ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS
1. NAME OF THE VETERINARY MEDICINAL PRODUCT

COXEVC suspension for injection for cattle and goats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Inactivated *Coxiella burnetii*, strain Nine Mile  ≥ 72 QF Units*

*QF (Q fever) Unit: relative potency of phase I antigen measured by ELISA in comparison with a reference item.

Excipient:
Thiomersal  ≤ 120 μg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Whitish, opalescent, homogeneous suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and goats

4.2 Indications for use, specifying the target species

Cattle:
For the active immunisation of cattle to lower the risk for non-infected animals vaccinated when non-pregnant to become shedder (5 times lower probability in comparison with animals receiving a placebo), and to reduce shedding of *Coxiella burnetii* in these animals via milk and vaginal mucus.
Onset of immunity: not established.
Duration of immunity: 280 days after completion of the primary vaccination course.

Goats:
For the active immunisation of goats to reduce abortion caused by *Coxiella burnetii* and to reduce shedding of the organism via milk, vaginal mucus, faeces and placenta.
Onset of immunity: not established.
Duration of immunity: one year after completion of the primary vaccination course.

4.3 Contraindications

None.
4.4 Special warnings for each target species

Vaccination of animals already infected at the time of vaccination will have no adverse effect.

No efficacy data are available concerning the use of COXEVAC in male animals. However, in safety laboratory trials, the use of COXEVAC in males proved to be safe. In the case that it is decided to vaccinate the whole herd, it is advisable to vaccinate the male animals at the same time.

There are no benefits of the vaccine (as described in the indications for cattle), when used in infected and/or pregnant cows.

The biological significance of the levels of reduction shown in shedding in cattle and goats is not known.

4.5 Special precautions for use

Special precautions for use in animals

It is advisable to vaccinate all the animals in the herd at the same time.

Under field conditions, vaccination with COXEVAC has commonly been followed by a decrease in milk production in goats. Since stress could contribute to this adverse reaction, appropriate precautions should be taken to reduce stress as much as possible during the administration of the product.

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

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

4.6 Adverse reactions (frequency and seriousness)

Cattle:
It is very common to see a palpable reaction of maximum diameter of 9 to 10 cm at the injection site, which may last for 17 days. The reaction gradually reduces and disappears without need for treatment.

Goats:
It is very common to see a palpable reaction of 3 to 4 cm diameter at the injection site which may last for 6 days. The reaction reduces and disappears without need for treatment.
It is very common to observe a slight increase of rectal temperature for 4 days post-vaccination without other general signs.

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

4.7 Use during pregnancy, lactation or lay

In cattle and goats the vaccine can be used during lactation. Under field conditions, vaccination with COXEVAC has commonly been followed by a decrease in milk production in goats. Since stress could contribute to this adverse reaction, appropriate precautions should be taken to reduce stress as much as possible during the administration of the product.
**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**

Subcutaneous use.
Shake well before use.

Administer the vaccine as follows:
- **Cattle:** 4 ml in the neck region.
- **Goats:** 2 ml in the neck region.

**Cattle from 3 months of age:**

Primary vaccination:
Two doses should be given subcutaneously with an interval of 3 weeks. Under normal conditions the timing of vaccination should be planned so that the primary course is completed by 3 weeks before artificial insemination or mating.

Re-vaccination:
Every 9 months, as described for primary vaccination, based on duration of immunity of 280 days.

**Goats from 3 months of age:**

Primary vaccination:
Two doses should be given subcutaneously with an interval of 3 weeks. Under normal conditions the timing of vaccination should be planned so that the primary course is completed by 3 weeks before artificial insemination or mating.

Re-vaccination:
One dose should be given yearly.

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

**Cattle:**
With double dose, a palpable reaction of maximum diameter of 10 cm was observed at the injection site, lasting for 16 days. The reaction gradually reduced and disappeared without need for treatment.

**Goats:**
With double dose, a moderate palpable reaction of diameter of 4 to 5 cm was observed at the injection site, lasting for 4 days. The reaction reduced and disappeared without need for treatment.

**4.11 Withdrawal period(s)**

Meat, milk and offal: Zero days.

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**5. IMMUNOLOGICAL PROPERTIES**

Pharmacotherapeutic group: immunologicals for bovidae, inactivated bacterial vaccines for cattle.
ATCvet code: QI02AB.

The vaccine contains phase I *Coxiella burnetii* as active ingredient inducing active immunity against Q fever in cattle and goats.

6. **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

- Thiomersal
- Sodium chloride
- Disodium hydrogen phosphate
- Potassium dihydrogen phosphate
- Water for injections

6.2 **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: 2 years.
Shelf life after first opening the immediate packaging: 10 hours.

6.4 **Special precautions for storage**

Store and transport refrigerated (2 °C – 8 °C).
Do not freeze.
Protect from light.

6.5 **Nature and composition of immediate packaging**

Carton box with 1 plastic (LDPE) bottle, containing 40 ml of suspension.
Carton box with 1 plastic (LDPE) bottle, containing 100 ml of suspension.
Each container is closed with a 20 mm bromobutyl rubber stopper and a central tear-off aluminium-plastic 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 product should be disposed of in accordance with local requirements.

7. **MARKETING AUTHORISATION HOLDER**

CEVA Sante Animale
10 avenue de la Ballastiere
33500 Libourne
FRANCE
8. MARKETING AUTHORISATION NUMBER(S)

EU/2/10/110/001-002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30/09/2010.
Date of last renewal:

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

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

The manufacture, import, possession, sale, supply and/or use of COXEvac may be prohibited in a Member State on the whole or part of its territory pursuant to national legislation. Any person intending to manufacture, import, possess, sell, supply and use COXEvac must consult the relevant Member State’s competent authority on the current vaccination policies prior to the manufacture, import, possession, sale, supply and/or use.

6
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

CEVA-Phylaxia Veterinary Biologicals Co. Ltd.
Szállás u. 5
1107 Budapest
HUNGARY

Name and address of the manufacturer responsible for batch release

CEVA-Phylaxia Veterinary Biologicals Co. Ltd.
Szállás u. 5
1107 Budapest
HUNGARY

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

According to Article 71 of Directive 2001/82/EC of the European Parliament and of the Council as amended, a Member State may, in accordance with its national legislation, prohibit the manufacture, import, possession, sale, supply and/or use of immunological veterinary medicinal products on the whole or part of its territory if it is established that:

a) the administration of the product to animals will interfere with the implementation of a national programme for the diagnosis, control or eradication of animal diseases, or will cause difficulties in certifying the absence of contamination in live animals or in foodstuffs or other products obtained from treated animals.

b) the disease to which the product is intended to confer immunity is largely absent from the territory in question.

C. STATEMENT OF THE MRLs

The active substance being a principle of biological origin intended to produce active 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.

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORIZATION

Specific pharmacovigilance requirement(s):

The MAH should provide an additional PSUR.
ANNEX III

LABELLING AND PACKAGE LEAFLET
A. LABELLING
<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON THE OUTER PACKAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARTON BOX for 40 ml or 100 ml plastic bottle</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1. NAME OF THE VETERINARY MEDICINAL PRODUCT</th>
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<tbody>
<tr>
<td>COXEVAC suspension for injection for cattle and goats</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated <em>Coxiella burnetii</em>, strain Nine Mile ≥ 72 QF Units/ml</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. PHARMACEUTICAL FORM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspension for injection</td>
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</tbody>
</table>

<table>
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<tr>
<th>4. PACKAGE SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 ml</td>
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<tr>
<td>100 ml</td>
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</tbody>
</table>

<table>
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<tr>
<th>5. TARGET SPECIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle and goats</td>
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</tbody>
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<table>
<thead>
<tr>
<th>6. INDICATION(S)</th>
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</table>

<table>
<thead>
<tr>
<th>7. METHOD AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous use. Read the package leaflet before use.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>8. WITHDRAWAL PERIOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrawal period: zero days.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>9. SPECIAL WARNING(S), IF NECESSARY</th>
</tr>
</thead>
</table>
10. **EXPIRY DATE**

EXP {month/year}
Once broached, use within 10 hours.

11. **SPECIAL STORAGE CONDITIONS**

Store and transport refrigerated.
Do not freeze.
Protect from light.

12. **SPECIAL 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**

CEVA Sante Animale
10 avenue de la Ballastiere
33500 Libourne
FRANCE

16. **MARKETING AUTHORISATION NUMBER(S)**

EU/2/10/110/001 (40 ml)
EU/2/10/110/002 (100 ml)

17. **MANUFACTURER'S BATCH NUMBER**

Batch {number}
PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100 ml plastic bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

COXEVAC suspension for injection for cattle and goats

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Inactivated *Coxiella burnetii*, strain Nine Mile ≥ 72 QF Units/ml

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle and goats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

SC
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period: zero days.

9. SPECIAL WARNING(S), IF NECESSARY
10. **EXPIRY DATE**

EXP {month/year}
Once broached, use within 10 hours.

11. **SPECIAL STORAGE CONDITIONS**

Store and transport refrigerated.
Do not freeze.
Protect from light.

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

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”**

15. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

CEVA Sante Animale
10 avenue de la Ballastiere
33500 Libourne
FRANCE

16. **MARKETING AUTHORISATION NUMBER(S)**

EU/2/10/110/002

17. **MANUFACTURER’S BATCH NUMBER**

Batch {number}
### MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

**40 ml plastic bottle**

| 1. NAME OF THE VETERINARY MEDICINAL PRODUCT |
| COXEVAC suspension for injection for cattle and goats |

| 2. QUANTITY OF THE ACTIVE SUBSTANCE(S) |
| Inactivated *Coxiella burnetii*, strain Nine Mile \( \geq 72 \text{ QF Units/ml} \) |

| 3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES |
| 40 ml |

| 4. ROUTE(S) OF ADMINISTRATION |
| SC |

| 5. WITHDRAWAL PERIOD |
| Withdrawal period: zero days. |

| 6. BATCH NUMBER |
| Batch {number} |

| 7. EXPIRY DATE |
| EXP {month/year} |
| Once broached, use within 10 hours. |

| 8. THE WORDS “FOR ANIMAL TREATMENT ONLY” |
| For animal treatment only. |
B. PACKAGE LEAFLET
1. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Marketing authorisation holder:
CEVA Sante Animale
10 avenue de la Ballastiere
33500 Libourne
FRANCE

Manufacturer responsible for batch release:
CEVA-Phylaxia Veterinary Biologicals Co. Ltd.
Szállás u. 5
1107 Budapest
HUNGARY

2. **NAME OF THE VETERINARY MEDICINAL PRODUCT**

COXEVAC suspension for injection for cattle and goats

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

Each ml contains:

**Active substance:**
Inactivated *Coxiella burnetii*, strain Nine Mile ≥ 72 QF Units*
*QF (Q fever) Unit: relative potency of phase I antigen measured by ELISA in comparison with a reference item.

**Excipients:**
Thiomersal ≤ 120 μg.

Whitish, opalescent, homogeneous suspension.

4. **INDICATION(S)**

**Cattle:**
For the active immunisation of cattle to lower the risk for non-infected animals vaccinated when non-pregnant to become shedder (5 times lower probability in comparison with animals receiving a placebo), and to reduce shedding of *Coxiella burnetii* in these animals via milk and vaginal mucus. Onset of immunity: not established. Duration of immunity: 280 days after completion of the primary vaccination course.

**Goats:**
For the active immunisation of goats to reduce abortion caused by *Coxiella burnetii* and to reduce shedding of the organism via milk, vaginal mucus, faeces and placenta. Onset of immunity: not established. Duration of immunity: one year after completion of the primary vaccination course.
5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

Cattle:
It is very common to see a palpable reaction of maximum diameter of 9 to 10 cm at the injection site, which may last for 17 days. The reaction gradually reduces and disappears without need for treatment.

Goats:
It is very common to see a palpable reaction of 3 to 4 cm diameter at the injection site which may last for 6 days. The reaction reduces and disappears without need for treatment.
It is very common to observe a slight increase of rectal temperature for 4 days post-vaccination without other general signs.

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

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle and goats

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

Subcutaneous use.

Administer the vaccine as follows:
Cattle: 4 ml in the neck region.
Goats: 2 ml in the neck region.

Cattle from 3 months of age:

Primary vaccination:
Two doses should be given subcutaneously with an interval of 3 weeks. Under normal conditions the timing of vaccination should be planned so that the primary course is completed by 3 weeks before artificial insemination or mating.

Re-vaccination:
Every 9 months, as described for primary vaccination, based on a duration of immunity of 280 days.
Goats from 3 months of age:

Primary vaccination:
Two doses should be given subcutaneously with an interval of 3 weeks. Under normal conditions the timing of vaccination should be planned so that the primary course is completed by 3 weeks before artificial insemination or mating.

Re-vaccination:
One dose should be given yearly.

9. ADVICE ON CORRECT ADMINISTRATION
Shake well before use.
Respect normal aseptic conditions.

10. WITHDRAWAL PERIOD
Meat, milk and offal: Zero days.

11. SPECIAL STORAGE PRECAUTIONS
Keep out of the sight and reach of children.
Store and transport refrigerated (2 °C – 8 °C).
Do not freeze.
Protect from light.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after {EXP}.
Shelf life after first opening the container: 10 hours.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Vaccination of animals already infected at the time of vaccination will have no adverse effect.

No efficacy data are available concerning the use of the vaccine in male animals. However, in safety laboratory trials, the use of the vaccine in males proved to be safe. In the case that it is decided to vaccinate the whole herd, it is advisable to vaccinate the male animals at the same time.

The biological significance of the levels of reduction shown in shedding in cattle and goats is not known.

Special precautions for use in animals:
It is advisable to vaccinate all the animals in the herd at the same time.

Under field conditions, vaccination with COXEVAC has commonly been followed by a decrease in milk production in goats. Since stress could contribute to this adverse reaction, appropriate precautions should be taken to reduce stress as much as possible during the administration of the product.
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 the label, to the physician.

Pregnancy:
The there are no benefits of the vaccine (as described in the indications for cattle), when used in infected and/or pregnant cows.

Lactation:
The vaccine can be used during lactation.

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 (symptoms, emergency procedures, antidotes):
Cattle:
With double dose, a palpable reaction of maximum diameter of 10 cm was observed at the injection site, lasting for 16 days. The reaction gradually reduced and disappeared without need for treatment.
Goats:
With double dose, a moderate palpable reaction of diameter of 4 to 5 cm was observed at the injection site, lasting for 4 days. The reaction reduced and disappeared without need for treatment.

Incompatibilities:
Do not mix with any other veterinary medicinal product.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY
Ask your veterinary surgeon 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
The vaccine contains phase I Coxiella burnetii as active ingredient inducing active immunity against Q fever in cattle and goats.
Pack sizes: 40 ml or 100 ml in a plastic LDPE bottle.
Not all pack sizes may be marketed.

The manufacture, import, possession, sale, supply and/or use of COXEVAC may be prohibited in a Member State on the whole or part of its territory pursuant to national legislation. Any person intending to manufacture, import, possess, sell, supply and use COXEVAC must consult the relevant Member State’s competent authority on the current vaccination policies prior to the manufacture, import, possession, sale, supply and/or use.