ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BioBos RCC suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2ml dose contains:

Active substances:

Inactivated *E. coli* expressing F5 (K99) adhesin, strain O8:K35	RP ≥ 1*
Inactivated bovine rotavirus, serotype G6P1, strain TM-91	RP ≥ 1*
Inactivated bovine coronavirus, strain C-197	RP ≥ 1*

* Relative potency (RP): level of antibodies in sera of vaccinated guinea pigs as determined by ELISA in comparison with the reference serum obtained after vaccination of guinea pigs with a vaccine batch that has successfully passed the challenge test in the target animals.

Adjuvants:

Aluminium hydroxide	6 mg
Quillaja saponin (Quil A)	≤ 0.4 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Thiomersal	0.2 mg
Formaldehyde	≤ 1 mg
Sodium chloride	-
Potassium chloride	-
Potassium dihydrogen phosphate	-
Disodium phosphate dodecahydrate	-
Water for injections	-

3. CLINICAL INFORMATION

3.1 Target species

Cattle (pregnant heifers and cows).

3.2 Indications for use for each target species

Active immunisation of pregnant heifers and cows in order to stimulate the development of antibodies against bovine rotavirus, bovine coronavirus and *E. coli* expressing F5 (K99) adhesin and to increase the level of passive immunity of calves against neonatal diarrhoea caused by bovine rotavirus, bovine coronavirus and *E. coli* expressing F5 (K99) adhesin.
In calves fed with colostrum and milk from vaccinated cows for the first week of life, laboratory studies conducted with heterologous challenge strains (a G6 BRV strain, a BCV strain, and a K99 *E. coli* strain) have demonstrated that these antibodies:

- prevent neonatal diarrhoea caused by bovine rotavirus and *E. coli* expressing F5 (K99) adhesin,

- reduce the incidence and severity of neonatal diarrhoea caused by bovine coronavirus,
- reduce faecal shedding of virus in calves infected with bovine rotavirus and bovine coronavirus.

Onset of immunity:
In calves fed with colostrum from vaccinated heifers or cows passive immunity commences with colostrum feeding and is dependent on calves receiving sufficient colostrum after birth.

Duration of immunity:
Calves fed with colostrum and milk from vaccinated dams for the first week of life are protected against bovine rotavirus for 7 days and against bovine coronavirus for 14 days.
The duration of immunity against infections caused by *E. coli* expressing F5 (K99) adhesin was not studied since such disease is usually observed in calves less than 3 days of age and susceptibility to enterotoxigenic *E.coli* is age dependent.

3.3 Contraindications

None.

3.4 Special warnings

Vaccinate healthy animals only.

3.5 Special precautions for use

Special precautions for safe use in the target species:

To achieve optimum results and to reduce infection pressure on the farm, a whole herd cow vaccination policy should be adopted, as well as standard infectious diseases control practices.

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

In case of adverse reactions following accidental self-injection, 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

Very common (>1 animal / 10 animals treated):	An increase in mean body temperature of 1.0°C was very commonly observed in laboratory and field studies; in individual cases, the maximum increase may reach 2.1°C, with body temperatures resolving to normal levels within 2 days without impairing the general health status of the vaccinated animals.
Common (1 to 10 animals / 100 animals treated):	A localised mild swelling (≤ 5 cm in diameter) at the injection site resolving within 2 days was commonly observed in field studies.

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 its local representative or the national competent authority via the national reporting system. See also the last section of the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Can be used during pregnancy.
The effect of vaccination on pre- or post-partum lactation was not studied.

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

Slowly warm up to room temperature and gently shake the content of the vial before administration.

Administration:
One dose of 2 ml by intramuscular injection.
A single injection should be given during each pregnancy between 12 and 3 weeks before the expected calving.

Colostrum feeding:
Calves are born without protection from antibodies. Immunity against calf diarrhoea is provided by rapid uptake of colostral antibodies from vaccinated dams. The first colostrum intake should take place as soon as possible, ideally within 2 hours and at most 6 hours after birth. In dairy calves, it should represent a volume equivalent to approximately 10% of the body weight, followed by a similar volume within 12 hours. Beef calves should stand and suckle within 2 hours of calving.

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

Not applicable.

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

For administration only by a veterinarian.

3.12 Withdrawal periods

Zero days.

4. IMMUNOLOGICAL INFORMATION

4.1 ATCvet code:

ATCvet code: QI02AL01
Pharmacotherapeutic group: immunologicals for Bovidae, inactivated viral and inactivated bacterial vaccines for cattle.

Vaccination of pregnant heifers and cows induces specific antibodies that are present at high levels from 3 to 12 weeks after vaccination for passive immunisation of calves via colostrum intake against bovine rotavirus, bovine coronavirus and *E. coli* expressing F5 (K99) adhesin.

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 first opening the immediate packaging: 10 hours

5.3 Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C).
Once open, the vials should not be stored above 25°C.

Protect from frost.
Protect from light.

5.4 Nature and composition of immediate packaging

Type I glass vials of 3 or 10 ml with chlorobutyl elastomer closure and aluminium or flip off caps.
Type II glass vials of 50 or 100 ml with chlorobutyl elastomer closure and aluminium or flip off caps.
Translucent plastic (HDPE) vials of 15, 60 or 120 ml with chlorobutyl elastomer closure and aluminium or flip off caps.

Plastic box of 2, 10 or 20 vials of 1 dose (2 ml)
Cardboard box of 1 glass or plastic vial of 5 doses (10 ml)
Plastic box of 5 or 10 glass or plastic vials of 5 doses (10 ml)
Cardboard box of 1, 12 or 24 glass or plastic vials of 25 doses (50 ml)
Cardboard box of 1 glass or plastic vial of 50 doses (100 ml)

Not all pack sizes may be marketed.

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

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

Bioveta, a,.s., Komenského 212/12, Ivanovice na Hané, Czech Republic

7. MARKETING AUTHORISATION NUMBER(S)

To be completed after the Marketing Authorisation

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: *To be completed after the Marketing Authorisation*

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

To be completed after the Marketing Authorisation

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.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Plastic box of 2, 10 or 20 vials of 1 dose (2 ml)
Cardboard box of 1 vial of 5 doses (10 ml)
Plastic box of 5 or 10 vials of 5 doses (10 ml)
Cardboard box of 1, 12 or 24 vials of 25 doses (50 ml)
Cardboard box of 1 vial of 50 doses (100 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BioBos RCC suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Per 1 d. (2 ml):

Inactivated *E. coli* expressing F5 (K99) adhesin, strain O8:K35	RP* ≥ 1
Inactivated bovine rotavirus, serotype G6P1, strain TM-91	RP* ≥ 1
Inactivated bovine coronavirus, strain C-197	RP* ≥ 1

*Relative potency

3. PACKAGE SIZE

2 x 1 dose,
10 x 1 dose,
20 x 1 dose
1 x 5 doses,
5 x 5 doses,
10 x 5 doses
1 x 25 doses,
12 x 25 doses,
24 x 25 doses
1 x 50 doses

4. TARGET SPECIES

Cattle (pregnant heifers and cows). 

5. INDICATIONS

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6. ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Intramuscular use.

7. WITHDRAWAL PERIODS

Withdrawal period(s): Zero days.

8. EXPIRY DATE

Exp. {month/year}
Once opened use within 10 hours.

9. SPECIAL STORAGE PRECAUTIONS

Store and transport refrigerated.
Protect from frost.
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

Bioveta, a,.s., Komenského 212/12, Ivanovice na Hané, Czech Republic

14. MARKETING AUTHORISATION NUMBERS

To be completed locally

15. BATCH NUMBER

Lot

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100 ml vial (50 doses)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BioBos RCC suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Per 1 d. (2 ml):
Inactivated *E. coli* expressing F5 (K99) adhesin, strain O8:K35 RP* ≥ 1
Inactivated bovine rotavirus, serotype G6P1, strain TM-91 RP* ≥ 1
Inactivated bovine coronavirus, strain C-197 RP* ≥ 1
*Relative potency

3. TARGET SPECIES

Cattle (pregnant heifers and cows).

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Intramuscular use.

5. WITHDRAWAL PERIODS

Withdrawal period: Zero days.

6. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 10 hours.

7. SPECIAL STORAGE PRECAUTIONS

Store and transport refrigerated.
Protect from frost.
Protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Bioveta, a,.s., Komenského 212/12, Ivanovice na Hané, Czech Republic

9. BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of 1 dose (2ml), 5 doses (10 ml) and 25 doses (50 ml)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BioBos RCC suspension for injection

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Per 1 d. (2 ml):
Inactivated *E. coli* expressing F5 (K99) adhesin, strain O8:K35 RP* ≥ 1
Inactivated bovine rotavirus, serotype G6P1, strain TM-91 RP* ≥ 1
Inactivated bovine coronavirus, strain C-197 RP* ≥ 1
*Relative potency

3. BATCH NUMBER

Lot

4. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 10 hours.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

BioBos RCC suspension for injection

2. Composition

Each 2mldose contains:

Active substance<s>:

Inactivated *E. coli* expressing F5 (K99) adhesin, strain O8:K35	RP ≥ 1*
Inactivated bovine rotavirus, serotype G6P1, strain TM-91	RP ≥ 1*
Inactivated bovine coronavirus, strain C-197	RP ≥ 1*

* Relative potency (RP): level of antibodies in sera of vaccinated guinea pigs as determined by ELISA in comparison with the reference serum obtained after vaccination of guinea pigs with a vaccine batch that has successfully passed the challenge test in the target animals.

Adjuvants:

Aluminium hydroxide	6 mg
Quillaja saponin (Quil A)	≤ 0.4 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal produc**t
Thiomersal	0.2 mg
Formaldehyde	≤ 1 mg
Sodium chloride	-
Potassium chloride	-
Potassium dihydrogen phosphate	-
Disodium phosphate dodecahydrate	-
Water for injections	-

3. Target species

Cattle (pregnant heifers and cows).

4. Indications for use

Active immunisation of pregnant heifers and cows in order to stimulate the development of antibodies against bovine rotavirus, bovine coronavirus and *E. coli* expressing F5 (K99) adhesin and to increase the level of passive immunity of calves against neonatal diarrhoea caused by bovine rotavirus, bovine coronavirus and *E. coli* expressing F5 (K99) adhesin.
In calves fed with colostrum and milk from vaccinated cows for the first week of life, laboratory studies conducted with heterologous challenge strain (a G6 BRV strain, a BCV strain, and a K99 *E. coli* strain) have demonstrated that these antibodies:

- prevent neonatal diarrhoea caused by bovine rotavirus and *E. coli* expressing F5 (K99) adhesin,
- reduce the incidence and severity of neonatal diarrhoea caused by bovine coronavirus,
- reduce faecal shedding of virus in calves infected with bovine rotavirus and bovine coronavirus.

Onset of immunity:
In calves fed with colostrum from vaccinated heifers or cows passive immunity commences with colostrum feeding and is dependent on calves receiving sufficient colostrum after birth.

Duration of immunity:
Calves fed with colostrum and milk from vaccinated dams for the first week of life are protected against bovine rotavirus for 7 days and against bovine coronavirus for 14 days.
The duration of immunity against infections caused by *E. coli* expressing F5 (K99) adhesin was not studied since such disease is usually observed in calves less than 3 days of age and susceptibility to enterotoxigenic *E.coli* is age dependent.

5. Contraindications

None.

6. Special warnings

Special warnings:
Vaccinate healthy animals only.

Special precautions for safe use in the target species:
To achieve optimum results and to reduce infection pressure on the farm, a whole herd cow vaccination policy should be adopted, as well as standard infectious diseases control practices.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
In case of adverse reactions following accidental self-injection, 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.

Pregnancy and lactation:
Can be used during pregnancy.
The effect of vaccination on pre- or post-partum lactation was not studied.

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:
Not applicable.

Special restrictions for use and special conditions for use:
For administration only by a veterinarian.

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

7. Adverse events

Very common (>1 animal / 10 animals treated):	An increase in mean body temperature of 1.0°C was very commonly observed in laboratory and field studies; in individual cases, the maximum increase may reach 2.1°C, with body temperatures resolving to normal levels within 2 days without impairing the general health status of the vaccinated animals.
Common (1 to 10 animals / 100 animals treated):	A localised mild swelling (≤ 5 cm in diameter) at the injection site resolving within 2 days was commonly observed in field studies.

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 its local representative or the national competent authority via the national reporting system. See also the last section of the package leaflet for respective contact details.

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

Administration:
One dose of 2 ml by intramuscular injection.
A single injection should be given during each pregnancy between 12 and 3 weeks before the expected calving.

Colostrum feeding:
Calves are born without protection from antibodies. Immunity against calf diarrhoea is provided by rapid uptake of colostral antibodies from vaccinated dams. The first colostrum intake should take place as soon as possible, ideally within 2 hours and at most 6 hours after birth. In dairy calves, it should represent a volume equivalent to approximately 10% of the body weight, followed by a similar volume within 12 hours. Beef calves should stand and suckle within 2 hours of calving.

9. Advice on correct administration

Slowly warm up to room temperature and gently shake the content of the vial before administration.

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 frost.
Protect from light.

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

Shelf life after first opening the container: 10 hours

12. Special precautions for disposal

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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Package size:
Plastic box of 2, 10 or 20 glass vials of 1 dose (2 ml)
Cardboard box of 1 glass or plastic vial of 5 doses (10 ml)
Plastic box of 5 or 10 glass or plastic vials of 5 doses (10 ml)
Cardboard box of 1, 12 or 24 glass or plastic vials of 25 doses (50 ml)
Cardboard box of 1 glass or plastic vial of 50 doses (100 ml)

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.

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Bioveta, a,.s., Komenského 212/12, Ivanovice na Hané, Czech Republic

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