

b. Paragraph (a) would be revised to read as set forth below.

c. Paragraph (b) the introductory text would be revised to read as set forth below.

d. Paragraph (b)(5) would be revised to read as set forth below.

e. Paragraph (c) would be redesignated as paragraph (e) and new paragraphs (c) and (d) would be added to read as set forth below.

f. In redesignated paragraph (e), in the introductory text, the reference to ''paragraph (b)'' would be removed and ''Paragraphs (b) and (c)'' would be added in its place. In paragraph (e)(4), the reference to ''paragraphs (c)(1),'' would be removed and ''paragraphs (e)(1),'' would be added in its place.

§ 113.8 In vitro potency tests for serial release.

(a) Master Seed which has been established as pure, safe, and immunogenic shall be used for preparing seed for production as specified in the Standard Requirements or in the filed Outline of Production. The Administrator may exempt a product from a required animal potency test for release when an evaluation can, with reasonable certainty, be made by:

(1) Subjecting the master seed to the applicable requirements prescribed in §§ 113.64, 113.100, 113.200, and 113.300;

(2) Testing the Master Seed for immunogenicity in a manner acceptable to the Animal and Plant Health Inspection Service (APHIS);

(3) Establishing a satisfactory potency for live products based on the protective dose used in the Master Seed immunogenicity test plus an adequate overage allowance for adverse conditions and test error; and

(4) For inactivated products, determining the potency of each serial or subserial, or both, using an accepted test system. Acceptable potency tests shall include:

(i) Determining the $\log_{10}$ live virus titer;

(ii) Determining the live bacterial count; or

(iii) For inactivated products, determining the relative antigen content, as compared with a reference, using a parallel line immunoassay.

(b) In the case of live products, each serial and subserial of desiccated product derived from an approved Master Seed and bulk or final container samples of each serial of completed liquid product derived from an approved Master Seed shall be evaluated by a test procedure acceptable to APHIS. On the basis of the results of the test, as compared with the required minimum potency, each serial and subserial shall either be released to the firm for marketing or withheld from the market. The evaluation of such products shall be made in accordance with the following criteria:

(1) * * *

* * * * *

(5) *Exceptions.* When a product is evaluated in terms other than $\log_{10}$ virus titer or organism count, an appropriate difference between the average potency value obtained in the retests and the potency value obtained in the initial test shall be established for use in paragraphs (b)(3) or (b)(4) of this section to evaluate such products and shall be specified in the Product Standard Requirement or filed Outline of Production.

(c) In the case of inactivated products, bulk or final container samples of completed product from each serial derived from an approved Master Seed, shall be evaluated for relative antigen content (potency), as compared with a reference, by a parallel line immunoassay procedure acceptable to APHIS. Firms currently using immunoassays which do not meet the requirements of a parallel line assay shall have 2 years from the effective date of the final rule to update their filed Outlines of Production to be in compliance with this requirement. On the basis of the results of such test procedures, each serial that meets the required minimum potency shall be released to the firm for marketing; each serial not meeting the required minimum potency shall be withheld from the market. The evaluation of such products shall be made in accordance with the following criteria:

(1) A test that results in no valid lines is considered a no test and may be repeated.

(2) An initial test that results in valid lines that are not parallel is considered a valid equivocal test. Release of the serial may not be based on such test since the result cannot be termed ''satisfactory'' or ''unsatisfactory''.

(3) If the initial test shows that potency equals or exceeds the required minimum potency, the serial is satisfactory without additional testing.

(4) If the initial test is an equivocal test due to lack of parallelism, the serial may be retested up to three times: *Provided*, That, if the test is not repeated, the serial shall be deemed unsatisfactory.

(i) If more than 50% of all valid repeat tests show that potency equals or exceeds the required minimum potency, the serial is satisfactory.

(ii) If greater than 50% of all valid repeat tests show either lack of parallelism or that potency is less than the required minimum potency, the serial is unsatisfactory.

(5) If the initial test shows that potency is less than the required minimum potency, the serial may be retested. If retested, two additional tests, must be conducted: *Provided,* That, if the serial is not retested, the serial shall be deemed unsatisfactory.

(i) If more than 50% of all valid tests show that potency equals or exceeds the required minimum potency, the serial is satisfactory.

(ii) If more than 50% of all valid tests show either lack of parallelism or that potency is less than the required minimum potency, the serial is unsatisfactory.

(d) *Repeat immunogenicity tests.*

(1) The accuracy of the protective dose established for live products in the Master Seed immunogenicty test and defined as live virus titer or live bacterial count shall be confirmed in 3 years in a manner acceptable to APHIS, unless use of the lot of Master Seed previously tested is discontinued.

(2) All determinations of relative antigen content using parallel line immunoassays shall be conducted with an unexpired reference. The lot of reference used to determine antigenic content shall have an initial dating period equal to the dating of the product or as supported by data acceptable to APHIS. Prior to the expiration date, such reference may be granted an extension of dating by confirming its immunogenicity using a Qualifying Serial of product. Tests to establish or confirm immunogenicity of references shall be conducted in a manner acceptable to APHIS. The dating period of the Master Reference and Working Reference may be extended as supported by data acceptable to APHIS if the minimum potency of the Master Reference is determined to be adequately above the minimum level needed to provide protection in the host animal. If a new Master Reference is established, it shall be allowed an initial dating period equal to the dating of the product or as supported by data acceptable to APHIS.

* * * * *

Done in Washington, DC, this 11th day of May 1995.

Terry L. Medley,

Acting Administrator, Animal and Plant Health Inspection Services.

[FR Doc. 95–12152 Filed 5–16–95; 8:45 am]

BILLING CODE 3410–34–M

9 CFR Part 113

[Docket No. 93–039–2]

Viruses, Serums, Toxins, and Analogous Products; Standard Requirement or Escherichia Coli Bacterin

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Notice of reopening and extension of comment period.

SUMMARY: We are reopening and extending the comment period for the proposed Standard Requirement for *Escherichia coli* bacterin. This extension will provide interested persons with additional time in which to prepare comments on the proposed rule.

DATES: Consideration will be given only to written comments on Docket No. 93–039–1 that are received on or before August 15, 1995.

ADDRESSES: Please send an original and three copies of your comments to Docket No. 93–039–1, Regulatory Analysis and Development, PPD, APHIS, Suite 3C03, 4700 River Road Unit 118, Riverdale, MD 20737–1238. Please state that your comments refer to Docket No. 93–039–1. Comments received may be inspected at USDA, room 1141, South Building, 14th Street and Independence Avenue SW., Washington, DC, between 8 a.m. and 4:30 p.m., Monday through Friday, except holidays. Persons wishing to inspect comments are requested to call ahead on (202) 690–2817 to facilitate entry into the comment reading room.

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

SUPPLEMENTARY INFORMATION: On October 11, 1994, we published in the **Federal Register** (59 FR 51390–51392, Docket No. 93–039–1) a proposed rule to amend the regulations in 9 CFR 113.124 to include a Standard Requirement for *Escherichia coli* bacterins. Comments on the proposed rule were required to be received on or before December 12, 1994.

So that we may consider comments submitted after that date, we are reopening and extending the public comment period on Docket No. 93–039–1 until 90 days after the date of publication of this notice in the **Federal Register**. During this period, interested persons may submit their comments for our consideration.

Authority: 21 U.S.C. 151–159, 7 CFR 2.17, 2.51, and 371.2(d). Done in Washington, DC, this 11th day of May 1995.

Lonnie J. King,

Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 95–12151 Filed 5–16–95; 8:45 am]

BILLING CODE 3410–34–M

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 71

[Airspace Docket No. 95–ANE–23]

Proposed Establishment of Class E Airspace; Portland, ME

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking.

SUMMARY: This proposed rule would establish Class E airspace at Portland International Jetport, Portland, Maine, that coincides with the hours that the associated radar approach control facility is not in operation. Since the Portland Class C airspace is predicated on an operational air traffic control tower (ATCT) serviced by a radar control approach facility (TRACON), Class E airspace must be defined for the hours when that facility is not in operation. This proposal would not change the designated boundaries or altitudes of the Portland Class C airspace, but only establish the necessary Class E airspace to provide sufficient controlled airspace for those aircraft operating under instrument flight rules during the hours when the Portland ATCT and TRACON are not in operation.

DATES: Comments must be received on or before June 16, 1995.

ADDRESSES: Send comments on the proposal in triplicate to: Manager, System Management Branch, ANE–530, Federal Aviation Administration, 12 New England Executive Park, Burlington, MA 01803–5299; telephone (617) 238–7530; fax (617) 238–7596.

The official docket may be examined in the Office of the Assistant Chief Counsel for the New England Region, ANE–7, 12 New England Executive Park, Burlington, MA 01803–5299; telephone (617) 238–7049; fax (617) 238–7055.

An informal docket may also be examined during normal business hours in the Office of the Manager, System Management Branch, Air Traffic Division, ANE–530, at the first address shown above.