

LEPTOSPIRA VACCINES

Description

Leptospirosis is a zoonotic disease affecting most mammalian species worldwide amongst which farm animals and pets. If the majority of Leptospira infections are either sub-clinical or result in a mild disease, a small proportion develops into a serious disease that can affect various organs (brain, heart, spleen, liver or kidneys (Weil's disease)) and which can be fatal. The control of leptospirosis is therefore important for both an animal and public health perspectives.

Leptospira species have been historically subdivided in serovars based on the expression of surface-exposed lipopolysaccharide (LPS). Serovars containing overlapping antigenic determinants are classified into larger serogroups.

Leptospira animal vaccines have been in use for decades, whilst only a few commercial human vaccines exist¹: a monovalent vaccine (Spirolet) from IMAXIO, France; a bivalent vaccine from Shanghai Institute of Biological Products and a trivalent product Vax-Spiral from the Finlay Institute in Cuba. These vaccines are used only for workers in high risk of infection. All current Leptospira human and animal health vaccines are conventionally produced and their efficacy is limited to the serovars included in their composition.

Canine vaccination

Although infection of cats is much rarer than dogs, both animals can shed Leptospira via their urine leading to potential human exposure. Canine leptospirosis is caused primarily by Leptospira interrogans and Leptospira kirschneri. The most common canine Leptospira interrogans serovars thought to infect dogs before the introduction of vaccines 50 years ago were Canicola and Icterohaemorrhagiae. It is suspected that the development and use of vaccines based on these two serovars gave rise to opportunistic infections with additional serovars in Europe such as Grippotyphosa, Australis and Sejroe². The European canine Leptospira vaccines offer is slowly adapting in reaction to the serovar changes observed in the field with the recent introduction of new Leptospira combination vaccines. This evolution is captured in a comparison table of major canine Leptospira vaccines, built around the clinical claims agreed on the SPC (Summary of Product Characteristics) of vaccines commercially available in Europe. Although these products were registered using various routes of EU registration, their assessment was made against the same set of EU directives, guidelines and European Pharmacopoeia monographs, allowing some comparison of their clinical claims.

All canine Leptospira vaccines registered in EU contain inactivated organisms. Their safety is not a differentiation factor. Their registered efficacy claims show some differences, which could translate a difference in

- the qualitative and/or quantitative composition of the Leptospira strain(s) used in the vaccine or the vaccination scheme,
- the inactivation method/duration resulting in some antigenic variations
- a positive or negative effect of an adjuvant or of a combination with multiple viral components
- the development methods (clinical trials design and/or statistical power)
- the challenge model and/or isolate used to reproduce the disease
- the interpretation between reduction and prevention claims by regulatory assessors.

EU regulators (CVMP) have tried to harmonise the efficacy claims across vaccines by adopting a position paper in 2003 on the wording of European veterinary vaccines claims (EMA/CVMP/042/97-Rev). A concept paper was issued in 2011 to investigate the need to write a guideline to harmonise the interpretation of the reduction and prevention claims across regulatory agencies in EU and to add new claims expected from future biopharmaceutical products. This topic has not been updated since the end of consultation in December 2011 and is not on the CVMP Immunological Working Party work plan for 2015.

Other canine Leptospira vaccines are available outside Europe. These were not considered for comparison as they might include serogroups with less or no relevance to European field situation. They were also registered using other sets of technical guidelines rendering the comparison meaningless.

Cantum Biosciences Ltd is an independent organisation helping veterinary biologicals producers with their product development and registration. The documentation presented has been selected, reviewed and assembled without any guidance or financial support from any company, organisation or individual.

The product profiles captured in the table are based on published information available at the time of composing the table (June 2015). The table is provided for comparison purposes only. Always refer to the latest officially published SPC of each product before purchasing, using or recommending the product, as SPC do get updated from time to time. Product tradenames may differ between countries. This information is provided free of charge. Cantum Biosciences Ltd will not accept any responsibility or liability resulting from the use, mistakes or omissions in the information provided. The information presented does not constitute an incentive to use any of the vaccines reviewed.

¹ Stokes, W et al (2013) Report on the international workshop on alternative methods for Leptospira vaccine potency testing. *Biologicals* 41, 279-294.

² Ellis, W. A. (2010) Control of canine leptospirosis in Europe: time for a change? *Veterinary Record* 167, 602-605.

Efficacy comparison table of major canine Leptospira vaccines registered in Europe

Vaccine name	Minimum age at vaccination	Strains composition	Strains ID	Clinical registered claims (SPC)										Date 1st registration (or licence review)	Registration: Centralised Decentralised Procedure Mutual Recognition Procedure National		
				Reduction					Prevention				Immunity				
				Clinical signs	Infection	Urinary excretion	Kidney lesions	Kidney colonisation	Mortality	Clinical signs	Infection	Urinary excretion	Mortality			Onset	Duration
Canigen L4*	Unpublished June 2015	1. PO serogroup Canicola 2. CO serogroup Icterohaemorrhagiae 3. DA serogroup Grippotyphosa 4. BR serogroup Australis	1. Ca-12-000 2. Ic-02-001 3. As-05-073 4. Gr-01-005		Y	Y									Unpublished June 2015	Pending EC May 2015	C
Versican L4 mono & various combos Biocan Novel L4 combos	6 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae 3. GR serogroup Grippotyphosa 4. BR serogroup Australis	1. MSLB 1090 2. MSLB 1089 3. MSLB 1091 4. MSLB 1088		Y					Y		Y		4 w	12 m	2014	C, DCP
Nobivac L4*	6 weeks	1. PO serogroup Canicola 2. CO serogroup Icterohaemorrhagiae 3. DA serogroup Grippotyphosa 4. BR serogroup Australis	1. Ca-12-000 2. Ic-02-001 3. As-05-073 4. Gr-01-005		Y	Y								3 w	12 m	2012	C
Versican L3 various combos	8 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae 3. GR serogroup Grippotyphosa	1. MSLB 1010 2. MSLB 1008 3. MSLB 1009	Y	Y	N								4 w	12 m	2012	MRP
Canixin (Canigen) mono & various combos	8 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	1. 601903 2. 601895	Y	Y	Y	Y	Y				Y	5 w 2 w	12 m	2012	MRP, N	
Eurican CHPPI2-LR	12 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	1. 16070 2. 16069	Y		Y			Y				2 w	12 m	2005	MRP	
Virbagen L	8 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	Unpublished	Y									3 w	12 m	2005	N	
Vanguard Lepto Ci	7 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	1. C51 2. NADL 11403	Y									2 w	12 m	2005	MRP	
Eurican L	7-8 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	1. 16070/LC87K1 2. 16069/LI84	Y								Y	2 w	12 m	2004	N	
Duramune (Galaxy) various combos	6 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	Unpublished	Y								Y	2 w	12 m	2003	MRP	
Nobivac or Canigen Lepto 2	8 weeks	1. PO serogroup Canicola 2. CO serogroup Icterohaemorrhagiae	1. Ca-12-000 2. 820K		Y								4 w	12 m 6 m	2002	MRP	
Maxivac various combos	8 weeks	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	Unpublished							Y				12 m	2001	N	
Vanguard (Enduracell) various combos	7-8 weeks (8-12 weeks)	1. CA serogroup Canicola 2. IC serogroup Icterohaemorrhagiae	1. C51 2. NADL 11403	Y	Y								2 w	12 m	1997	N	

* Nobivac L4 and Canigen L4 have an identical qualitative and quantitative strains composition, claims and Market Authorisation Holder
Y: claim agreed on SPC – N: claim specifically denied on SPC

Comparison table composed in June 2015

BR = L.interrogans serovar Bratislava; **CA** = L.interrogans serovar Canicola; **CO** = L.interrogans serovar Copenhageni; **DA** = L.kirschneri serovar Dadas; **IC** = L.interrogans serovar Icterohaemorrhagiae; **GR** = L.kirschneri serovar Grippotyphosa; **PO** = L.interrogans serovar Portland-vere.