Code 2693 2661.00

FILE—VSC 188

OUTLINE OF PROCEDURE FOR THE PREPARATION OF LEPTOSPIRA CANICOLA BACTERIN

Code 2693

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U. S. Veterinary
License No. 188

July 31, 1973

Supersedes April 2, 1973
" Feb. 19, 1968

I. COMPOSITION, ETC., OF THE PRODUCT

A. Organisms or viruses.

Leptospira canicola.

B. Source and date of accession of each organism.

[redacted] (b) (4)

C. Strains.

[redacted] (b) (4)

D. Proportions of each strain.

Not applicable.

II. CULTURES

A. Brief description of methods of identifying each organism or virus and the frequency with which these methods are applied.

1. Method of Identification.

[redacted] (b) (4)

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VETERINARY SERVICES
★ AUG 31 1973 ★
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NO ENDORSEMENT
EXPRESSED OR IMPLIED

Code 2693
U. S. Veterinary
License No. 188

January 17, 1974
Supersedes Page 13 of Outline
Dated July 31, 1973

IV. A. continued

9. Amount of antigenic or virus material per dose or doses in final container.

[redacted]

B. Include any additional pertinent information regarding the product not shown under A.

Not applicable.

V. TESTING

Indicate the stages in the preparation of the biological product at which the samples are collected. Refer to all applicable Standard Requirements by number. Outline all additional tests in detail.

A. Purity

1. Bulk Container Completed Product

a. Bacteria and fungi

Tests of samples removed from bulk containers are conducted as per the procedures of 9 CFR 113.26 prior to the time the product is assembled into batch lots. Tests should indicate that the product is free of contaminating organisms. Because of the size of the containers being tested, retests are not limited as stated in the section referred to.

[redacted]

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(b) (4)

Code 2661.00
U. S. Veterinary
License No. 188

October 16, 1996
Supersedes Page 14 Dated
April 11, 1991

V. A. 1. continued

b. Inactivation

[redacted]

2. Final container product.

Final container product will be tested according to the provisions of 9 CFR 113.26.

[redacted]

Disposition will be as indicated therein.

B. Safety

Test will be conducted in the manner prescribed in 9 CFR 113.38 with disposition as indicated therein. Sample will be either final bulk or final container product.

C. Potency

Final bulk or final container product will be tested [redacted] ions of 9 CFR 113.103 with disposition [redacted] to.

(b) (6)

(b)(6)

[redacted]

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Code 2661.00
U. S. Veterinary
License No. 188

February 25, 1977
Supersedes Page 15 of Outline
Dated July 31, 1973

V. continued

E. Any other tests.

Each serial or one subserial of product will be tested for viricidal activity in accordance with the test shown in 9 CFR 113.35. Only those serials that satisfactorily pass such tests will be eligible for packaging as a diluent for desiccated fractions in combination packages.

VI. POST PREPARATORY STEPS

A. Form, size, etc. of containers of product distributed.

1. Form of containers.

Please see Special Outline No. 28.

2. Size of containers.

Bottles used are commonly referred to as 6 ml., 10 ml., 30 ml., 60 ml., 120 ml., and 250 ml. Bottles are filled as shown in IV A 6. Please see Special Outline No. 28.

3. Labeling of containers.

Labeling is done by printing directly on the glass or plastic bottles using a screen-printing process. Please see Special Outline No. 29.

4. Final package.

Final containers, see Special Outline No. 28, are packaged in a folding carton imprinted with directions for proper use of the completed product. A circular containing other [illegible]ion is also placed in each carton.

(b)(6)

(b)(6)

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★ MAR 14 1977 ★
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EXPRESSED OR IMPLIED

Code 2665.01

FILE-VSC 188

2665.01

OUTLINE OF PROCEDURE
FOR THE PREPARATION OF

LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2665.01

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U. S. Veterinary
License No. 188

February 27, 1980

New

I. COMPOSITION, ETC., OF THE PRODUCT.

A. Micro-organisms used. Give the isolation and passage history.

1. Leptospira canicola.

[redacted] (b) (4)

2. Leptospira grippotyphosa.

[redacted] (b) (4)

3. Leptospira hardjo.

[redacted] (b) (4)

4. Leptospira icterohaemorrhagiae.

[redacted] (b) (4)

5. [redacted]

[redacted] (b) (4)

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LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-
ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2665.01 September 11, 2008
U.S. Veterinary License No. 188 Supersedes Page 22 dated February 27, 1980

IV. I. Amount of antigenic material per dose or doses in final container.

(b) (4)

- added J. Bulk container purity. "added" -

- moved from V.A.1.a. deleted "a. Bacteria and fungi.")

Tests of samples collected from bulk containers are conducted as per procedures of 9 CFR 113.26 prior to the time the product is assembled into serial lots. Tests should indicate that the product is free of contaminating micro-organisms. Because of the size of the containers being tested, retests are not limited as stated in the Section of 9 CFR referred to.

V. TESTING

Indicate the stages in the preparation of the biological product at which time the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirement for each satisfactory test.

A. Purity

- was V.A.2. 1. Final container product.

Completed product in final containers will be tested as prescribed in 9 CFR 113.26. Determination of a satisfactory test will be as stated therein.

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(b) (6)

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SEP 23 2008

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NO ENDORSEMENT
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A08

LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-
ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2665.01 | September 11, 2008
U.S. Veterinary License No. 188 | Supersedes Page 23 Dated May 21, 1991

V. A. 1. continued

[redacted] (b) (4) [redacted]

2. Dilution of Preservative

Colorado Serum Company submitted a study concerning the dilution of preservative with respect to test medium volume. The acceptance date from the CVB, [redacted] pertaining to this study was May 10, 2008.

B. Safety

Test will be conducted in the manner prescribed in 9 CFR 113.38 with disposition as indicated therein. Samples will be either final bulk or final container product. The route of injection will be subcutaneous.

C. Potency

Sampling and testing will comply with 9 CFR 113.7.

Leptospira canicola, Leptospira grippotyphosa, Leptospira icterohaemorrhagiae, and Leptospira pomona fractions of the final bulk or final container bacterin will be tested in accordance with the provisions of 9 CFR's 113.101, 113.102, 113.103, and 113.104, with conclusions and disposition being based therein.

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[redacted]

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LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2665.01
U. S. Veterinary
License No. 188

February 27, 1980

New

V. C. continued

(b) (4)

(b) (4)

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VETERINARY SERVICES
MAR 10 1980
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Code 2665.01
U. S. Veterinary
License No. 188

February 27, 1980

New

V. C. 3. continued

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LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-
ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2665.01
U.S. Veterinary
License No. 188

April 11, 1991
Supersedes Page 26 Dated
February 27, 1980

V. C. continued

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Code 2665.01
U. S. Veterinary
License No. 188

February 27, 1980

New

V. C. 6. b. continued

(b) (4)

D. Moisture, if desiccated.

Not applicable.

E. Any other tests.

Each serial or one subserial of product will be tested for viricidal activity in accordance with the test shown in 9 CFR 113.35. Only those serials that satisfactorily pass such test will be eligible for packaging as a diluent for desiccated fractions in combination packages.

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CODE 2675.00

FILE—VSC 188

2675.00

OUTLINE OF PROCEDURE
FOR THE PREPARATION OF
LEPTOSPIRA GRIPPOTYPHOSA BACTERIN

Code 2695

2675
axw

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U. S. Veterinary
License No. 188

January 29, 1975

New

I. COMPOSITION, ETC., OF THE PRODUCT.

A. Micro-organisms used. Give the isolation and passage history.

1. Micro-organisms.

Leptospira grippotyphosa.

2. Isolation and passage history.

[redacted] (b) (4)

B. Source and date of accession of each micro-organism.

1. Source of the micro-organism.

[redacted] (b) (4)

2. Date of accession of the micro-organism.

[redacted] (b) (4)

C. Strains.

[redacted] (b) (4)

D. Proportions of each strain.

Not applicable.

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APR 9 1975
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PROCUREMENT
EXCLUDED AS EXPIRED

Code 2695
U. S. Veterinary
License No. 188

January 29, 1975

New

IV. continued

I. Amount of antigenic material per dose or doses in final

(b) (4)

V. TESTING

Indicate the stages in the preparation of the biological product at which time the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirement for each satisfactory test.

A. Purity

1. Bulk container completed product.

a. Bacteria and fungi.

Tests of samples collected from bulk containers are conducted as per procedures of 9 CFR, §113.26, prior to the time the product is assembled into serial lots. Tests should indicate that the product is free of contaminating micro-organisms. Because of the size of the containers being tested, retests are not limited as stated in the Section of 9 CFR referred to.

b. Inactivation.

(b) (4)

Pg. 15
Supersedes
15 + 16

LEPTOSPIRA GRIPPOTYPHOSA BACTERIN

Code 2675.00
U.S. Veterinary
License No. 188

April 11, 1991
Supersedes Page 15 Dated
March 1, 1977

V. A. 1. b. continued

(b) (4)

2. Final container product.

Completed product in final containers will be tested as prescribed in 9 CFR 113.26. Determination of a satisfactory test will be as stated therein.

B. Safety

Test will be conducted in the manner prescribed in 9 CFR 113.38 with disposition as indicated therein. Sample will be either final bulk or final container product.

C. Potency

Final bulk or final container product will be potency tested according to the provisions of 9 CFR 113.104 with disposition relating directly thereto.

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COLORADO SERUM COMPANY

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Code 2675.00
U. S. Veterinary
License No. 188

March 1, 1977
Supersedes Page 17 of Outline
Dated January 29, 1975

V. continued

D. Moisture, if desiccated.

Not applicable.

E. Any other tests.

Each serial or one subserial of product will be tested for viricidal activity in accordance with the test shown in 9 CFR 113.35. Only those serials that satisfactorily pass such test will be eligible for packaging as a diluent for desiccated fractions in combination packages.

VI. POST PREPARATORY STEPS

A. Form and size of final containers in which the product is to be distributed.

1. Form of containers.

Please see Special Outline No. 28.

2. Size of containers.

Bottles used are commonly referred to as 10 ml., 30 ml., 60 ml., and 120 ml. Bottles are filled as shown in Section IV F. Please see Special Outline No. 28.

3. Labeling of final containers.

Labeling is done by printing directly on the glass or plastic bottles using a screen-printing process. Please

[redacted]

#6 JH

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MAR 14 1977
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NO ENDORSEMENT
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Code 2863.00

FILE-VSC #188

OUTLINE OF PROCEDURE
FOR THE PREPARATION OF

CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-
POMONA BACTERIN

Code 2863.00

Colorado Serum Company
4950 York St-Box 16428
Denver, Colorado 80216

U.S. Veterinary
License No. 188

August 2, 1985
Supercedes
November 12, 1981

I. COMPOSITION, ETC. OF THE PRODUCT

A. Micro-organisms used. Give isolation and passage history.

1. Micro-organisms used.

a. Campylobacter fetus fraction.

Campylobacter fetus, subsp. fetus isolated from cattle.

b. Leptospira fraction.

Leptospira canicola, Leptospira grippotyphosa, Leptospira hardjo, Leptospira icterohaemorrhagiae, and Leptospira pomona.

2. Isolation and passage history.

a. Campylobacter fetus fraction.

[redacted] (b) (4)

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VETERINARY SERVICES
OCT 28 1985
BIOLOGICAL SERVICES
NO RESPONSIBILITY
EXPRESSED ON CONTENT

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CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-
POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

August 2, 1985
Supercedes
November 12, 1981

IV. I

(b) (4)

V. T

Indicate the stages in the preparation of the biological product at which the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirements for each satisfactory test.

This product contains more than one immunogenic fraction and will be evaluated by tests applicable to each fraction in accordance with Section 113.7, 9 CFR.

A. Purity

1. Bulk containers.

Prior to assembly of product into serial lots samples are removed from bulk containers of each individual fraction or serotype and tested per procedures of 9 CFR 113.26. Holding of the tests may be shortened to 7 days in some instances. Growth should not be observed in any of these tests. Retests will be run as indicated by reasonable

(b) (4)

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CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

October 8, 1996
Supersedes Page 15
Dated August 2, 1985

V. A. continued

2. Final containers.

Final container product will be tested according to the provisions of 9 CFR 113.26.

[redacted] (b) (4)

Disposition will be as indicated therein.

B. Safety

Bulk or final container samples of completed product will be tested for safety as provided in 9 CFR 113.38.

C. Potency

1. Campylobacter fetus.

[redacted] (b) (4)

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[redacted] (b) (6)

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LICENSING & POLICY
DEVELOPMENT
NO ENDORSEMENT EXPRESSED

CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

October 8, 1996

New Page

V. C. 1. continued

(b) (4)

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CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

August 2, 1985
Sueprcedes
November 12, 1981

V. C. 1. continued

(b) (4)

2. Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona.

Potency testing of the completed bulk or final container product to determine potency of the L. canicola, L. grippotyphosa, L. icterohaemorrhagiae, and L. pomona fractions will be in accordance with the provisions of 9 CFR 113.88, 113.89, 113.87, and 113.86 respectively, with conclusions and disposition being based thereon.

(b) (4)

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(b)(6), (b)(7)(C)

CA

LEPTOSPIRA CANICOLA-GRI

(b) (4

Code 2863.00
U.S. Veterinary
License No. 188

V. C. 2. continued

[redacted]

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CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-
POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

August 2, 1985
Supercedes
November 12, 1981

V. C. 2. [redacted]

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CAMPYLOBACTER FETUS
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-
POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

August 2, 1985
Supercedes
November 12, 1981

V. C. 2. [redacted] (b) (4)

[redacted] (b) (4)

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CAMPYLOBACTER FETUS -
LEPTOSPIRA CANICOLA-GRIPPOTYPHOSA-HARDJO-ICTEROHAEMORRHAGIAE-
POMONA BACTERIN

Code 2863.00
U.S. Veterinary
License No. 188

August 22, 2005
Supersedes Page 20 Dated
August 2, 1985

V. C. 2. f. ii. continued

(b) (4)

D. Moisture, if desiccated.

Not applicable.

"Any" deleted

E. Other tests.

revised Residual free formaldehyde content shall not exceed 0.74 grams per liter when measured by the ferric chloride method in accordance with 9 CFR 113.100 (f).

VI. POST PREPARATORY STEPS

A. Form and size of final containers in which the product is to be distributed.

~~Final containers may be either glass or plastic and are commonly referred to as 30 ml and 120 ml serum bottles. These will be filled as shown under IV F. A screen-printing method is used for labeling directly on the glass or plastic surface of the bottle. Folding cartons, properly labeled, are used for packaging. Because all necessary information for use of the product appears on the final container and carton labels a package insert may not be used.~~

 #6 MPE

(b) (6)

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OCT 18 2005

POLICY, EVALUATION, AND LICENSING
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EXPRESSED

30.05

Code 4059.00

FILE—VSC 188

OUTLINE OF PROCEDURE
FOR THE PREPARATION OF
BOVINE RHINOTRACHEITIS VACCINE
Modified Live Virus, Bovine Tissue Culture Origin
LEPTOSPIRA GRIPPOTYPHOSA - HARDJO - POMONA BACTERIN

Code 4059.00

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U. S. Veterinary
License No. 188

December 30, 1980

New

I. COMPOSITION, ETC. OF THE PRODUCT

This outline covers the packaging of two completed products as fractions of an eventual final combination which comes into being when the lyophilized vaccine portion is rehydrated and thoroughly mixed with the liquid inactivated bacterin. The vaccine is a modified live virus and will be referred to as the Vaccine Fraction. The bacterin is an inactivated whole culture and will be referred to as the Bacterin Fraction.

A. Micro-organisms used. Give the isolation and passage history.

1. Micro-organisms used.

a. Vaccine Fraction.

Bovine Rhinotracheitis Virus.

b. Bacterin Fraction.

Leptospira grippotyphosa, Leptospira hardjo, and Leptospira pomona.

2. Isolation and passage history.

a. Vaccine Fraction.

(b) (4)

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VETERINARY SERVICES
MAR 16 1981
BIOLOGICS STAFF
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Code 4059.00
U. S. Veterinary
License No. 188

December 30, 1980

New

I. continued

C. Strains

1. Vaccine Fraction

[redacted] (b) (4)

2. Bacterin Fraction.

a. Leptospira grippotyphosa.

[redacted] (b) (4)

b. Leptospira hardjo.

[redacted] (b) (4)

c. Leptospira pomona.

[redacted] (b) (4)

D. Proportions

II. CULTURES

III. HARVEST

IV. PREPARATION OF THE PRODUCT

Please refer to current approved outlines for the individual product codes.

V. TESTING

Please refer to individual outlines for testing procedure.

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MAR 16 1981
NO ENDORSEMENT
EXPRESSED OR IMPLIED

Code 4129.00

Est. 188

OUTLINE OF PRODUCTION FOR THE PREPARATION OF

BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE, Modified Live Virus, LEPTOSPIRA CANICOLA - GRIPPOTYPHOSA - HARDJO - ICTEROHAEMORRHAGIAE - POMONA BACTERIN

Code 4129.00

Complete Revision

Dated: September 8, 1998

Supersedes Outline Dated January 12, 1981
and all individual pages:
Page 9 Dated June 6, 1986

COLORADO SERUM COMPANY
4950 York St. - Box 16428
Denver, Colorado 80216

U.S. Veterinary
License No. 188

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BIOLOGICS

OCT 29 1998

LICENSING & POLICY
DEVELOPMENT
NO ENDORSEMENT EXPRESSED

BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE, Modified Live Virus,
LEPTOSPIRA CANICOLA - GRIPPOTYPHOSA - HARDJO -
ICTEROHAEMORRHAGIAE - POMONA BACTERIN

Code 4129.00
U.S. Veterinary
License No. 188

May 11, 2001
Supersedes Page 9
Dated September 8, 1998

V. TESTING

Please refer to individual outlines for testing procedure.

VI. POST PREPARATORY STEPS.

A. Form and size of final containers in which the product is to be distributed.

Lyophilized vaccine fraction is supplied in 10 dose and 50 dose containers. These are accompanied with similar sizes of the bacterin fraction for rehydration which completes the combination. Components for this product: Code 1121.00 (Bovine Rhinotracheitis-Parainfluenza3 Vaccine, Modified Live Virus), and Code 2665.01 (Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin).

B. Collection, storage, and submission of representative samples. Indicate at which stage in production these samples are taken.

Not applicable.

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(b) (6)

5-29-01

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BIOLOGICS

JUN - 5 2001

LICENSING & POLIC'
DEVELOPMENT
NO ENDORSEMENT
EXPRESSED

Code 4339.00

FILE—VSC 188

OUTLINE OF PROCEDURE
FOR THE PREPARATION OF
BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus, Bovine Tissue Culture Origin
LEPTOSPIRA CANICOLA - GRIPPOTYPHOSA - HARDJO -
ICTEROHAEMORRHAGIAE - POMONA BACTERIN

Code 4339.00

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U. S. Veterinary
License No. 188

January 21, 1981

New

I. COMPOSITION, ETC. OF THE PRODUCT

This outline covers the packaging of two completed products as fractions of an eventual final combination which comes into being when the lyophilized vaccine portion is rehydrated and thoroughly mixed with the liquid inactivated bacterin. The vaccine consists of a true combination of modified live bovine rhinotracheitis and virus diarrhea viruses and will be referred to as the Vaccine Fraction. The bacterin is also a true combination and consists of a mixture of inactivated whole cultures of Leptospira canicola, Leptospira grippotyphosa, Leptospira hardjo, Leptospira icterohaemorrhagiae, and Leptospira pomona and will be referred to as the Bacterin Fraction.

A. Micro-organisms used. Give the isolation and passage history.

1. Micro-organisms used.

a. Vaccine Fraction

Bovine rhinotracheitis virus and Bovine diarrhea virus.

b. Bacterin Fraction.

Leptospira canicola, Leptospira grippotyphosa, Leptospira hardjo, Leptospira icterohaemorrhagiae, and Leptospira pomona.

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BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE, Modified Live Virus, - deleted "Bovine Tissue Culture Origin" not on Summary Chart
LEPTOSPIRA CANICOLA - GRIPPOTYPHOSA - HARDJO -
ICTEROHAEMORRHAGIAE - POMONA BACTERIN

Code 4339.00
U.S. Veterinary
License No. 188

June 24, 1998
Supersedes Page 8
Dated January 21, 1981

I. continued

D. Proportions

II. CULTURES

III. HARVEST

IV. PREPARATION OF THE PRODUCT

Please refer to current approved outlines for the individual product codes.

V. TESTING

Please refer to individual outlines for testing procedure.

VI. POST PREPARATORY STEPS

A. Form and size of final containers in which the product is to be distributed.

Lyophilized vaccine fraction is supplied in 10 dose and 50 dose containers. These are accompanied with similar sizes of the bacterin fraction for rehydration which completes the combination. [Components for the product: Code 1151.00 (Bovine Rhinotracheitis - Virus Diarrhea Vaccine, Modified Live Virus), and 2665.01 added (Leptospira Canicola - Grippotyphosa - Hardjo - Icterhaemorrhagiae - Pomona - Bacterin).]

B. Collection, storage, and submission of representative samples. Indicate at which stage in production these samples are taken.

Not applicable.

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188

Code 1101.00

OUTLINE OF PRODUCTION
FOR
BOVINE RHINOTRACHEITIS VACCINE
Modified Live Virus

Code 1101.00

Complete Revision

Date: February 11, 1992

Supersedes Outline Dated December 27, 1982 and all individual pages
Page 8 Dated September 30, 1985
Page 11 Dated January 21, 1991
Page 12 Dated January 21, 1991
Page 13 Dated June 11, 1985

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BOVINE RHINOTRACHEITIS VACCINE
Modified Live Virus

Code 1101.00
U.S. Veterinary
License No. 188

February 9, 1999
Supersedes Page 10
Dated September 12, 1996

IV. G. continued

2. Method of sealing final containers.

Fluted rubber stoppers are partially inserted into the bottles at the time of filling. When drying is completed the bottles are vacuum stoppered. Aluminum seals are crimped on to hold the rubber stoppers securely in place.

H. Desiccation, including moisture control. Give maximum percent moisture.

[redacted] (b) (4)

I. Amount of antigenic material per dose or doses in final containers.

[redacted] (b) (4)

V. TESTING

Indicate the stages in the preparation of the biological product at which the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirements for each satisfactory test.

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#6025

BOVINE RHINOTRACHEITIS VACCINE
Modified Live Virus

Code 1101.00
U.S. Veterinary
License No. 188

April 20, 2005
Supersedes Page 10A Dated
February 9, 1999

V. continued

A. Purity

1. Bacteria and fungi.

Final container product will be tested according to the provisions of 9 CFR 113.27.

(b) (4)

Disposition will be indicated as therein.

2. Mycoplasma.

Bulk pooled product from each serial or final container samples will be tested per 9 CFR 113.28. Any serial found to contain mycoplasma will be destroyed.

B. Safety

The mouse safety test prescribed in Section 113.33 (a) and the calf safety test prescribed in Section 113.41 of 9 CFR will be conducted. [An exemption has been granted to replace 113.33 (a) with 113.33 (b) per CVB Notice No. 05-01 by a letter from CVB PEL dated March 3, 2005] Disposition and conclusions will be as stipulated therein. - added

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[redacted]

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RB 4-26-05

BOVINE RHINOTRACHEITIS VACCINE
Modified Live Virus

Code 1101.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 11
Dated August 20, 1999

V. C. Potency.

Final container samples will be tested for virus titer according to the provisions of 9 CFR 113.310 (d) (3) (b) (4)

(b) (4)

(b) (4)

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BOVINE RHINOTRACHEITIS VACCINE
Modified Live Virus

Code 1101.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 11A
Dated April 9, 1999

was "continued" deleted; not on Summary
V. D. Other tests. — added; not noted on Summary

was indented & numbered 2. → Virus Identity.

was indented → One or both of the Virus Identity Tests listed in 9 CFR 113.300 (c) will be conducted on final container samples from each serial or first subserial.

formatting [illegible] & not listed on Summary

VI. POST PREPARATORY STEPS

A. Form and size of final containers in which the product is to be distributed.

Vaccine is filled into vials that will permit rehydration to 50 doses (100 ml.) and 10 doses (20 ml.).

B. Collection, storage, and submission of representative samples. Indicate at which steps in the production these samples are taken.

Final container samples will be selected in accordance with 9 CFR 113.3.

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$) FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

NEW

"2" - 2015

Date: May 1, 2008

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1 5/8" margin

1 1/2 at base of "1"

Comment - may require Δ based on use by the EVB - PLL

SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$) FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

Colorado Serum Company	U.S. Veterinary	"2" on 2015 May 1, 2008
4950 York Street - Box 16428	License No. 188	New
Denver, Colorado 80216		

I. OBJECTIVE

To describe the steps necessary to titrate live viruses causing cytopathic effect (CPE) on cell cultures.

II. DEFINITIONS

A. $TCID_{50}$ - Tissue Culture Infective Dose, 50% endpoint
B. FBS - Fetal bovine serum
C. MLV - Modified Live Virus
D. EBK Cells - Cells derived from embryonic bovine kidneys
E. MEM - Minimum Essential Medium
F. F-12 - A supplement frequently added to Minimum Essential Medium
G. SOP - Standard Operating Procedure
H. CO_2 - Carbon dioxide
I. C after a temperature number - Centigrade
J. 1:10 dilution - 1 part of one solution plus 9 parts of a different solution, or variations thereof
K. µl - Microliter

III. SPECIAL NOTES

A. This test applies to seeds, live production harvests, and final potency tests for the following licensed MLV vaccines: Product Codes 1201.00, 1101.00, 1121.00, 1151.00, and 1171.00. Titrations are run in 96-well tissue culture plates and expressed as a tissue culture infective dose - 50% endpoint ($TCID_{50}$).

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$)
FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

Colorado Serum Company
U.S. Veterinary License No. 188

"2"
May 1, 2008
New

III. SPECIAL NOTES, Continued

B. Titrations are expressed as $TCID_{50}$/ml for Master Seeds, Working Seeds, Production Seeds and bulk harvests. Titrations for final product and final potency titrations are expressed as $TCID_{50}$/dose.

C. Cells used for conducting titrations will be chosen according to the virus being titered. The cells are to be susceptible to the growth of the particular virus being titered. The cells used for titrations are to be free of extraneous agents as required by the Code of Federal Regulations, Title 9, Section 113.51 or 113.52. (113.51.c) (113.52.5.e)

D. EBK cells are used for potency testing of products listed in Section III. A.

E. When potency titers are conducted for final products containing two or three different viral components (bivalent vaccine), specific antiserum for each virus is required in order to neutralize all viruses except the one being titered.

F. Unless otherwise noted, all virus titrations are to be run on a "Day 0" time cell seeding. That is, cells are seeded onto the microtiter plates first, and the viral dilutions are added within 0.5 to 8 hours on the same day.

IV. MATERIALS AND EQUIPMENT

A. Monolayer of susceptible cells for titration. Passes 1 through 5 are used when using primary cells such as EBK.

B. 96-well tissue culture microtiter plates

C. Cell growth media - MEM with 5-10% FBS and F-12 supplement (See Special Outline No. 25)

D. Sterile 1 ml, 5 ml, and 25 ml pipettes with pipette aid

E. Specific antiserums - if needed

F. 17 x 100 mm sterile plastic tubes with tube rack

G. 100 µl Eppendorf repeating pipettor (or equivalent) with sterile pipette tips

H. 100, 200 and 1000 µl pipettors with sterile pipette tips

I. CO_2 incubator

J. Biological Safety Cabinet

K. Vortex mixer

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$)
FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

"2"-2016

Colorado Serum Company — May 1, 2008
U.S. Veterinary License No. 188 — New

IV. MATERIALS AND EQUIPMENT, Continued

L. Water bath set at 36-38°C
M. Inverted microscope
N. Marking pen

V. PROCEDURES

A. Prepare cell growth media according to Special Outline No. 25.
B. Add cells to microtiter plate:
1. Determine which cell type to use for the titration. (See Section III. C.)
2. Unless otherwise noted, cells are seeded on the day the test begins.
3. The microtiter plates contain 96-wells configured in a 12 x 8 rectangle. Titrations are run with 5 wells per dilutions and in duplicate. The microtiter plate is marked to contain one dilution per row at 10 wells across (5 wells/dilution, in duplicate). Each plate can hold 8 different dilutions. For example: 10^{-1} through 10^{-8}. At least 3 wells are used as negative controls. See Section V.C.4.d.
4. Cells are seeded at 100 µl per well using an Eppendorf® repeater™ pipettor at a cell count of 1.2 to 2.0 x 10^4 cells per 100 µl. The wells used for dilutions and the wells held for negative controls are seeded in an identical manner.

C. Procedures for Titration of a Monovalent Virus (only one viral component):
1. Dilute the virus to be titered using 10-fold dilutions (0.5 ml virus into 17 x 100 mm tube containing 4.5 ml cell growth media).
2. 0.5 ml of virus is added to tube # 1 using a 1000 µl tip. The tube is mixed for 2-5 seconds by means of a Vortex mixer. This tube is the 1:10 dilution (10^{-1}).
3. Using an unused sterile pipette tip, 0.5 ml from the 1:10 dilution tube is transferred to the next tube. This tube is the 1:100 dilution (10^{-2}). The tube is mixed for 2-5 seconds by means of a Vortex mixer. This process is repeated for every dilution tube.

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$)
FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

Colorado Serum Company
U.S. Veterinary License No. 188

"2" - 2015
May 1, 2008
New

V. PROCEDURES, Continued

C. 4. The viral dilutions are added to the microtiter plate(s) as follows:
   a. Using an Eppendorf® repeater™ pipettor (or equivalent)
   b. Working bottom to top on the microtiter plate
   c. Beginning with the highest dilution (least virus), and using only one pipette tip for addition of the viral dilutions, add 100 µl of the viral dilutions to the proper wells which identify the dilutions.
   d. Using a sterile unused pipette tip, add 100 µl cell growth media to the virus-free wells designated as negative controls.

5. The microtiter plate(s) are placed in a 5% CO_2 incubator at 36-38°C for 5-7 days.

D. Procedures for Titration of a Bivalent Virus (two viral components):

1. Prepare media and microtiter plates as per Sections V.A. and V.B.
2. In a 17 x 100 ml tube, add 1.0 ml of the test vaccine and 4.0 ml cell growth media. This is a 1:5 dilution. Mix for 2-5 seconds using a Vortex mixer.
3. In a 17 x 100 ml tube, mix the following for 2-5 seconds using a Vortex mixer:
   a. 500 µl of the 1:5 dilution from Section V.D.2.
   b. 500 µl antiserum against the virus not being titered

   This is a 1:2 dilution of the 1:5 dilution, thus becoming a 1:10 dilution. This tube is labeled as the 10^{-1} dilution.
4. Incubate the 1:10 dilution tube in a 36-38°C water bath for 60 minutes ± 15 minutes (45-75 minutes).
5. Continue the process as per Section V.C.1. through V.C.5.

E. Reading the plates for CPE

1. At the end of the incubation period, examine the plates for CPE using an inverted light microscope at 100x magnification. Observe the negative control wells before the cells containing virus.
2. The plates are read with the covers on. Wells displaying one or more CPE foci are considered to be positive for virus.

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$)
FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

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Colorado Serum Company
U.S. Veterinary License No. 188

May 1, 2008
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V. PROCEDURES, Continued

E. 3. Results are recorded comparing the number of CPE-positive wells with the total number of wells examined for each dilution of the test virus. An example including calculations is described in Section VI.

VI. RESULTS AND TITRATION EXAMPLE

A. (b) (4) [redacted]

B.

C.

(b) (4) [redacted]

Therefore, the average of the duplicate titers is 5.0.

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$)
FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

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May 1, 2008
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VI. RESULTS AND TITRATION EXAMPLE, Continued

C. Continued

Inoculum = amount of diluted virus added to each well of the test plate

Test vaccine dose = manufacturer recommended vaccination dose

1. Example # 1: If the virus above was a seed or harvest material, it would be calculated as $TCID_{50}$/ml.

(b) (4)

[redacted]

2. Example # 2: If the virus above was a vaccine or a component of a

(b) (4)

[redacted]

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SPECIAL OUTLINE NO. 72

TISSUE CULTURE INFECTIVE DOSE 50% ENDPOINT ($TCID_{50}$)
FOR THE TITRATION OF LIVE VIRUSES IN MICROTITER PLATES

"2"- 2015

Colorado Serum Company — May 1, 2008
U.S. Veterinary License No. 188 — New

VII. INTERPRETATION OF RESULTS

A. For a valid assay:
   1. The negative control cells cannot exhibit any CPE.
   2. The lowest dilution (most virus) must exhibit a 100% positive CPE (5/5), while the highest dilution (least virus) must exhibit no positive CPE (0/5). Otherwise, the test will not have been considered endpointed, and the titration is considered a "No Test" and is repeated until an endpoint is reached.

B. When testing a vaccine for potency and the validity requirements are met and the test vaccine is greater than or equal to the titer contained in the Outline of Production, the vaccine is considered "Satisfactory".

C. If the validity requirements are met and the test vaccine is less than the titer contained in the Outline of Production, the test vaccine is retested according to 9 CFR 113.8.b.

Subsidiaries:

Americana Laboratories, Inc.
Continental Pharmacal Company
Denver Colorado Laboratories, Inc.
Empire Veterinary Company
International, Inc.
Metropolitan Medical Company
Professional Biological Company
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OKW
3 June 08

6-3-08

Code 2681.00

FILE—VSC 188 2681.00

OUTLINE OF PROCEDURE
FOR THE PREPARATION OF

LEPTOSPIRA GRIPPOTYPHOSA-HARDJO-POMONA BACTERIN
Lepto-3

Code 2681.00

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U. S. Veterinary
License No. 188

August 30, 1979
Supersedes March 17, 1978

I. COMPOSITION, ETC., OF THE PRODUCT.

ASRTS:

A. Micro-organisms used. Give the isolation and passage history.

L. Grippotyphosa 12-19-01

1. Leptospira grippotyphosa.

[redacted] (b) (4)

L. Hardjo 12-19-01

2. Leptospira hardjo.

[redacted] (b) (4)

L. Pomona 12-19-

3. Leptospira pomona.

[redacted] (b) (4)

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August 30, 1979

Supersedes March 17, 1978

IV. continued

H. Desiccation, including moisture control.

Product is not desiccated.

I. Amount of antigenic material per dose or doses in final container

[redacted] (b) (4)

V. TESTING

Indicate the stages in the preparation of the biological product at which time the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirement for each satisfactory test.

A. Purity

1. Completed bulk container product.

a. Bacteria and fungi.

Tests of samples collected from bulk containers are conducted as per procedures of 9 CFR 113.26 prior to the time the product is assembled into serial lots. Tests should indicate that the product is free of contaminating micro-organisms. Because of the size of the containers being tested, retests are not limited as stated in the Section of 9 CFR referred to.

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October 28, 1996
Supersedes Page 22 Dated
May 21, 1991

V. A. 1. continued

b. Inactivation

(b) (4)

2. Final container product.

Final container product will be tested according to the provisions of 9 CFR 113.26.

(b) (4)

Disposition will be as indicated therein.

B. Safety

Test will be conducted in the manner prescribed in 9 CFR 113.38 with disposition as indicated therein. Samples will be either final bulk or final container product.

C. Potency

Leptospira grippotyphosa and Leptospira pomona fractions of the completed bulk or final container bacterin will be tested in accordance with the provisions of 9 CFR's 113.101 and 113.104, with conclusions and disposition being based thereon.

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August 30, 1979

Supersedes March 17, 1978

V. C. continued

[redacted]

(b) (4)

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August 30, 1979

Supersedes March 17, 1978

V. C. 3. continued

(b) (4)

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LEPTOSPIRA GRIPPOTYPHOSA-HARDJO-POMONA BACTERIN
LEPTO - 3

Code 2681.00
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April 16, 1991
Supersedes Page 25 Dated
August 30, 1979

V. C. continued

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Code 2681.00
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License No. 188

August 30, 1979

Supersedes March 17, 1978

V. C. 6. b. continued

(b) (4)

D. Moisture, if desiccated.

Not applicable.

E. Any other tests.

Each serial or one subserial of product will be tested for viricidal activity in accordance with the test shown in

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Code 2681.00
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September 30, 1980
Supersedes Page 27 of Outline
Dated August 30, 1979

V. E. continued

9 CFR 113.35. Only those serials that satisfactorily pass such test will be eligible for packaging as a diluent for desiccated fractions in combination packages.

VI. POST PREPARATORY STEPS

A. Form and size of final containers in which the product is to be distributed.

1. Form of containers.

Please see Special Outline No. 28.

2. Size of containers.

Bottles are commonly referred to as 60 ml., 120 ml., and 250 ml. Bottles are filled as shown in Section IV F. Please see Special Outline No. 28.

3. Labeling of final containers.

Labeling is done by printing directly on the glass or plastic bottles using a screen-printing process. Please see Special Outline No. 29. Label will state that the product may be used alone or for rehydration of accompanying desiccated vaccine when packaged as a fraction of a combination.

4. Final package.

Each bottle is packaged in a folding carton which is printed with all required label information including the date of expiration and serial number. An enclosure containing other useful information is also placed in each carton.

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Code 1121.00

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OUTLINE OF PREPARATION
FOR
BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE
Modified Live Virus

Code 1121.00

Complete Revision

Date: January 28, 1992

Supersedes Outline Dated December 27, 1979 and all individual pages

Page 4	Dated 9-30-85
Page 5	Dated 5-05-86
Page 9	Dated 1-23-91
Page 10	Dated 1-23-91
Page 13	Dated 3-31-86

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BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE
Modified Live Virus

Code 1121.00
U.S. Veterinary
License No. 188

September 12, 1992
Supersedes Page 7
Dated January 28, 1992

IV. continued

I. Amount of antigenic material per dose or doses in final containers.

See V. C. 1.

V. TESTING

Indicate the stages in the preparation of the biological product at which the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirements for each satisfactory test.

A. Purity.

1. Bacteria and fungi.

Final container product will be tested according to the provisions of 9 CFR 113.27.

[redacted] (b) (4)

Disposition will be as indicated therein.

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[redacted] (b) (6)

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BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE
Modified Live Virus

Code 1121.00
U.S. Veterinary
License No. 188

April 20, 2005
Supersedes Page 7A Dated
September 12, 1996

V. A. continued

2. Mycoplasma.

Bulk pooled material from each serial or final container samples will be tested as prescribed in 9 CFR 113.28. Any serial found to contain mycoplasma will be destroyed.

B. Safety

The mouse safety test prescribed in Section 113.33(a) and the calf safety test prescribed in Section 113.41 of 9 CFR will be conducted. [An exemption has been granted to replace 113.33 (a) with 113.33 (b) per CVB Notice No. 05-01 by a letter from CVB PEL dated March 3, 2005.] Disposition and conclusions will be as stipulated therein. - added

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(b) (6)

#6 MRC

RL 4-26-05

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JUN 0 1 2005

POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
EXPRESSED

BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE
Modified Live Virus

Code 1121.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 8
Dated January 5, 2000

V. C. Potency.

1. Bovine Rhinotracheitis Virus.

For release, serials of vaccine will be tested in vitro for potency in accordance with 9 CFR 113.310 (d) (3). [redacted] (b) (4) See Special Outline No. 72.

(b) (4)

(b) (4)

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[redacted]

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POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
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BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE
Modified Live Virus

Code 1121.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 8A
Dated January 5, 2000
deleted "New" - not in summary

V. C. continued

2. Parainfluenza$_3$ Virus.

needs a comma or wording chg.

For release, serials of vaccine will be tested in vitro for potency in accordance with 9 CFR 113.309 (d) (3). [redacted] (b) (4)
See Special Outline No. [redacted]

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[redacted] (b) (6)

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EXPRESSED

#6
GRW
3 June 08
NC

BOVINE RHINOTRACHEITIS - PARAINFLUENZA$_3$ VACCINE
Modified Live Virus

Code 1121.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 9
Dated April 9, 1999

V. C. 2. continued

(b) (4)

D. Any other tests.

(1) Virus Identity Test.

One or both of the virus identity tests listed in 9 CFR 113.300 (4) (c) will be conducted on final harvest samples from individual fractions before assembling into serial form.

(b) (6)

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JUN 0 4 2008

POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
EXPRESSED

Est. 188

Code 1151.00

OUTLINE OF PRODUCTION
FOR
BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00

Date: February 5, 1999

Supersedes Outline Cover Page Dated January 28, 1992

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U.S. Veterinary
License No. 188

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APR - 9 1999

LICENSING & POLICY
DEVELOPMENT
NO ENDORSEMENT EXPRESSED

BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00
U.S. Veterinary
License No. 188

February 5, 1999
Supersedes Page 7
Dated September 16, 1996

IV. continued

H. Desiccation, including moisture control. Give maximum percent moisture.

(b) (4)

I. Amount of antigenic material per dose or doses in final containers.

(b) (4)

V. TESTING

Indicate the stages in the preparation of the biological product at which the samples are collected. Refer to all applicable Standard Requirements. Outline all additional tests in detail and state the minimum requirements for each satisfactory test.

A. Purity

1. Bacteria and fungi.

Final container product will be tested according to the provisions of 9 CFR 113.27.

(b) (6)

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APR - 5 1999

LICENSING & POLICY
DEVELOPMENT
NO ENDORSEMENT EXPRESSED

BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00
U.S. Veterinary
License No. 188

September 16, 1996

New Page

V. A. 1. continued

(b) (4)

Disposition will be as indicated therein.

2. Mycoplasma.

Bulk pooled material from each serial or final container samples will be tested as prescribed in 9 CFR 113.28. Any serial found to contain mycoplasma will be destroyed.

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(b) (6)

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NO ENDORSEMENT
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BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 8
Dated April 20, 2005

V. B. Safety.

The mouse safety test prescribed in Section 113.33 (a) and the calf safety test prescribed in Section 113.41 of 9 CFR will be conducted. An exemption has been granted to replace 113.33 (a) with 113.33 (b) per CVB Notice No. 05-01 by a letter from CVB PEL dated March 3, 2005. Disposition and conclusions will be as stipulated therein.

C. Potency.

1. Bovine Rhinotracheitis Virus.

For release serials of vaccine will be tested in vitro for potency in accordance with 9 CFR 113.310 (d) (3) [redacted] (b) (4) [redacted] (b) (4) [redacted] Special Outline No. 72.

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[redacted] (b) (6)

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BIOLOGICS

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POLICY, EVALUATION, AND LICENSING
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EXPRESSED

#6
3 June 08

BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00
U.S. Veterinary
License No. 188

January 4, 2000

New

V. C. 1. continued (table moved from pg. 8) ✓

(b) (4)

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(b) (6)

#6GB

05-15-00

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DEVELOPMENT
NO ENDORSEMENT
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BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 9
Dated April 9, 1999

V. C. "Continued" deleted & was in line w/ "V. C."

V. C. 2. Bovine Virus Diarrhea Vaccine moved #2 in line w/ "V. C."

moved #2 up

For release serials of vaccine will be tested in vitro for potency in accordance with 9 CFR 113.311 (d) (3). [redacted] (b) (4) [redacted] (b) (4) See Special Outline No. 72. added

[redacted] (b) (4)

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[redacted] (b) (6)

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BIOLOGICS

JUN 0 4 2008

POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
EXPRESSED

#6
3 June 08
NL

BOVINE RHINOTRACHEITIS - VIRUS DIARRHEA VACCINE
Modified Live Virus

Code 1151.00
U.S. Veterinary
License No. 188

May 15, 2008
Supersedes Page 9A
Dated April 9, 1999

V. D. Any other tests.

Virus identification.

Samples of each virus used in this combination are collected at harvest time, see section III. C., and are used for one or both of the virus identity tests listed in 9 CFR 113.300 (c). Tests will be concluded prior to combination of the viruses.

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JUN 0 4 2008

POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
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Est. 188
S.O. #37

Est. 188
S.O. #37

Added Cover page*

OUTLINE OF PRODUCTION

FOR

MODIFIED STUART'S MEDIUM

Special Outline No. 37

Date: July 6, 2006

Complete Revision

Supersedes Outline Dated March 28, 1972

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U.S. Vet. License No. 188

*: Not in Summary of Changes

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JUL 27 2006

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Increased top margin

Deleted "Outline of Procedure for the Preparation of" *

MODIFIED STUART'S MEDIUM

Insert "Outline"

~~Special~~ No. 37

Outline "*

[redacted]

Colorado Serum Company
4950 York Street
Denver, Colorado 80216

U.S. Veterinary
License No. 188

July 6, 20[redacted]

Complete Revision

A. FORMULA

[redacted]

Chg from "Cond[redacted]

B. METHOD

Chg from "agita[redacted]
motor-driven
to completely d[redacted]
salts."

[redacted]

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MODIFIED STUART'S MEDIUM

Insert "Outline"

Special No. 37

Outline

U.S. Veterinary
License No. 188

July 6, 2006
Complete Revision

B. 1. continued

new

new

added → 2.

add

added → 3.

(b) (4)

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JUL 27 2006

POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
EXPRESSED

MODIFIED STUART'S MEDIUM

Insert "Outline"

Special Outline No. 37

U.S. Veterinary
License No. 188

July 6, 2006
Complete Revision

B. continued

(b) (4)

Producing Subsidiaries:

Americana Laboratories, Inc.
Continental Pharmacal Company
Denver Colorado Laboratories, Inc.
Empire Veterinary Company
International, Inc.
Metropolitan Medical Company
Professional Biological Company
Scientific Laboratories, Inc.
Universal Laboratories, Inc.

#6 VMBE

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COLORADO SERUM COMPANY

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BIOLOGICS

JUL 27 2006

POLICY, EVALUATION, AND LICENSING
NO ENDORSEMENT
EXPRESSED

RS
7-12-06