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.

Excipients:

Qualitative composition of excipients and other constituents
Sodium chloride
Potassium chloride
Potassium dihydrogen phosphate
Disodium phosphate dihydrate
Water for injections

Colourless suspension.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each 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/Liangguang to reduce infection and urinary excretion.

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

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:
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.

Special precautions for the protection of the environment
Not applicable.

3.6 Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Injection site swelling[1], Injection site nodule[1], Injection site pain[2], Elevated temperature[3], Decreased activity[4], Decreased appetite[4].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction[5], Immune mediated haemolytic anaemia, Immune mediated thrombocytopenia, Immune mediated polyarthritis.

[1] ≤ 4 cm; subsides within 14 days.
[2] Subsides within 14 days.
[3] ≤ 1 °C, up to 3 days.
[4] In pups.
[5] Reactions are transient. This includes anaphylaxis (sometimes fatal). If such reaction occurs, appropriate treatment should be administered without delay.

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

Can be used during pregnancy.

3.8 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 in the Nobivac range 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 in the Nobivac range 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 in the Nobivac range against *Bordetella bronchiseptica*. When this vaccine is administered in association with the inactivated vaccine in the Nobivac range 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.

3.9 Administration routes and dosage

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 schedule:

Primary 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 this vaccine. The mixed vaccines should be at room temperature (15 °C – 25 °C) before they are administered by subcutaneous injection.

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

No adverse reactions other than those mentioned in section 3.6 were observed after the administration of a double dose of vaccine. However, these reactions may be more severe and/or last longer. For example, injection site 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.

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

Not applicable.

4. IMMUNOLOGICAL INFORMATION

4.1 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/Liangguang.

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

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product except those mentioned in section 3.8 above.

5.2 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.

5.3 Special precautions for storage

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

5.4 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.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Intervet International B.V.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/12/143/001-004

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 16/07/2012.

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

{MM/YYYY}

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

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

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac L4 suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Inactivated *Leptospira* strains

3. 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)

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use immediately.

9. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator.
Do not freeze.
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

Intervet International B.V.

14. 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)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

GLASS VIAL LABEL of 1 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac L4

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

1 ml (1 dose)
Inactivated *Leptospira* strains

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use immediately.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Nobivac L4 suspension for injection for dogs

2. 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.

Colourless suspension.

3. Target species

Dogs.

4. Indications for use

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/Liangguang to reduce infection and urinary excretion.

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

5. Contraindications

None.

6. Special warnings

Special warnings:
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 in the Nobivac range 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 in the Nobivac range 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 in the Nobivac range against *Bordetella bronchiseptica*.
When this vaccine is administered in association with the inactivated vaccine in the Nobivac range 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:
No adverse reactions other than those mentioned in section "Adverse events" were observed after the administration of a double dose of vaccine. However, these reactions may be more severe and/or last longer. For example, injection site 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.

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

7. Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Injection site swelling[1], Injection site nodule[1], Injection site pain[2], Elevated temperature[3], Decreased activity[4], Decreased appetite[4].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction[5], Immune mediated haemolytic anaemia, Immune mediated thrombocytopenia, Immune mediated polyarthritis.

[1] ≤ 4 cm; subsides within 14 days.
[2] Subsides within 14 days.
[3] ≤ 1 °C, up to 3 days.
[4] In pups.
[5] Reactions are transient. This includes anaphylaxis (sometimes fatal). If such reaction occurs, appropriate treatment should be administered without delay.

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

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 schedule:
Primary 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 this vaccine. 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 periods

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 after Exp. The expiry date referes to the last day of that month.

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

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

EU/2/12/143/001-004

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

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, manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Intervet International B.V., Wim de Körverstraat 35, 5831 AN Boxmeer, The Netherlands

België/Belgique/Belgien
Tél/Tel: + 32 (0)2 370 94 01

Република България
Тел: + 359 28193749

Česká republika
Tel: + 420 233 010 242

Danmark
Tlf: + 45 44 82 42 00

Deutschland
Tel: + 49 (0)8945614100

Eesti
Tel: + 37052196111

Lietuva
Tel: + 37052196111

Luxembourg/Luxemburg
Tél/Tel: + 32 (0)2 370 94 01

Magyarország
Tel.: + 36 1 439 4597

Malta
Tel: + 39 02 516861

Nederland
Tel: + 32 (0)2 370 94 01

Norge
Tlf: + 47 55 54 37 35

Ελλάδα
Τηλ: + 30 210 989 7452

España
Tel: + 34 923 19 03 45

France
Tél: + 33 (0)241228383

Hrvatska
Tel: + 385 1 6611339

Ireland
Tel: + 353 (0) 1 2970220

Ísland
Sími: + 354 535 7000

Italia
Tel: + 39 02 516861

Κύπρος
Τηλ: + 30 210 989 7452

Latvija
Tel: + 37052196111

Österreich
Tel: + 43 (1) 256 87 87

Polska
Tel.: + 48 22 18 32 200

Portugal
Tel: + 351 214 465 700

România
Tel: + 40 21 311 83 11

Slovenija
Tel: + 385 1 6611339

Slovenská republika
Tel: + 420 233 010 242

Suomi/Finland
Puh/Tel: + 358 10 2310 750

Sverige
Tel: + 46 (0)8 522 216 60

United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

17. Other information

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.