ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4 lyophilisate for oral suspension for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of vaccine contains:

Live non-pathogenic *Escherichia coli* O8:K87[1].(F4ac).....1.3 x10^8 to 9.0 x10^8 CFU[2]/dose

[1]not attenuated

[2]CFU – colony forming units

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White or whitish lyophilisate for oral suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs

4.2 Indications for use, specifying the target species

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

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

Onset of immunity: 7 days after vaccination.

Duration of immunity: 21 days after vaccination.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Do not vaccinate animals undergoing immunosuppressive treatment.

Do not vaccinate animals undergoing antibacterial treatment effective against *Escherichia coli*.

Vaccinate healthy animals only.

4.5 Special precautions for use

Special precautions for use in animals
Apply the usual aseptic precautions to all administration procedures.

The vaccine strain may be excreted by vaccinated piglets for at least 14 days following vaccination. The vaccine strain readily spreads to other pigs in contact to vaccinated pigs. Unvaccinated pigs in contact with vaccinated pigs will harbour and shed the vaccine strain 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.

4.6 Adverse reactions (frequency and seriousness)

A transient reduced weight gain was observed during the first week after vaccination in studies.
Shivering was very commonly observed after vaccination in studies.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The use of this veterinary medicinal product is not recommended during pregnancy.

4.8 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.

4.9 Amounts to be administered and administration route

Oral use and in drinking water use.

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

Oral use. Vaccination by drench application:

- 50-dose presentation: Reconstitute the lyophilisate by adding 5 ml of tap water to the vial. Shake well and transfer the suspension into a graduated container, mix again with tap water to complete to a total volume of 100 ml. Shake well and use immediately. Administer a single 2 ml dose orally to pigs (from 18 days of age), irrespective of body weight.
- 200-dose presentation: Reconstitute the lyophilisate by adding 10 ml of tap water to the vial. Shake well and transfer the suspension into a graduated container, mix again with tap water to complete to a total volume of 400 ml. Shake well and use immediately. Administer a single 2 ml dose orally to pigs (from 18 days of age), irrespective of body weight.

The suspension should be administered within 4 hours after preparation.

In drinking water use. Vaccination via the drinking water:
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 5 ml (50-dose presentation) or 10 ml (200-dose presentation) of tap 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 in a 4-hour time period of number of pig(s)		
	1	50	200
4.5	0.11 l	5.5 l	22 l
6.8	0.17 l	8.5 l	34 l
9.0	0.23 l	11.5 l	46 l

- 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 l and a dosing pump rate of 1%, the volume of the stock solution should be 22 l x 0.01 = 220 ml.

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

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

No adverse reactions other than those stated under section 4.6 have been observed after administration of 10 times the recommended dose.

4.11 Withdrawal period(s)

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: immunologicals for Suidae live bacterial vaccines for pigs.
ATCvet code: QI09AE03.
To stimulate active immunity against enterotoxigenic F4-positive *Escherichia coli* in pigs.
Live non-pathogenic vaccine to reduce diarrhoea, faecal shedding and intestinal colonization associated with F4-positive enterotoxigenic *Escherichia coli* in pigs.
The vaccine induces an intestinal immunity and a serological response against F4-positive *Escherichia coli* in pigs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextran 40 000
Sucrose
Monosodium glutamate
Purified water

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale : 18 months.

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

6.4. Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Type I glass vial of 6 ml containing 50 doses and of 11 ml containing 200 doses with a chlorobutyl rubber stopper sealed with an aluminum cap.

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

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Prevtec Microbia GmbH
Geyerspergerstr 27
80689 München
GERMANY

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/14/180/001–003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:16/03/2015
Date of latest renewal: dd/mm/yyyy

10 DATE OF REVISION OF THE TEXT

11/2019

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/)

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

Name and address of the manufacturer of the biological active substance and the manufacturer responsible for batch release:
CZ Veterinaria S.A.
Poligono La Relva, Torneiros s/n
36410 Porriño (Pontevedra)
SPAIN

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

The active substance being a principle of biological origin intended to produce a state of immunity is not within the scope of Regulation (EC) No 470/2009.

The excipients listed in section 6.1 of the SPC are either allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

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 lyophilisate for oral suspension for pigs.

2. STATEMENT OF ACTIVE SUBSTANCES

Live non-pathogenic *Escherichia coli* O8:K87 (F4ac): 1.3 x10^8 to 9.0 x10^8 CFU/dose

3. PHARMACEUTICAL FORM

Lyophilisate for oral suspension

4. PACKAGE SIZE

50 doses
4 x 50 doses
200 doses

5. TARGET SPECIES

Pigs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use and in drinking water use.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s): Zero days.

9. SPECIAL WARNING(S), IF NECESSARY

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

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated.
Protect from light.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Prevtec Microbia GmbH
80689 München
GERMANY

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/14/180/001 – 003

17. MANUFACTURER'S 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 lyophilisate for oral suspension for pigs.

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Live *E.coli,* O8:K87 (F4ac).

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

50 doses
200 doses

4. ROUTE(S) OF ADMINISTRATION

Oral use and in drinking water use.

5. WITHDRAWAL PERIOD(S)

Withdrawal period(s): Zero days.

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Coliprotec F4
lyophilisate for oral suspension for pigs

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

Marketing authorisation holder:
Prevtec Microbia GmbH
Geyerspergerstr. 27
80689 München
GERMANY

Manufacturer responsible for batch release:
CZ Veterinaria S.A.
Poligono La Relva, Torneiros s/n
36410 Porriño (Pontevedra)
SPAIN

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4 lyophilisate for oral suspension for pigs

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

Each dose of vaccine contains:
Live non-pathogenic *Escherichia coli* O8:K87 (F4ac)[1].....1.3x 10^8 to 9.0 x10^8 CFU[2]/dose

[1] not attenuated
[2] CFU = colony forming units

White or whitish lyophilisate.

4. INDICATION(S)

For active immunisation of pigs against enterotoxigenic F4-positive *Escherichia coli* in order to:
- reduce the incidence of moderate to severe post-weaning *Escherichia coli* diarrhoea (PWD) in pigs
- reduce the colonisation of the ileum and faecal shedding of enterotoxigenic F4-positive *Escherichia coli* from infected pigs.

Onset of immunity: 7 days after vaccination.
Duration of immunity: 21 days after vaccination.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

A transient reduced weight gain was observed during the first week after vaccination in studies.
Shivering was very commonly observed after vaccination in studies.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

7. TARGET SPECIES

Pigs

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

Oral use and in drinking water use.

9. ADVICE ON CORRECT ADMINISTRATION

Oral use and in drinking water use.

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.

Oral use. Vaccination by drench application:
- 50-dose presentation: Reconstitute the lyophilisate by adding 5 ml of tap water to the vial. Shake well and transfer the suspension into a graduated container, mix again with tap water to complete to a total volume of 100 ml. Shake well and use immediately. Administer a single 2 ml dose orally to pigs (from 18 days of age), irrespective of body weight.
- 200-dose presentation: Reconstitute the lyophilisate by adding 10 ml of tap water to the vial. Shake well and transfer the suspension into a graduated container, mix again with tap water to complete to a total volume of 400 ml. Shake well and use immediately. Administer a single 2 ml dose orally to pigs (from 18 days of age), irrespective of body weight.

The suspension should be administered within 4 hours after preparation.

In driniking water use. Vaccination via the drinking water:
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 5 ml (50-dose presentation) or 10 ml (200-dose presentation) of tap 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 in a 4-hour time period of number of pig(s)		
	1	50	200
4.5	0.11 l	5.5 lL	22 l
6.8	0.17 l	8.5 l	34 l
9.0	0.23 l	11.5 l	46 l

- 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 l and a dosing pump rate of 1%, the volume of the stock solution should be 22 l x 0.01 = 220 ml.

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

10. WITHDRAWAL PERIOD(S)

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 dilution according to directions: 4 hours.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Vaccinate healthy animals only.
Do not vaccinate animals undergoing immunosuppressive treatment. Do no vaccinate animals undergoing antibacterial treatment effective against *Escherichia coli*.

Special precautions for use in animals:

Apply the usual aseptic precautions to all administration procedures.

The vaccine strain may be excreted by vaccinated piglets for at least 14 days following vaccination. The vaccine strain readily spreads to other pigs in contact to vaccinated pigs. Unvaccinated pigs in contact with vaccinated pigs will harbour and shed the vaccine strain 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 and lactation:
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. 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 (symptoms, emergency procedures, antidotes):

No adverse reactions other than those stated for single dose use have been observed after administration of 10 times the recommended dose

Incompatibilities:

Do not mix with any other veterinary medicinal product.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

15. OTHER INFORMATION

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.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.