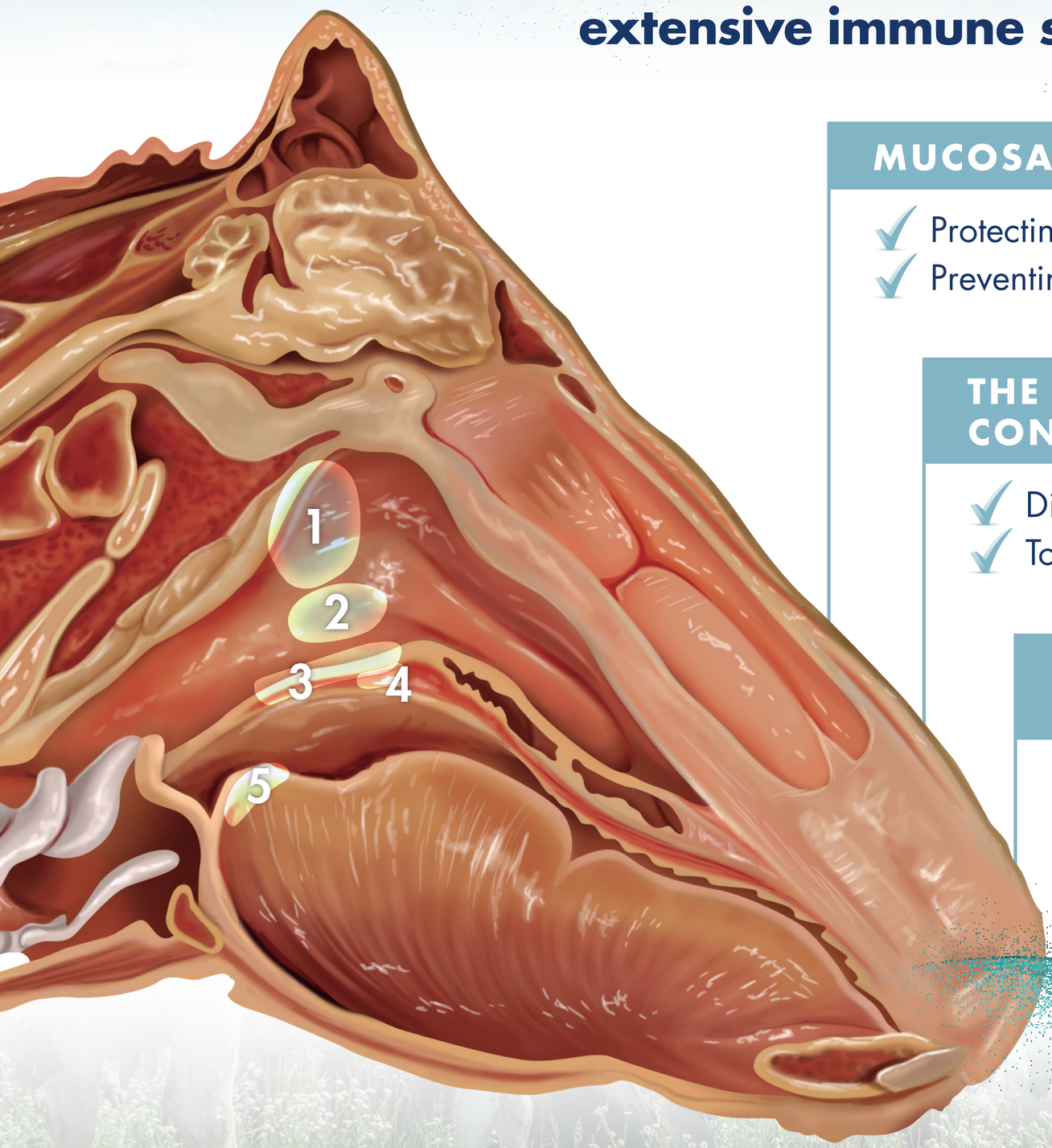
BOVALTO
Respi INTRANASAL

# EASY AND EFFECTIVE
# AS PREDICTED

Boehringer
Ingelheim

# RELEASE THE FULL POWER

## Triggering mucosal immunity activates the most extensive immune system present in cattle[1]




### MUCOSAL IMMUNE RESPONSES ARE KEY FOR[2]:

- ✓ Protecting the mucosa from dangerous microbes
- ✓ Preventing harmful immune responses

### THE RESPIRATORY SYSTEM IN CATTLE CONTAINS:

- ✓ Diffuse lymphoid tissue scattered along the mucosa[3,4,5]
- ✓ Tonsils in different locations[5,6,7]

### MOST IMPORTANT FOR THE NASAL AIRWAYS ARE:

- ✓ The nasopharynx (NALT*):
  The pharyngeal + tubal tonsils[3]

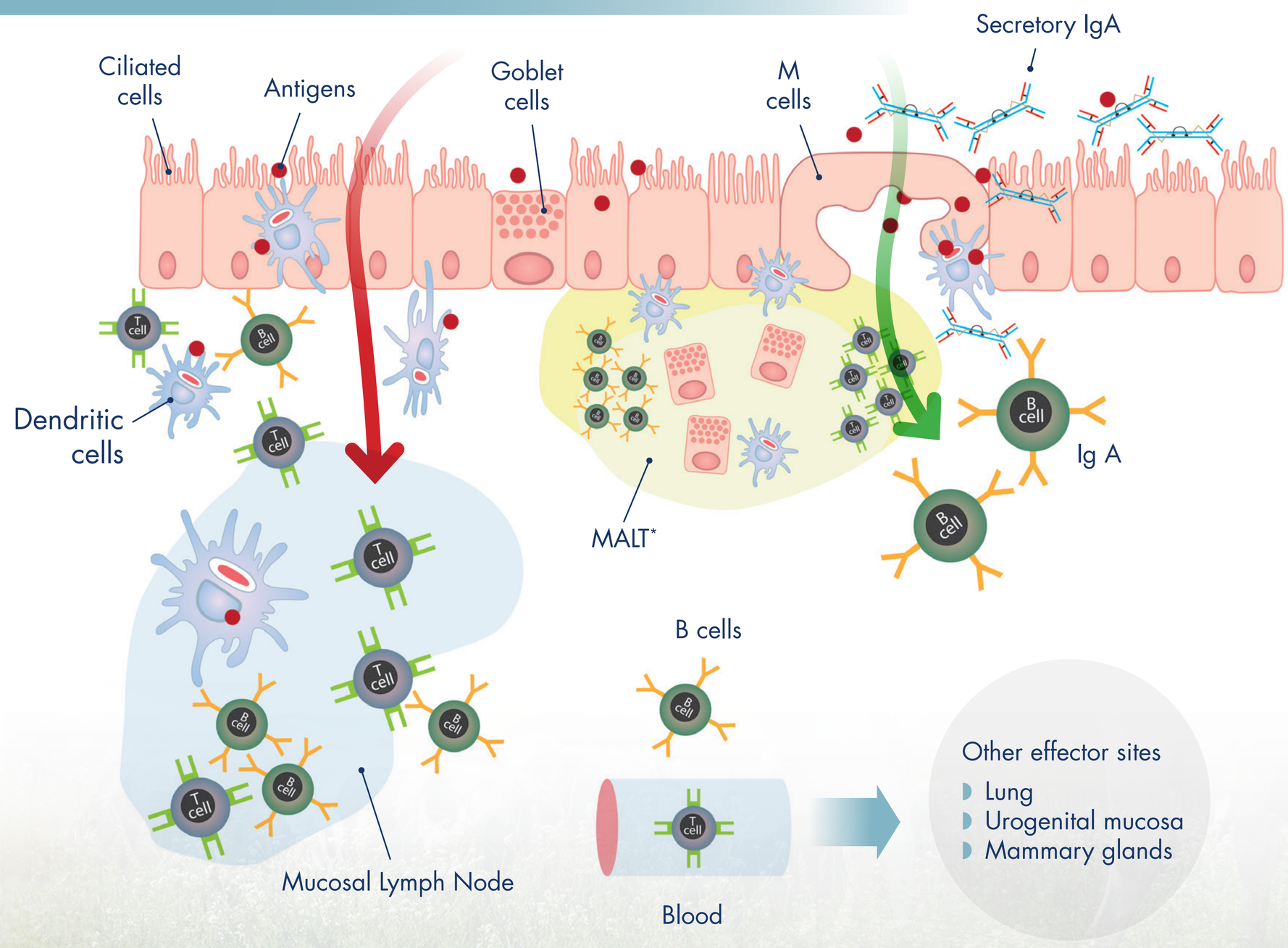
* **NALT:** nasopharynx-associated lymphoid tissue

# OF MUCOSAL IMMUNITY

## Intranasal vaccination is the most effective way to prevent pathogens from colonising the lungs[8]

### THE CALF RESPIRATORY MUCOSA IS PRIMED FOR ACTION[5]

1. **Innate immunity** acts quickly[8]
2. **Dendritic cells and/or M cells** transport the antigen to be presented[2]
3. **Humoral and cellular responses** are triggered[9]
4. **IgA production** is key (first line of defence)[10]
5. **Protective immune response**.




ANTIGEN TRANSPORT AND PRESENTATION ROUTES:

→ VIA DENDRITIC CELLS OUTSIDE THE TONSILS

→ VIA M CELLS

* **MALT:** mucosa-associated lymphoid tissue

# A SIMPLE VACCINATION:

## Bovine respiratory disease is a major problem in modern beef and dairy production[11,12]

## Vaccination at a young age is an important tool to help face these challenges[13]

### THE RESPONSE TO VACCINATION IN THE PRESENCE OF MATERNAL ANTIBODIES CAN BE COMPLEX AND VARIABLE, AND DEPENDS ON:[14,15]

- ✓ The calf age
- ✓ The amount of MDA (maternal derived antibodies)
- ✓ The type of vaccine/formulation
- ✓ The route of administration
- ✓ The critical amount of antigen in the vaccine

### BOVALTO INTRANASAL IS SIMPLE AND GIVES PREDICTABLE RESULTS:[16]

- ✓ Contains live parainfluenza virus (PI3) and bovine respiratory syncytial virus (RSV)
- ✓ Effective in the presence of maternal antibodies
- ✓ Early immunisation from 10 days of age
- ✓ Proven by challenge studies[17]

# A PREDICTABLE RESULT

## The efficacy of Bovalto Respi IN in calves has been proven by challenge[17]

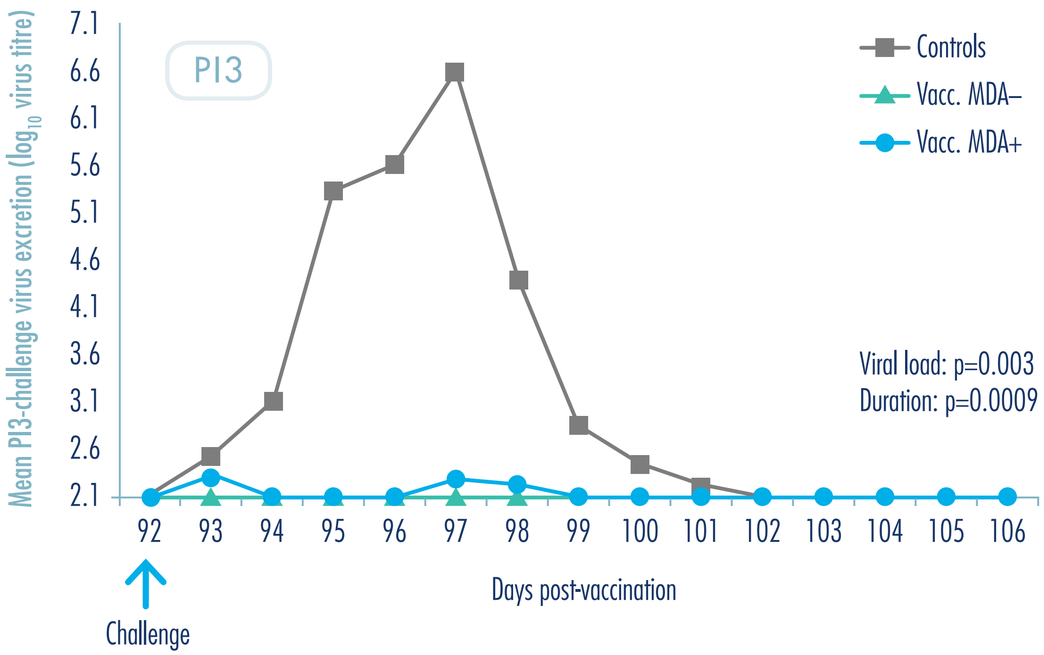
### Two studies performed (BRSV* and PI3*):

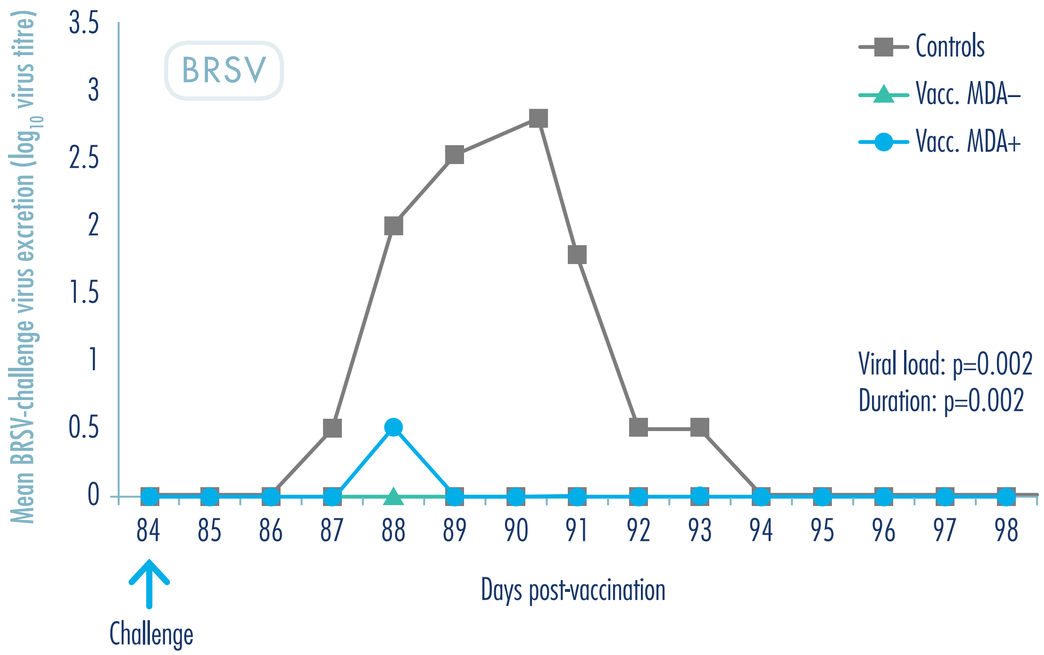

- 5 vaccinated calves (MDA–)
- 5 vaccinated calves (MDA+)
- 5 non-vaccinated control-group calves (MDA+)

**V1** — **BRSV CHALLENGE** — **PI3 CHALLENGE**
D0 — D84 — D92
3 months

Challenged around 3 months post-vaccination for each antigen

## NASAL EXCRETION AFTER CHALLENGE




**All vaccinated animals, whether MDA+ or MDA–** at the time of vaccination, showed a **significant reduction** in both the viral titre and the duration of virus excretion compared to the non-vaccinated group.

**The MDA levels were comparable** to MDA levels from **254 field samples** from 6 European countries.

* **BRSV:** bovine respiratory syncytial virus
**PI3:** bovine parainfluenza-3 virus

# TIPS FOR MASTERING

## THE RIGHT DROPLET SIZE

## THE CORRECT DISTRIBUTION PATTERN

## A COMFORTABLE AND EASY EXPERIENCE

**BOVALTO Fine Spray (30 to 100 µm)**

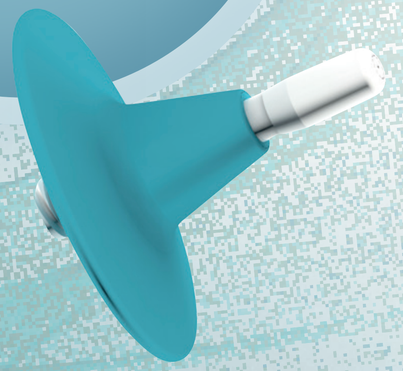
**=**

**optimal pattern and droplet size for induction of immunity**


**BOVALTO Respisafe applicator**

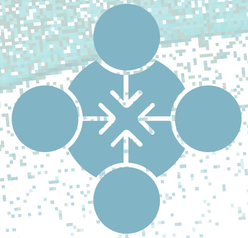
**=**

**reduced risk of injury to nasal mucosa and optimal positioning for administration**



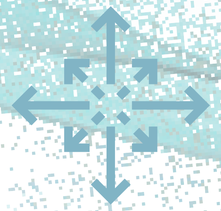
# THE INTRANASAL TECHNIQUE[18-23]

## GOOD CONCENTRATION/ VOLUME BALANCE



Dose of
1 ml
per nostril
=
appropriate
volume per
calf nostril

## INCREASE THE MUCOSAL SURFACE



Treat both
nostrils
=
increased antigen
absorption

## DON'T FORGET!

### EFFICIENT DELIVERY = OPTIMAL EFFICACY

- Maximise antigen exposure to induce an effective immune response

# BOVALTO Respi INTRANASAL

**EFFICACIOUS IN THE PRESENCE OF MATERNAL ANTIBODIES**

**EARLY PROTECTION**

**IMMUNITY DURING CRITICAL PERIODS**

**ANTIGENS WITH PROVEN EFFICACY AGAINST RECENT ISOLATES[24]**

**UNIQUE VACCINATION EXPERIENCE**

# EASY AND EFFECTIVE AS PREDICTED

**REFERENCES:** 1. Mestecky J *et al.* (eds) (2005) Mucosal Immunology 3rd edn. Academic Press, San Diego. 2. Holmgren J, Czekinsky C (2005) Mucosal immunity and vaccines. Nature medicine 11: 4. 3. Meuusen E (2011) Exploiting mucosal surfaces for the development of mucosal vaccines. Vaccine 29: 8506-8511. 4. Sephahi A, Salinas I (2016) The evolution of nasal immune systems in vertebrates. Molecular immunology 69: 131-138. 5. Pabst R (2015) Mucosal vaccination by the intranasal route. Nose-associated lymphoid tissue (NALT) - Structure, function and species differences. Vaccine 33: 4406-4413. 6. Casteleyn *et al.* (2011) The Tonsils Revisited: Review of the anatomical Localization and Histological Characteristics of the Tonsils of Domestic and Laboratory Animals. Immunology 472460. 7. Liebler-Tenorio E, Pabst R (2006) MALT structure and function in farm animals. Vet. Res 37: 257-280. 8. McNeilly TN, McClure SJ, Huntley JF (2008) Mucosal immunity in sheep and implications for mucosal vaccine development. Small Ruminant Research 76: 83-91. 9. Lycke N (2012) Recent progress in mucosal vaccine development: potential and limitations. Nature 12: 592-605. 10. Brandtzaeg P (2013) Secretory IgA: designed for anti-microbial defense. Frontiers Immunology 4: 222. 11. Woolums AR *et al.* (2013) Producer survey of herd-level risk factors for nursing beef calf respiratory disease. JAVMA 243: 538 -547. 12. Rasby R (2007) Early weaning beef calves. Veterinary Clinics of North America: Food Animal Practice 23: 29 -40. 13. Ellis J *et al.* (2001) Effect of maternal antibodies on induction and persistence of vaccine-induced immune responses against bovine viral diarrhea virus type II in young calves. JAVMA 219: 351 -356. 14. Chamorro MF *et al.* (2016) Vaccination of calves against common respiratory viruses in the face of maternally derived antibodies (IFMA). 15. Woolums AR (2007) Vaccinating calves: new information on the effects of maternal immunity. Proceedings of 40th Annual Conference. 16. SPC Bovalto Respi Intranasal. 17. Internal data. 18. FDA Guidance (April 2003). Bioequivalence (BE) and bioavailability (BA) studies for nasal sprays and nasal aerosols for local action. 19. Heyder J *et al.* (1986) Deposition of particles in the human respiratory tract in the size range 0.005 to 15 µm. Aerosol Sci., 17: 811-825. 20. Thomas RJ *et al.* (2008) Characterization and Deposition of Respirable Large- and Small-Particle Bioaerosols. Appl. Environ. Microbiol. 74: 20 6437-6443. 21. Visweswaraiah A *et al.* (2002) Tracking the tissue distribution of marker dye following intranasal delivery in mice and chinchillas: a multifactorial analysis of parameters affecting nasal retention. Vaccine, 20: 3209-3220. 22. Shekunov BY *et al.* (2006) Particle Size Analysis in Pharmaceutics: Principles, Methods and Applications. Pharmaceutical Reseach, 24: 2 203-227. 23. Kublik H, Vidgren MT (1998) Nasal delivery systems and their effect on deposition and absorption. Advanced Drug Delivery Reviews 29: 157-77. 24. Philippe-Reversat C *et al.* (2017) Duration of immunity of a four-valent vaccine against bovine respiratory diseases. Acta Vet. Brno 86: 325-332.

Bovalto Respi Intranasal, nasal spray, lyophilisate and solvent for suspension contains Bovine parainfluenza 3 virus (PI3V), modified live virus, strain Bio 23/A $10^{5.0} – 10^{7.5}$ $TCID_{50}$ and Bovine respiratory syncytial virus (BRSV), modified live virus, strain Bio 24/A $10^{4.0} – 10^{6.0}$ $TCID_{50}$. For the active immunisation of calves from the age of 10 days against bovine respiratory syncytial virus (BRSV) and bovine parainfluenza 3 virus (PI3V), to reduce the quantity and duration of nasal excretion of both viruses. UK: POM-V IE: POM(E). For information about side effects, precautions, warnings and contraindications please refer to the product packaging and package leaflet. Further information available in the SPCs or from Boehringer Animal Health UK Ltd, RG12 8YS, UK. UK Tel: 01344 746959 (sales) or 01344 746957 (technical), IE Tel: 01 291 3985 (all queries). Bovalto and the steerhead logo are registered trademarks of the Boehringer Ingelheim Group.  Date of preparation: Jun 2019. AHD12529. Use Medicines Responsibly.

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