ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18 lyophilisate for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of vaccine contains:

Active substances:
Live non-pathogenic *Escherichia coli* O8:K87* (F4ac):.....$1.3x10^8$ to $9.0x10^8$ CFU**
Live non-pathogenic *Escherichia coli* O141:K94* (F18ac):.....$2.8x10^8$ to $3.0x10^9$ CFU**

*not attenuated
**CFU – colony-forming units

Excipients:

Qualitative composition of excipients and other constituents
Dextran 40,000
Sucrose
Monosodium glutamate
Purified water

White or whitish powder.

3. CLINICAL INFORMATION

3.1 Target species

Pigs.

3.2 Indications for use for each target species

For active immunisation of pigs from 18 days of age against enterotoxigenic F4-positive and F18-positive *Escherichia coli* in order to:

- reduce the incidence of moderate to severe post-weaning *E. coli* diarrhoea (PWD) in infected pigs;
- reduce the faecal shedding of enterotoxigenic F4-positive and F18-positive *E. coli* from infected pigs.

Onset of immunity: 1 week after vaccination
Duration of immunity: 3 weeks after vaccination

3.3 Contraindications

None.

3.4 Special warnings

It is not recommended to vaccinate animals undergoing immunosuppressive treatment or to vaccinate animals undergoing antibacterial treatment effective against *E. coli*.

Vaccinate healthy animals only.

3.5 Special precautions for use

Special precautions for safe use in the target species:
The vaccine strains may be excreted by vaccinated piglets for at least 14 days following vaccination. The vaccine strains readily spread to other pigs in contact with vaccinated pigs. Unvaccinated pigs in contact with vaccinated pigs will harbour and shed the vaccine strains similarly to vaccinated pigs. During this time, the contact of immunosuppressed pigs with vaccinated pigs should be avoided.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Personal protective equipment consisting of protective disposable gloves and safety glasses should be worn when handling the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. In case of spillage onto skin, rinse with water and seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Pigs:
No adverse events have been observed.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
The use is not recommended during pregnancy.

3.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

3.9 Administration routes and dosage

Oral use.
Vaccination schedule: administer a single dose orally from 18 days of age.

All materials used in preparing and administering the vaccine must be free of antimicrobials, detergent or disinfectant residues to prevent inactivation.

The reconstituted vaccine is a transparent to opaque white-yellowish suspension depending on the volume of water used for dilution.

Vaccination by drench application:
- 50-dose presentation: Reconstitute the lyophilisate by adding 10 ml of water to the vial. Shake well and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 100 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.
- 200-dose presentation: Reconstitute the lyophilisate by adding 20 ml of water to the vial. Shake well and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 400 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.

Vaccination via the drinking water system:
The drinking water systems have to be cleaned and intensively rinsed with untreated water to avoid any residues of antimicrobials, detergents or disinfectants.

Withhold drinking water supply for 1 to 2 hours prior to the planned vaccination to stimulate drinking of the vaccine suspension.

Reconstitute the lyophilisate by adding 10 ml (50-dose presentation) or 20 ml (200-dose presentation) of water to the vial. Shake well.

The final suspension containing the vaccine should be consumed within 4 hours after preparation. Provide enough space so that all pigs can drink the required amount. The actual amount of water consumed may however vary considerably depending on several factors. Therefore, it is recommended to assess the actual water intake during a 4-hour time period the day before vaccination. Alternatively, refer to the following table:

Body weight (kg)	Water consumption (litres) in a 4-hour time period		
	1 pig	50 pigs	200 pigs
Up to 4.5	0.11 litres	5.5 litres	22 litres
4.6 to 6.8	0.17 litres	8.5 litres	34 litres
6.9 to 9.0	0.23 litres	11.5 litres	46 litres

- For administration using bowls or tanks, dilute the reconstituted vaccine in the volume of water that the pigs will drink during a 4-hour time period.
- For administration through water lines using a dosing pump (proportioner), dilute the reconstituted vaccine in the needed volume of the dosing pump stock solution. The volume of stock solution is calculated using the volume of water that the pigs will drink during a 4-hour time period multiplied by the dosing pump rate (in decimal). As an example, for a 4-hour consumption of 22 litres and a dosing pump rate of 1%, the volume of the stock solution should be 22 litres x 0.01 = 220 ml.

In case of concerns about the presence of disinfectant residues in the drinking water, such as chlorine, it is recommended to add skimmed milk powder as a stabiliser into the drinking water prior to adding the vaccine. The final concentration of the skimmed milk powder should be 5 g/litre.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

A rectal temperature up to 41.2 °C may occur in individual animals within the first 24 hours after administration of a 10-fold overdose.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Zero days.

4. IMMUNOLOGICAL INFORMATION

4.1 ATCvet code: QI09AE03

To stimulate active immunity against enterotoxigenic F4-positive and F18-positive *E. coli* in pigs.

The vaccine induces an intestinal immunity and a serological response against F4-positive and F18-positive *E. coli* in pigs. The vaccine confers cross-protection against F18ab-positive *E. coli*, as demonstrated by challenge for both the 7-day onset of immunity and the 21-day duration of immunity. Antibodies triggered by the vaccine provide cross-reactivity against F4ab and F4ad-positive *E. coli* strains.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after reconstitution and dilution according to directions: 4 hours.

5.3 Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C).
Protect from light.

5.4 Nature and composition of immediate packaging

Type I glass vial of 11 ml containing 50 doses and type II glass vial of 50 ml containing 200 doses with a chlorobutyl rubber stopper sealed with an aluminium cap.

Cardboard box of one vial of 50 or 200 doses.
Cardboard box of four vials of 50 doses.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco GmbH

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/16/202/001-003

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 09/01/2017

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18 lyophilisate for oral suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Live non-pathogenic *E. coli* O8:K87 (F4ac): $1.3x10^8$ to $9.0x10^8$ CFU/dose
Live non-pathogenic *E. coli* O141:K94 (F18ac): $2.8x10^8$ to $3.0x10^9$ CFU/dose

3. PACKAGE SIZE

1 x 50 doses
4 x 50 doses
1 x 200 doses

4. TARGET SPECIES

Pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use

7. WITHDRAWAL PERIODS

Withdrawal period: zero days

8. EXPIRY DATE

Exp. {mm/yyyy}

Once reconstituted use within 4 hours.

9. SPECIAL STORAGE PRECAUTIONS

Store and transport refrigerated.
Protect from light.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco GmbH

14. MARKETING AUTHORISATION NUMBERS

EU/2/16/202/001-003

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vials (50 or 200 doses)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

50 / 200 doses live *E. coli* O8:K87 (F4ac) and live *E. coli* O141:K94 (F18ac)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once reconstituted use within 4 hours.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Coliprotec F4/F18 lyophilisate for oral suspension

2. Composition

Each dose of vaccine contains:
Live non-pathogenic *E. coli* O8:K87* (F4ac):.....1.3x10^8 to 9.0x10^8 CFU**
Live non-pathogenic *E. coli* O141:K94* (F18ac):.....2.8x10^8 to 3.0x10^9 CFU**

*not attenuated
**CFU – colony-forming units

White or whitish powder.

3. Target species

Pigs

4. Indications for use

For active immunisation of pigs from 18 days of age against enterotoxigenic F4-positive and F18-positive *E. coli* in order to:

- reduce the incidence of moderate to severe post-weaning *E. coli* diarrhoea (PWD) in infected pigs;
- reduce the faecal shedding of enterotoxigenic F4-positive and F18-positive *E. coli* from infected pigs.

Onset of immunity: 1 week after vaccination
Duration of immunity: 3 weeks after vaccination

5. Contraindications

None

6. Special warnings

Special warnings:
It is not recommended to vaccinate animals undergoing immunosuppressive treatment or to vaccinate animals undergoing antibacterial treatment effective against *E. coli*.

Vaccinate healthy animals only.

Special precautions for safe use in the target species:
The vaccine strains may be excreted by vaccinated piglets for at least 14 days following vaccination. The vaccine strains readily spread to other pigs in contact with vaccinated pigs. Unvaccinated pigs in contact with vaccinated pigs will harbour and shed the vaccine strains similarly to vaccinated pigs. During this time, the contact of immunosuppressed pigs with vaccinated pigs should be avoided.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Personal protective equipment consisting of protective disposable gloves and safety glasses should be worn when handling the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. In case of spillage onto skin, rinse with water and seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy:
The use is not recommended during pregnancy.

Interaction with other medicinal products and other forms of interaction:
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Overdose:
A rectal temperature up to 41.2 °C may occur in individual animals within the first 24 hours after administration of a 10-fold overdose.

Major incompatibilities:
Do not mix with any other veterinary medicinal product.

7. Adverse events

Pigs:
No adverse events have been observed.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

Oral use.
Administer a single dose of vaccine from 18 days of age.

9. Advice on correct administration

All materials used in preparing and administering the vaccine must be free of antimicrobials, detergent or disinfectant residues to prevent inactivation.

Vaccination schedule: administer a single dose orally from 18 days of age.

The reconstituted vaccine is transparent to opaque white-yellowish suspension depending on the volume of water used for dilution.

Vaccination by drench application:

- 50-dose presentation: Reconstitute the lyophilisate by adding **10 ml** of water to the vial. **Shake well** and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 100 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.
- 200-dose presentation: Reconstitute the lyophilisate by adding **20 ml** of water to the vial. **Shake well** and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 400 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.

Vaccination via the drinking water system:

The drinking water systems have to be cleaned and intensively rinsed with untreated water to avoid any residues of antimicrobials, detergents or disinfectants.

Withhold drinking water supply for 1 to 2 hours prior to the planned vaccination to stimulate drinking of the vaccine suspension.

Reconstitute the lyophilisate by adding **10 ml** (50-dose presentation) or **20 ml** (200-dose presentation) of water to the vial. **Shake well**.

The final suspension containing the vaccine should be consumed within 4 hours after preparation. Provide enough space so that all pigs can drink the required amount. The actual amount of water consumed may however vary considerably depending on several factors. Therefore, it is recommended to assess the actual water intake during a 4-hour time period the day before vaccination. Alternatively, refer to the following table:

Body weight (kg)	Water consumption (litres) in a 4-hour time period		
	1 pig	50 pigs	200 pigs
Up to 4.5	0.11 litres	5.5 litres	22 litres
4.6 to 6.8	0.17 litres	8.5 litres	34 litres
6.9 to 9.0	0.23 litres	11.5 litres	46 litres

- For administration using bowls or tanks, dilute the reconstituted vaccine in the volume of water that the pigs will drink during a 4-hour time period.
- For administration through water lines using a dosing pump (proportioner), dilute the reconstituted vaccine in the needed volume of the dosing pump stock solution. The volume of stock solution is calculated using the volume of water that the pigs will drink during a 4-hour time period multiplied by the dosing pump rate (in decimal). As an example, for a 4-hour consumption of 22 litres and a dosing pump rate of 1%, the volume of the stock solution should be 22 litres x 0.01 = 220 ml.

In case of concerns about the presence of disinfectant residues in the drinking water, such as chlorine, it is recommended to add skimmed milk powder as a stabiliser into the drinking water prior to adding the vaccine. The final concentration of the skimmed milk powder should be 5 g/litre.

10. Withdrawal periods

Zero days.

11. Special storage precautions

Keep out of the sight and reach of children.
Store and transport refrigerated (2 °C – 8 °C).
Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

Shelf life after reconstitution and dilution according to directions: 4 hours.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Marketing authorisation numbers:
EU/2/16/202/001-003

Pack sizes:
Cardboard box of one vial of 50 or 200 doses.
Cardboard box of four vials of 50 doses.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

België/Belgique/Belgien
Tél/Tel: +3233000338
PV.BEL@elancoah.com

Република България
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PV.CZE@elancoah.com

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Latvija
Tel: +3728840390
PV.LVA@elancoah.com

United Kingdom (Northern Ireland)
Tel: +443308221732
PV.XXI@elancoah.com

Manufacturer responsible for batch release:
Lohmann Animal Health GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

17. Other information

Immunological properties:
To stimulate active immunity against enterotoxigenic F4-positive and F18-positive *E. coli* in pigs. The vaccine induces an intestinal immunity and a serological response against F4-positive and F18-positive *E. coli* in pigs. The vaccine confers cross protection against F18ab-positive *E. coli*, as demonstrated by challenge for both the 7-day onset of immunity and the 21-day duration of immunity. Antibodies triggered by the vaccine provide cross-reactivity against F4ab and F4ad-positive *E. coli* strains.