ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli **Diluvac Forte**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per dose of two ml:

Active substances:

- F4ab (K88ab) fimbrial adhesin	≥ 9.0 $\log_2$ Ab titre[1]
- F4ac (K88ac) fimbrial adhesin	≥ 5.4 $\log_2$ Ab titre[1]
- F5 (K99) fimbrial adhesin	≥ 6.8 $\log_2$ Ab titre[1]
- F6 (987P) fimbrial adhesin	≥ 7.1 $\log_2$ Ab titre[1]
- LT toxoid	≥ 6.8 $\log_2$ Ab titre[1]

[1] Mean antibody titre (Ab) obtained after vaccination of mice with a 1/20 sow dose.

Adjuvant:

dl-α-tocopherol acetate	150 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (sows and gilts)

4.2 Indications for use, specifying the target species

For the passive immunisation of piglets by active immunisation of sows/gilts to reduce mortality and clinical signs such as diarrhoea due to neonatal enterotoxicosis during the first days of life, caused by those *E.coli* strains, which express the fimbrial adhesins F4ab (K88ab), F4ac (K88ac), F5 (K99) or F6 (987P).

4.3 Contraindications

None

4.4 Special warnings

None

4.5 Special precautions for use

Special precautions for use in animals

Before using the vaccine allow it to reach room temperature (15-25 °C) and shake well before use.
Use sterile syringes and needles.
Avoid introduction of contamination.
Vaccinate only healthy animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

In the case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the physician.

4.6 Adverse reactions (frequency and seriousness)

A mean transient increase in body temperature of about 1°C, in some pigs up to 3°C, may occur in the first 24 hours after vaccination. Reduced feed intake and listlessness may occur in approximately 10% of the animals on the day of vaccination, but returns to normal within 1-3 days. A transient swelling and redness at the injection site may be observed in approximately 5% of the animals. The diameter of the swelling is in general below 5 cm, but in some cases a larger swelling may occur. Swelling and redness at the injection site may occasionally last for at least 14 days.

4.7 Use during pregnancy, lactation or lay

The vaccine can be used during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy from concurrent use of this vaccine with any other. It is therefore recommended that no other vaccine should be administered within 14 days before or after vaccination with this product.

4.9 Amounts to be administered and administration route

Intramuscular injection in sows/gilts of 2 ml of the vaccine per animal in the neck in the area behind the ear.

Vaccination scheme:

Basic vaccination: Sows/gilts which have not yet been vaccinated with the product shall be given an injection preferably 6 to 8 weeks before the expected date of farrowing followed by a second injection 4 weeks later.

Revaccination: A single revaccination shall be carried out during the second half of each subsequent pregnancy, preferably 2 to 4 weeks before the expected date of farrowing.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No undesirable effects other than those observed and mentioned in the “Adverse reactions” section have been observed.

4.11 Withdrawal period(s)

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: inactivated bacterial vaccine. ATC vet code: QI09AB02.

Vaccine to stimulate active immunity of sows/gilts in order to provide passive immunity to their progeny against *E. coli* strains that express the fimbrial adhesins F4ab, F4ac, F5 and F6.

The fimbrial adhesins F4ab, F4ac, F5, and F6 are responsible for the adhesion and the virulence of *E.coli* strains, which cause neonatal enterotoxicosis in piglets. These immunogens are incorporated in an adjuvant in order to enhance a prolonged stimulation of immunity. Neonatal piglets derive passive immunity via ingestion of colostrum from vaccinated sows/gilts.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polysorbate 80
Potassium Chloride
Potassium Dihydrogen Phosphate
Simethicone emulsion
Sodium chloride
Disodium Phosphate Dihydate
DL-Alpha-Tocopherol Acetate
Water for injection

6.2 Incompatibilities

Do not mix with any other vaccine or immunological product.

6.3 Shelf life

2 years.
Shelf-life after first opening: 3 hours.

6.4. Special precautions for storage

Store in a refrigerator (+2°C to +8°C). Do not freeze.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 glass (hydrolytic type I) or 1 PET vial of 20, 50 or 100 ml with a halogenobutyl rubber stopper and a coded aluminium cap. Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands.

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/96/001/003-008

9. DATE OF RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

{MM/YYYY} or <month YYYY>

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO SAFE AND EFFECTIVE USE

D. STATEMENT OF THE MRLs

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substances

Intervet International B.V.
Wim de Körverstraat 35,
P.O. Box 31,
5830 AA Boxmeer,
The Netherlands.

Name and address of the manufacturer responsible for batch release

Intervet International B.V.
Wim de Körverstraat 35,
P.O. Box 31,
5830 AA Boxmeer,
The Netherlands.

B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

To be supplied only on veterinary prescription.

C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE PRODUCT

Not applicable.

D. STATEMENT OF THE MRLs

Annex II of Council Regulation (EEC) No 2377/90

Pharmacologically active substance	Animal Species	Other provisions
dl-α-tocopherol acetate[a] (Vitamin E)	All food-producing species	
Potassium chloride[b] (E508)	All food-producing species	
Potassium dihydrogen phosphate[c] (E340i)	All food-producing species	
Sodium chloride[d]	All food-producing species	
Disodium hydrogen phosphate[e] (E339ii)	All food-producing species	
Polysorbate 80[f]	All food-producing species	
Simethicone[g] (Dimethicone)	All food-producing species	

[a] OJ No L122 of 12.05.99
[b] OJ No L272 of 25.10.96
[c] OJ No L272 of 25.10.96
[d] OJ No L290 of 5.12.95
[e] OJ No L272 of 25.10.96
[f] OJ No L290 of 5.12.95
[g] OJ No L290 of 5.12.95

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli Diluvac Forte

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Per dose of two ml:

- F4ab (K88ab) fimbrial adhesin	≥ 9.0 $\log_2$ Ab titre[1]
- F4ac (K88ac) fimbrial adhesin	≥ 5.4 $\log_2$ Ab titre[1]
- F5 (K99) fimbrial adhesin	≥ 6.8 $\log_2$ Ab titre[1]
- F6 (987P) fimbrial adhesin	≥ 7.1 $\log_2$ Ab titre[1]
- LT toxoid	≥ 6.8 $\log_2$ Ab titre[1]

[1] Mean antibody titre (Ab) obtained after vaccination of mice with a 1/20 sow dose.

dl-α-tocopherol acetate 150 mg

3. PHARMACEUTICAL FORM

Suspension for injection.

4. PACKAGE SIZE

20 ml (10 doses)
50 ml (25 doses)
100 ml (50 doses)

5. TARGET SPECIES

Pigs (sows and gilts)

6. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.

IM injection of 2 ml

7. WITHDRAWAL PERIOD

Withdrawal period: Zero days

8. SPECIAL WARNING(S), IF NECESSARY

Accidental injection is dangerous.

9. EXPIRY DATE

EXP {month/year}
Once broached, use within 3 hours.

10. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Protect from light.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. . THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

13.. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE IN THE EEA, IF DIFFERENT

Intervet International B.V.
NL-5831 AN Boxmeer

14. NUMBERS IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS

EU/2/96/001/003	20 ml Glass
EU/2/96/001/006	20 ml PET
EU/2/96/001/004	50 ml Glass
EU/2/96/001/007	50 ml PET
EU/2/96/001/005	100 ml Glass
EU/2/96/001/008	100 ml PET

15. MANUFACTURER'S BATCH NUMBER

Batch: .....

16. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
20 ml & 50 ml (EU/2/96/001/003, EU/2/96/001/004, EU/2/97/001/006 & EU/2/96/001/007)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli Diluvac Forte

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Per dose of two ml:

- F4ab (K88ab) fimbrial adhesin	≥ 9.0 $\log_2$ Ab titre[1]
- F4ac (K88ac) fimbrial adhesin	≥ 5.4 $\log_2$ Ab titre[1]
- F5 (K99) fimbrial adhesin	≥ 6.8 $\log_2$ Ab titre[1]
- F6 (987P) fimbrial adhesin	≥ 7.1 $\log_2$ Ab titre[1]
- LT toxoid	≥ 6.8 $\log_2$ Ab titre[1]

[1] Mean antibody titre (Ab) obtained after vaccination of mice with a 1/20 sow dose.

dl-α-tocopherol acetate 150 mg

3. PHARMACEUTICAL FORM

Suspension for injection.

4. PACKAGE SIZE

20 ml (10 doses)
50 ml (25 doses)

5. TARGET SPECIES

Pigs (sows and gilts)

6. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.

IM injection of 2 ml

7. WITHDRAWAL PERIOD

Withdrawal period: Zero days

8. SPECIAL WARNING(S), IF NECESSARY

Accidental injection is dangerous.

9. EXPIRY DATE

EXP {month/year}
Once broached, use within 3 hours.

10. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Protect from light.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. . THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

13.. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE IN THE EEA, IF DIFFERENT

Intervet International B.V.
NL-5831 AN Boxmeer

14. NUMBERS IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS

EU/2/96/001/003	20 ml Glass
EU/2/96/001/006	20 ml PET
EU/2/96/001/004	50 ml Glass
EU/2/96/001/007	50 ml PET

15. MANUFACTURER'S BATCH NUMBER

Batch: .....

16. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
100 ml (EU/2/96/001/005 & EU/2/96/001/008)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli Diluvac Forte

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Per dose of two ml:

- F4ab (K88ab) fimbrial adhesin	≥ 9.0 $\log_2$ Ab titre[1]
- F4ac (K88ac) fimbrial adhesin	≥ 5.4 $\log_2$ Ab titre[1]
- F5 (K99) fimbrial adhesin	≥ 6.8 $\log_2$ Ab titre[1]
- F6 (987P) fimbrial adhesin	≥ 7.1 $\log_2$ Ab titre[1]
- LT toxoid	≥ 6.8 $\log_2$ Ab titre[1]

[1] Mean antibody titre (Ab) obtained after vaccination of mice with a 1/20 sow dose.

dl-α-tocopherol acetate 150 mg

3. PHARMACEUTICAL FORM

Suspension for injection.

4. PACKAGE SIZE

100 ml (50 doses)

5. TARGET SPECIES

Pigs (sows and gilts)

6. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.

IM injection of 2 ml

7. WITHDRAWAL PERIOD

Withdrawal period: Zero days

8. SPECIAL WARNING(S), IF NECESSARY

Accidental injection is dangerous.

9. EXPIRY DATE

EXP {month/year}
Once broached, use within 3 hours.

10. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Protect from light.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. . THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

13.. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE IN THE EEA, IF DIFFERENT

Intervet International B.V.
NL-5831 AN Boxmeer

14. NUMBERS IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS

EU/2/96/001/005	100 ml Glass
EU/2/96/001/008	100 ml PET

15. MANUFACTURER'S BATCH NUMBER

Batch: .....

16. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

17. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
20 ml vial labels (EU/2/96/001/003 & EU/2/96/001/006 only)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli Diluvac Forte

2. CONTENTS BY WEIGHT, BY VOLUME OR NUMBER OF DOSES

20 ml (10 doses)

3. ROUTE(S) OF ADMINISTRATION

IM injection

4. WITHDRAWAL PERIOD

Withdrawal period: Zero days

5. BATCH NUMBER

Batch: .....

6. EXPIRY DATE

EXP {month/year}
Once broached, use within 3 hours.

7. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE
50 ml & 100 ml vial labels (EU/2/96/001/004, EU/2/96/001/005, EU/2/97/001/007 & EU/2/96/001/008 only)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli Diluvac Forte

2. PACKAGE SIZE

50 ml (25 doses)
100 ml (50 doses)

3. TARGET SPECIES

Pigs (sows and gilts)

4. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
IM injection of 2 ml

5. WITHDRAWAL PERIOD

Withdrawal period: Zero days

6. EXPIRY DATE

EXP {month/year}
Once broached, use within 3 hours.

7. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

8. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

9. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE IN THE EEA, IF DIFFERENT

Intervet International B.V.
NL-5831 AN Boxmeer

10. NUMBER(S) IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS

EU/2/96/001/004	50 ml Glass
EU/2/96/001/007	50 ml PET
EU/2/96/001/005	100 ml Glass
EU/2/96/001/008	100 ml PET

11. MANUFACTURER'S BATCH NUMBER

Batch: .....

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR

PORCILIS PORCOLI DILUVAC FORTE

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE IN THE EEA, IF DIFFERENT

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Porcilis Porcoli Diluvac Forte suspension for injection

3. STATEMENT OF THE ACTIVE AND OTHER SUBSTANCE(S)

Each dose of two ml contains the F4ab (K88ab) fimbrial adhesin, the F4ac (K88ac) fimbrial adhesin, the F5 (K99) fimbrial adhesin, the F6 (987P) fimbrial adhesin and of LT toxoid, which induce a mean antibody titre of respectively ≥ 9.0 $\log_2$ Ab titre, ≥ 5.4 $\log_2$ Ab titre, ≥ 6.8 $\log_2$ Ab titre, ≥ 7.1 $\log_2$ Ab titre, and 6.8 $\log_2$ Ab titre after vaccination of mice with a 1/20 sow dose. The antigens are adjuvanted with 150 mg dl-α-tocopherol acetate per dose.

4. INDICATION(S)

For the passive immunisation of piglets by active immunisation of sows/gilts to reduce mortality and clinical signs such as diarrhoea due to neonatal enterotoxicosis during the first days of life, caused by those *E.coli* strains, which express the fimbrial adhesins F4ab (K88ab), F4ac (K88ac), F5 (K99) or F6 (987P).

5. CONTRA-INDICATIONS

None

6. ADVERSE REACTIONS

A mean transient increase in body temperature of about 1°C, in some pigs up to 3 °C, may occur in the first 24 hours after vaccination. Reduced feed intake and listlessness may occur in approximately 10% of the animals on the day of vaccination, but returns to normal within 1-3 days. A transient swelling and redness at the injection site may be observed in approximately 5% of the animals. The diameter of the swelling is in general below 5 cm, but in some cases a larger size swelling may occur. Swelling and redness at the injection site may occasionally last for at least 14 days.

If you notice any other side effects, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs (sows/gilts)

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Intramuscular injection in sows/gilts of 2 ml of the vaccine per animal in the neck in the area behind the ear.

Vaccination scheme:

Basic vaccination: Sows/gilts which have not yet been vaccinated with the product shall be given an injection preferably 6 to 8 weeks before the expected date of farrowing followed by a second injection 4 weeks later.

Revaccination: A single revaccination shall be carried out during the second half of each subsequent pregnancy, preferably 2 to 4 weeks before the expected date of farrowing.

9. ADVICE ON CORRECT ADMINISTRATION

- Before using the vaccine allow it to reach room temperature.
- Shake well before use.
- Use sterile syringes and needles.
- Avoid introduction of contamination.
- Vaccinate only healthy animals.

10. WITHDRAWAL PERIOD

Zero days

11. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator (+2°C to +8°C).
Do not freeze.
Shelf-life after first opening: 3 hours.

12. SPECIAL WARNING(S)

No information is available on the safety and efficacy from concurrent use of this vaccine with any other. It is therefore recommended that no other vaccine should be administered within 14 days before or after vaccination with this product.

In the absence of incompatibility studies this vaccine must not be mixed with other veterinary medical products.

In the case of accidental self-injection, seek medical advice immediately and show the package insert or label to the physician.

Keep out of the reach and sight of children.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Not all pack sizes may be marketed.

The fimbrial adhesins F4ab, F4ac, F5 and F6 are responsible for the adhesion and the virulence of *E. coli* strains, which cause neonatal enterotoxicosis in piglets. These immunogens are incorporated in an adjuvant in order to enhance a prolonged stimulation of immunity. Neonatal piglets derive passive immunity via ingestion of colostrum from vaccinated sows/gilts.

For animal treatment only.