ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac L4 suspension for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 1 ml contains:

Active substances:
Inactivated *Leptospira* strains:

- *L. interrogans* serogroup Canicola serovar Portland-vere (strain Ca-12-000)	3550–7100 U[1]
- *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni (strain Ic-02-001)	290–1000 U[1]
- *L. interrogans* serogroup Australis serovar Bratislava (strain As-05-073)	500–1700 U[1]
- *L. kirschneri* serogroup Grippotyphosa serovar Dadas (strain Gr-01-005)	650–1300 U[1]

[1] Antigenic mass ELISA units.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Colourless suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For active immunisation of dogs against:
- *L. interrogans* serogroup Canicola serovar Canicola to reduce infection and urinary excretion
- *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni to reduce infection and urinary excretion
- *L. interrogans* serogroup Australis serovar Bratislava to reduce infection
- *L. kirschneri* serogroup Grippotyphosa serovar Bananal/Lianguang to reduce infection and urinary excretion.

Onset of immunity: 3 weeks.
Duration of immunity: 1 year.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Vaccinate healthy animals only.

4.5 Special precautions for use

Special precautions for use in animals
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Avoid accidental self-injection or contact with the eyes. In case of ocular irritation seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

A mild and transient increase in body temperature (≤ 1 °C) has been observed very commonly in clinical studies for a few days after vaccination, with some pups showing less activity and/or a reduced appetite. A small transient swelling at the site of injection (≤ 4 cm), which can occasionally be firm and painful on palpation, has been observed very commonly in clinical studies. Any such swelling will either have disappeared or be clearly diminished by 14 days post-vaccination.
In very rare cases, clinical signs of immune-mediated haemolytic anaemia, immune-mediated thrombocytopenia, or immune-mediated polyarthritis have been reported. In very rare cases a transient acute hypersensitivity reaction may occur. Such reactions may evolve to a more severe condition (anaphylaxis), which may be life-threatening. If such reactions occur appropriate treatment is recommended.

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

Can be used during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

Safety and efficacy data are available which demonstrate that this vaccine can be mixed and administered with vaccines of the Nobivac series containing canine distemper virus, canine adenovirus type 2, canine parvovirus (strain 154) and/or canine parainfluenza virus components for subcutaneous administration. The product information of the relevant Nobivac vaccines should be consulted before administration of the mixed product. When mixed with these Nobivac vaccines, the demonstrated safety and efficacy claims for Nobivac L4 are no different from those described for Nobivac L4 alone. When mixed with Nobivac vaccines containing canine parainfluenza virus at annual revaccination, it has been established that there is no interference with the anamnestic response induced by the injectable canine parainfluenza virus component.

Safety and efficacy data are available which demonstrate that this vaccine can be administered on the same day but not mixed with vaccines of the Nobivac series containing *Bordetella bronchiseptica* and/or parainfluenza virus components for intranasal administration.

Safety data are available which demonstrate that this vaccine can be administered at the same time but not mixed with the inactivated vaccine of the Nobivac series against *Bordetella bronchiseptica*.
When this vaccine is administered in association with the inactivated vaccine of the Nobivac series against *Bordetella bronchiseptica* the demonstrated antibody response data and other immunity data of this vaccine are the same as when this vaccine is administered alone.

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product except the products mentioned above. 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.
Before use, ensure that the vaccine is at room temperature (15 °C – 25 °C).

Administer two vaccinations of 1 dose (1 ml) of vaccine with an interval of 4 weeks to dogs from 6 weeks of age onwards.

Vaccination scheme:
Basic vaccination: The first vaccination can be administered from 6 to 9(*) weeks of age and the second vaccination from 10 to 13 weeks of age.
Revaccination: Dogs should be re-vaccinated annually with one dose (1 ml) of vaccine.

(*) In case of high level of maternally derived antibodies, first vaccination is recommended at 9 weeks of age.

For simultaneous use, 1 dose of a Nobivac vaccine containing canine distemper virus, canine adenovirus type 2, canine parvovirus (strain 154), and/or canine parainfluenza virus components should be reconstituted with 1 dose (1 ml) of Nobivac L4. The mixed vaccines should be at room temperature (15 °C – 25 °C) before they are administered by subcutaneous injection.

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

No adverse reactions other than those mentioned in section 4.6 were observed after the administration of a double dose of vaccine. However, these reactions may be more severe and/or last longer. For example, local swelling, which can be up to 5 cm in diameter and which may take over 5 weeks to completely disappear, may be observed at the site of injection.

4.11 Withdrawal period

Not applicable.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Immunologicals for Canidae, inactivated bacterial vaccines.
ATCvet code: QI07AB01.

To stimulate active immunity in dogs against *L. interrogans* serogroup Canicola serovar Canicola, *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni, *L. interrogans* serogroup Australis serovar Bratislava, and *L. kirschneri* serogroup Grippotyphosa serovar Bananal/Lianguang.

In vitro and *in vivo* data in non-target species suggests that the vaccine may provide a degree of cross-protection against *L. interrogans* serogroup Icterohaemorrhagiae serovar Icterohaemorrhagiae and *L. kirschneri* serogroup Grippotyphosa serovar Grippotyphosa.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Potassium chloride
Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Water for injections

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product except those mentioned in section 4.8.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 21 months.
Shelf life after first opening the immediate packaging: use immediately.
Shelf life after reconstitution of Nobivac vaccines according to directions: 45 mins.

6.4. Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Protect from light.

6.5 Nature and composition of immediate packaging

Type I glass vial of 1 ml (1 dose) closed with a halogenobutyl rubber stopper and sealed with a coded aluminium cap.

Pack sizes:
Plastic box with 5, 10, 25 or 50 vials of 1 ml (1 dose).

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

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

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/12/143/001-004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16/07/2012.
Date of last renewal: 13/03/2017.

10 DATE OF REVISION OF THE TEXT

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 SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

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

Name and address of the manufacturer of the biological active substances

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

Name and address of the manufacturer responsible for batch release

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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BOX
Plastic box with 5, 10, 25 or 50 vials of 1 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac L4 suspension for injection for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

Four inactivated *Leptospira* strains.
Read the package leaflet before use.

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

5 x 1 ml (1 dose)
10 x 1 ml (1 dose)
25 x 1 ml (1 dose)
50 x 1 ml (1 dose)

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached, use immediately.

11. SPECIAL STORAGE CONDITIONS

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

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

Read the package leaflet before use.

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

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

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/12/143/001 (5 x 1 ml)
EU/2/12/143/002 10 x 1 ml)
EU/2/12/143/003 (25 x 1 ml)
EU/2/12/143/004 (50 x 1 ml)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL
Vial of 1 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac L4

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

See package leaflet.

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

1 ml

4. ROUTE(S) OF ADMINISTRATION

SC

5. WITHDRAWAL PERIOD(S)

Not applicable.

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once broached, use immediately.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Nobivac L4 suspension for injection for dogs

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

Marketing authorisation holder and manufacturer responsible for batch release:

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

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac L4 suspension for injection for dogs

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

Each dose of 1 ml contains:

Active substances:
Inactivated *Leptospira* strains:

- *L. interrogans* serogroup Canicola serovar Portland-vere (strain Ca-12-000)	3550–7100 U[1]
- *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni (strain Ic-02-001)	290–1000 U[1]
- *L. interrogans* serogroup Australis serovar Bratislava (strain As-05-073)	500–1700 U[1]
- *L. kirschneri* serogroup Grippotyphosa serovar Dadas (strain Gr-01-005)	650–1300 U[1]

[1] Antigenic mass ELISA units.

Colourless suspension.

4. INDICATION(S)

For active immunisation of dogs against:
- *L. interrogans* serogroup Canicola serovar Canicola to reduce infection and urinary excretion
- *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni to reduce infection and urinary excretion
- *L. interrogans* serogroup Australis serovar Bratislava to reduce infection
- *L. kirschneri* serogroup Grippotyphosa serovar Bananal/Lianguang to reduce infection and urinary excretion.

Onset of immunity: 3 weeks.
Duration of immunity: 1 year.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

A mild and transient increase in body temperature (≤ 1 °C) has been observed very commonly in clinical studies for a few days after vaccination, with some pups showing less activity and/or a reduced appetite. A small transient swelling at the site of injection (≤ 4 cm), which can occasionally be firm and painful on palpation, has been observed very commonly in clinical studies. Any such swelling will either have disappeared or be clearly diminished by 14 days post-vaccination.
In very rare cases, clinical signs of immune-mediated haemolytic anaemia, immune-mediated thrombocytopenia, or immune-mediated polyarthritis have been reported. In very rare cases a transient acute hypersensitivity reaction may occur. Such reactions may evolve to a more severe condition (anaphylaxis), which may be life-threatening. If such reactions occur appropriate treatment is recommended.

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

Dogs.

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

Subcutaneous use.

Administer two vaccinations of 1 dose (1 ml) of vaccine with an interval of 4 weeks to dogs from 6 weeks of age onwards.

Vaccination scheme:
Basic vaccination: The first vaccination can be administered from 6 to 9(*) weeks of age and the second vaccination from 10 to 13 weeks of age.
Revaccination: Dogs should be re-vaccinated annually with one dose (1 ml) of vaccine.

(*) In case of high level of maternally derived antibodies, first vaccination is recommended at 9 weeks of age.

For simultaneous use, 1 dose of a Nobivac vaccine containing canine distemper virus, canine adenovirus type 2, canine parvovirus (strain 154) and/or canine parainfluenza virus components should be reconstituted with 1 dose (1 ml) of Nobivac L4. The mixed vaccines should be at room temperature (15 °C – 25 °C) before they are administered by subcutaneous injection.

9. ADVICE ON CORRECT ADMINISTRATION

Before use, ensure that the vaccine is at room temperature (15 °C – 25 °C).

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store in a refrigerator (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.

Shelf life after first opening the immediate container: use immediately.
Shelf life after reconstitution of Nobivac vaccines according to directions: 45 mins.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Vaccinate healthy animals only.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Avoid accidental self-injection or contact with the eyes. In case of ocular irritation seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy:
Can be used during pregnancy.

Interaction with other medicinal products and other forms of interaction:
Safety and efficacy data are available which demonstrate that this vaccine can be mixed and administered with vaccines of the Nobivac series containing canine distemper virus, canine adenovirus type 2, canine parvovirus (strain 154), and/or canine parainfluenza virus components for subcutaneous administration. The product information of the relevant Nobivac vaccines should be consulted before administration of the mixed product. When mixed with these Nobivac vaccines, the demonstrated safety and efficacy claims for Nobivac L4 are no different from those described for Nobivac L4 alone. When mixed with Nobivac vaccines containing canine parainfluenza virus at annual revaccination, it has been established that there is no interference with the anamnestic response induced by the injectable canine parainfluenza virus component.
Safety and efficacy data are available which demonstrate that this vaccine can be administered on the same day but not mixed with vaccines of the Nobivac series containing *Bordetella bronchiseptica* and/or parainfluenza virus components for intranasal administration.

Safety data are available which demonstrate that this vaccine can be administered at the same time but not mixed with the inactivated vaccine of the Nobivac series against *Bordetella bronchiseptica*.
When this vaccine is administered in association with the inactivated vaccine of the Nobivac series against *Bordetella bronchiseptica* the demonstrated antibody response data and other immunity data of this vaccine are the same as when this vaccine is administered alone.

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product except the products mentioned above. 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 mentioned in section 6 were observed after the administration of a double dose of vaccine. However, these reactions may be more severe and/or last longer. For example,

local swelling, which can be up to 5 cm in diameter and which may take over 5 weeks to completely disappear, may be observed at the site of injection.

Incompatibilities:
Do not mix with any other veterinary medicinal products except the above mentioned vaccines.

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

15. OTHER INFORMATION

Pack sizes:
Plastic box with 5, 10, 25 or 50 vials of 1 ml (1 dose).

Not all pack sizes may be marketed.

In vitro and *in vivo* data in non-target species suggests that the vaccine may provide a degree of cross-protection against *L. interrogans* serogroup Icterohaemorrhagiae serovar Icterohaemorrhagiae and *L. kirschneri* serogroup Grippotyphosa serovar Grippotyphosa.