sale, which are intended for use in the
treatment of animals through the
detection or measurement of antigens,
antibodies, nucleic acids, or immunity; or
(iii) Substances, at any stage of
production, shipment, distribution, or
sale, which resemble or are represented
as biological products intended for use
in the treatment of animals through
appearance, packaging, labeling, claims
(either oral or written), representations,
and through any other means.
(3) The term “treatment” shall mean
the prevention, diagnosis, management,
or cure of diseases of animals.

Guidelines. Guidelines establish
principles or practices related to test
procedures, manufacturing practices,
product standards, scientific protocols,
labeling, and other technical or policy
considerations. Guidelines contain
procedures or standards of general
applicability that are usually not
regulatory in nature, but that are related
to matters that fall under the Virus-
Serum-Toxin Act. Guidelines issued by
the agency include Veterinary Biologics
Licensing Considerations, Memoranda,
Notices, and Supplemental Assay
Methods.

Done in Washington, DC, this 3rd day of
June 1997.
Terry L. Medley,
Administrator, Animal and Plant Health
Inspection Service.

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection
Service

9 CFR Part 113
[Docket No. 92–090–2]

Viruses, Serums, Toxins, and
Analogous Products; Revision of
Standard Requirements for
Clostridium Perfringens Types C and D
Toxoids and Bacterin-Toxoids

AGENCY: Animal and Plant Health
Inspection Service, USDA.

ACTION: Final rule.

SUMMARY: We are amending the
regulations pertaining to the Standard
Requirements for Clostridium
Perfringens Types C and Clostridium
Perfringens Types D toxoids and
bacterin-toxoids. The amendments will
reduce the minimum number of rabbits
required in order to pool their serum for
testing. This amendment will also
clarify the method of determining the
test vaccine dose in rabbits based on
the recommended vaccine dosage in cattle
and other host animal species.

These amended regulations will not
change the accuracy of the assays and,
under certain circumstances, will
reduce the number of required tests as
well as the number of mice needed for
testing. The amendment is necessary to
make the potency assays conform more
closely to the revised standard
requirements for Clostridium Novyi and
Clostridium Sordelli Bacterin-Toxoids
and more economical to run when
combination products containing these
fractions are tested.

EFFECTIVE DATE: July 9, 1997.

FOR FURTHER INFORMATION CONTACT:
Dr. David A. Espeseth, Director, Licensing
and Policy Development, Center for
Veterinary Biologics, VS, APHIS, USDA,
4700 River Road Unit 148, Riverdale,
MD 20737–1237, (301) 734–8245.

SUPPLEMENTARY INFORMATION:

Background

The regulations in 9 CFR part 113
pertain to standard requirements for the
preparation of veterinary biological
products. A standard requirement
consists of test methods, procedures,
and criteria established by the Animal
and Plant Health Inspection Service
(APHIS) to determine that a veterinary
biological product is pure, safe, potent,
efficacious and not worthless,
dangerous, contaminated, or harmful.

These regulations concerning potency
testing of Clostridium Perfringens Type
C Toxoid and Bacterin-Toxoid in
§ 113.111 and Clostridium Perfringens
Type D Toxoid and Bacterin-Toxoid in
§ 113.112 reduce certain test
requirements and decrease the cost of
performing these tests. This has been
accomplished without affecting the
accuracy and reliability of the tests.

On March 22, 1993, we published a
proposed rule in the Federal Register
(58 FR 15301–15303, Docket No. 92–
090–1) to amend the regulations in
§ 113.111 pertaining to Clostridium
Perfringens Type C Toxoid and
Bacterin-Toxoid and in § 113.112
pertaining to Clostridium Perfringens
Type D Toxoid and Bacterin-Toxoid.

We proposed to reduce the number of
mice needed for serum neutralization
testing in certain circumstances. Also,
the current test method uses half of the
recommended cattle or sheep dose. The
proposed rule provided for potency
testing of product recommended for use
in host animal species other than cattle
and sheep. The recommended method in
the proposed rule provided for
recommendations for a variety of host
animal species by prescribing the use of
half of the smallest host animal dose.

Current regulations in §§ 113.111(c)
and 113.112(c) provide for at least four
of eight rabbits which are initially
injected to be bled in the potency
determination of Clostridium
Perfringens Type C Toxoid and
Bacterin-Toxoid and Clostridium
Perfringens Type D Toxoid and
Bacterin-Toxoid. The amount of
antitoxin found in the rabbit sera after
injection with the toxoid or bacterin-
toxoid is proportional to the potency of
the antigen in the product tested.

The antitoxin response of vaccinated
rabbits is measured by a toxin
neutralization assay in mice. A standard
amount of Clostridium perfringens Beta
or Epsilon toxin is mixed with a
designated amount of the test rabbits’
sera. The mixture is allowed to
neutralize for one hour. Swiss white
mice are then injected with this toxin-
sera mixture to determine if the
standard amount of toxin was
neutralized by the test rabbit sera. Since
mice are particularly sensitive to these
antitoxins, the absence of mouse mortality
indicates sufficient toxin neutralization
and thus an adequate antitoxin response
in the rabbits tested. The result would
indicate an acceptable potency for the
toxoid or bacterin-toxoid antigen in the
product tested.

Under the current regulations in
§§ 113.111(c) and 113.112(c), if four to
seven rabbits are bled for potency
testing, the sera from each rabbit must
be assayed individually. This requires
the use of at least 20 to 35 mice (each
rabbit serum is tested in a minimum of
5 mice) for serum neutralization testing
as compared to a minimum of 5 mice
with the single pooled serum sample
which was proposed.

The proposed rule required the use of
at least seven rabbits in order for the
sera to be pooled into a single sample.
The potency test would then be
conducted on the single pooled sample.
Pooling the serum samples of seven
instead of eight rabbits would reduce
the number of toxin neutralization tests
required, the number of mice needed, the
time spent, and the expense of the
procedure.

We solicited comments concerning
our proposal for 60 days ending May 21,
1993. We received six comments by that
date from manufacturers of animal
health products and a national trade
association. One of the commenters
addressed concern that, as proposed, the
rule had the
unintended effect of making the potency test requirements more stringent. As a cure, the commenter recommended the use of half the cattle dose for testing the potency of all Clostridium Perfringens Toxoids.

Five other commenters also expressed concern about the proposed reduction in the volume of rabbit inoculum to half the smallest host animal dose. One firm indicated it would be forced to increase antigen content in order to pass the stringent requirement resulting from a reduced volume of rabbit inoculum, with the possible negative effect on host animal safety.

Three commenters indicated that the proposed inoculum volumes would be incompatible with those in the recently revised standard requirements for Clostridium Novyi and Clostridium Sordellii, which permitted utilization of the same group of rabbits for testing of sheep and cattle product fractions, the only two species addressed under that standard requirement. One commenter indicated that there is no need to change the volume of the rabbit inoculum under the current regulations.

Yet another commenter suggested that the volume of rabbit inoculum should be half of the largest dose indicated on the label for any species of animal for which the product is recommended. The commenter argued that this suggestion would not affect the potency test procedure for any licensed product, while it would address the dosage to be used for alternate species not specifically addressed under the current regulations, i.e., goats and swine.

In response to these comments, APHIS agrees that a volume of rabbit inoculum that is half the largest host animal dose for any species of animal for which the product is recommended is reasonable and also provides for more general indications that are appropriate for products not recommended for cattle or sheep. Reference to half of the largest host animal dose would, in most cases, result in the same rabbit test dosage that is used for testing these products in the current standard requirement. The proposal to require half the smallest host animal dose would have unnecessarily raised the potency requirement for some products and, in contrast to statements made in the proposed rule, would have resulted in test procedures that were not consistent with recent standard requirements for products containing Clostridium novyi and Clostridium sordellii. Therefore, in response to these comments, we are amending the regulations in §§ 113.111 and 113.112, paragraph (c)(2), to allow the use of half the largest recommended dose in host animals for the rabbit.

In further response to the comment that the standard requirement for Clostridium Perfringens should be consistent with those of Clostridium Novyi and Clostridium Sordellii, APHIS notes that the recently amended standard requirements for Clostridium Novyi and Clostridium Sordellii require that the strain of rabbit used for potency testing be acceptable to APHIS. APHIS believes that, for consistency, the requirement should apply equally to Clostridium Perfringens. Therefore, in response to this comment, we are adding the requirement in §§ 113.111 and 113.112, paragraph (c)(2), that the strain of rabbit used for potency testing Clostridium Perfringens be acceptable to APHIS.

Therefore, based on the rationale set forth in the proposed rule and in this document, we are adopting the provisions of the proposal as a final rule, with the changes discussed in this document.

Executive Order 12866 and Regulatory Flexibility Act

This 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. There are currently some 19 veterinary biologics establishments that may be affected by this rule. According to the Small Business Administration regulations, many of them would be classified as small entities. This rule will result in a reduction of the number of mice required to perform potency assays. The reduction in the number of mice needed will result in a reduction in the total cost of the assays. Therefore, the rule should provide an economic benefit to producers of veterinary biologics. In addition, this rule clarifies the dosage of rabbit inoculum to be used in potency tests for products recommended for species other than cattle or sheep.

Retests may be indicated if less than 80 percent of control mice, inoculated with standard antitoxin and 10 L. doses of standard toxin, die in the neutralization test. However, since the testing of the pooled serum sample requires fewer mice as compared to testing individual serum samples, the number of mice required for a retest will be less.

Manufacturers, as well as the National Veterinary Services Laboratories, will benefit from the revisions since they will improve efficiency and reduce costs but will not change the accuracy of the assays.

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 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 which must be exhausted prior to a judicial challenge to the provisions of this rule.

Paperwork Reduction Act

This rule contains no new information collection or record keeping 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, 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. Section 113.111 is amended by revising paragraphs (c)(2), (c)(3)(i), (c)(3)(ii), (c)(3)(iii), and (c)(5)(ii) to read as set forth below, and by removing paragraph (c)(5)(iv).

§ 113.111 Clostridium Perfringens Type C Toxoid and Bacterin-Toxoid.

* * * * *

(c) * * *

(2) Each of at least eight rabbits of a strain acceptable to APHIS, each
weighing 4–8 pounds, shall be injected subcutaneously with not more than half of the largest recommended dose for any species indicated on the product label. A second equivalent dose shall be given not less than 20 days nor more than 23 days after the first dose.

(3) * * *

(i) At least seven rabbits are required to make an acceptable serum pool.

(ii) Equal quantities of serum from each rabbit shall be combined and tested as a single pooled serum.

(iii) If less than seven rabbits are available, the test is invalid and shall be repeated: Provided, That, if the test is not repeated, the serial shall be declared unsatisfactory.

* * * * *

(5) * * *

(iii) If any mice inoculated with the mixture of serum with 10 Lr doses of Standard Toxin die, the serum is considered to contain less than 2 International Units per ml, and the serial is unsatisfactory.

§ 113.112 Clostridium Perfringens Type D Toxoid and Bacterin-Toxoid.

(c) * * *

(2) Each of at least eight rabbits of a strain acceptable to APHIS, each weighing 4–8 pounds, shall be injected subcutaneously with not more than half of the largest recommended dose for any species indicated on the product label. A second equivalent dose shall be given not less than 20 days nor more than 23 days after the first dose.

(3) * * *

(i) At least seven rabbits are required to make an acceptable serum pool.

(ii) Equal quantities of serum from each rabbit shall be combined and tested as a single pooled serum.

(iii) If less than seven rabbits are available, the test is invalid and shall be repeated: Provided, That, if the test is not repeated, the serial shall be declared unsatisfactory.

* * * * *

(5) * * *

(iii) If any mice inoculated with the mixture of serum with 10 Lr doses of Standard Toxin die, the serum is considered to contain less than 2 International Units per ml, and the serial is unsatisfactory.

Done in Washington, DC, this 3rd day of June 1997.

Donald W. Luchsinger,
Acting Administrator, Animal and Plant Health Inspection Service.

[FR Doc. 97–14996 Filed 6–6–97; 8:45 am]

BILLING CODE 3410–34–P

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 39

[Docket No. 97–NM–70–AD; Amendment 39–10045; AD 97–12–03]

RIN 2120–AA64

Airworthiness Directives; Boeing Model 747 Series Airplanes

AGENCY: Federal Aviation Administration, DOT.

ACTION: Final rule; request for comments.

SUMMARY: This amendment supersedes two existing airworthiness directives (AD) that are applicable to certain Boeing Model 747 series airplanes. One of those AD's currently requires inspections for cracking, corrosion, and fracturing of the lower horizontal clevis of the struts midspan fittings, and replacement of discrepant parts with new or serviceable parts, or repair, if necessary. That AD also requires inspection for removal of broken sealant of the clevis and the fasteners, and various follow-on actions. It also provides for optional terminating actions for the inspections. The other AD currently requires inspection for cracking of certain fastener holes of the upper and lower horizontal clevis legs. This amendment continues to require inspections to detect cracking, corrosion, and fracturing of the lower horizontal clevis; and adds corresponding inspections of the upper horizontal clevis, and replacement of discrepant parts with new parts, or rework, if necessary. This amendment also removes certain optional terminating actions. This amendment is prompted by reports of cracking of the lower and upper leg of the horizontal clevis of the midspan fitting. The actions specified in this AD are intended to detect and correct cracking and fracturing of the clevis, which could result in drooping of the strut at the strut-to-wing interface, and consequent separation of the engine and strut from the airplane.


The incorporation by reference of Boeing Alert Service Bulletin 747–54A2179, Revision 1, dated November 27, 1996, as listed in the regulations, is approved by the Director of the Federal Register as of June 24, 1997.

The incorporation by reference of the following publications listed in the regulations was approved by the Director of the Federal Register as of the specified dates:

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The incorporation by reference of certain other publications listed in the regulations also was approved previously by the Director of the Federal Register as of January 22, 1997 (60 FR 66201, December 12, 1996).

Comments for inclusion in the Rules Docket must be received on or before August 8, 1997.


The service information referenced in this AD may be obtained from Boeing Commercial Airplane Group, P.O. Box 3707, Seattle, Washington 98124–2207. This information may be examined at the FAA, Transport Airplane Directorate, 1601 Lind Avenue, SW., Renton, Washington; or at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.


SUPPLEMENTARY INFORMATION: On January 13, 1988, the FAA issued AD 87–04–13 R1, amendment 39–5836 (53 FR 2005, January 26, 1988), applicable to certain Boeing Model 747 series airplanes. That AD revised an existing AD to require inspection for cracking, and repair or replacement, as necessary, of the horizontal clevis of the cylinder midspan attach fitting. That action was prompted by reports of cracking and corrosion in the fastener holes of the