



PREVEXXION[®] RN

THE FUTURE IS NOW

PROTECTION • VALUE • INNOVATION

PREVEXXION[®] RN is a vaccine that contains a frozen Marek's disease chimera consisting of three serotype 1 strains and has been shown to be effective against very virulent Marek's disease.

PREVENTION WORKS
Shaping the future of poultry health

 **Boehringer
Ingelheim**

ABOUT

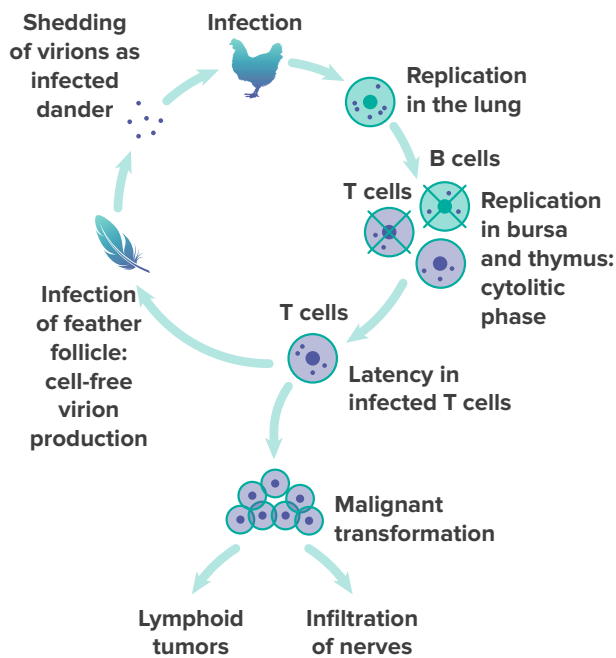
MAREK'S DISEASE

Marek's disease (MD) is a common **neoplastic** and **immunosuppressive** disease affecting poultry populations worldwide. It is caused by the Marek's disease virus (MDV), which is a ubiquitous **herpesvirus**. MD maintains a constant pressure on farms and keeping this disease under control through vaccination is critical.¹ During the past twenty years, several studies have shown the emergence of increasingly virulent strains.² This necessitated the development of a new vaccine.

IMPACT ON INDUSTRY

- Unpredictable outbreaks
- Immunosuppression
- Increased condemnation rate
- Decreased egg production
- Greatly affects long-lived birds

**\$1-2 billion
in losses
worldwide³**



PATHOGENESIS⁴

MDV infects birds by inhalation through the respiratory tract. The virus initially replicates in the lungs and then spreads to the lymphoid tissues. This cytolytic phase results in atrophy of the bursa of Fabricius and thymus, leading to immunosuppression.

About two weeks after infection, the virus starts replicating in feather follicle tissues, where cell-free virion production occurs, allowing the shedding of the virus as infected dander into the environment. Marek's disease persists throughout the life of the chicken, causing continuous contamination of the environment by the infected birds.

After several weeks, malignant transformation may occur in infected T cells, causing lymphomas to form in different tissues including the visceral tissues and peripheral nerves, ultimately leading to death.

CLINICAL SIGNS

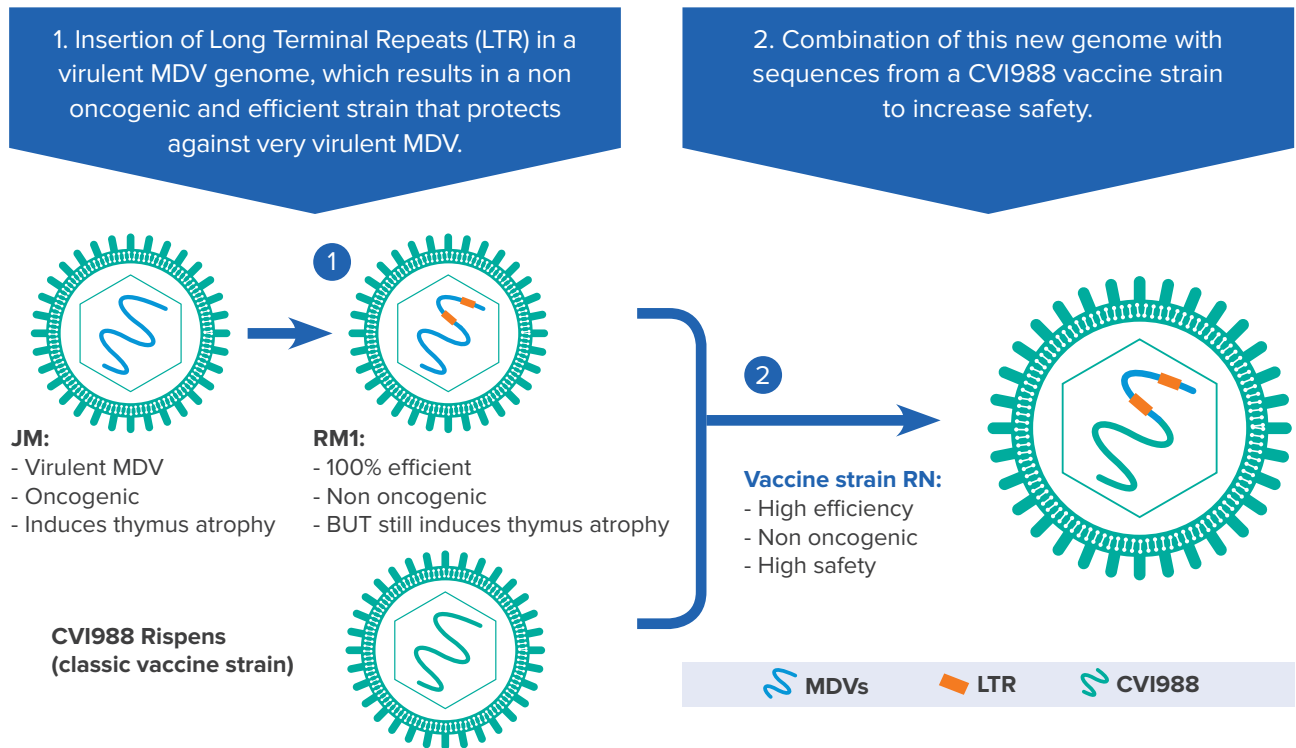
- Weight loss, paleness, anorexia and diarrhea
- Tumors in several organs
- Skin disorders
- Reduction in egg production and mortality in layers
- Progressive paralysis



PREVEXXION® RN

THE NEXT GENERATION MAREK'S VACCINE

PREVEXXION® RN is the result of an innovative and controlled process of attenuation of a virulent Marek's disease virus. It takes the best traits from different existing strains. The result is a vaccine that is both safe and efficacious against very virulent Marek's disease viruses. PREVEXXION® RN was developed in two steps:



WHY THIS NEW PROCESS OF ATTENUATION?

Classic vaccines are developed through passages in cell cultures. But while each passage of attenuation increases the safety of the vaccine, it also has the potential to decrease the vaccine's efficacy.⁵ Thanks to the innovative attenuation process used, PREVEXXION® RN delivers the right balance between safety⁶ and efficacy.⁷

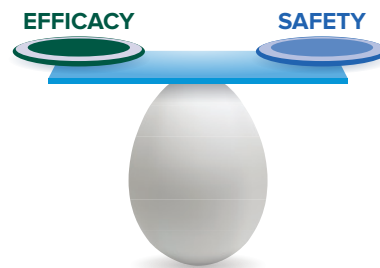
Classic CVI988 Rispens vaccines development

Number of passages of attenuation



Concessions have to be made, either on safety or efficacy

PREVEXXION® RN development



Controlled development, allowing both high safety and high efficacy

SAFETY

CLINICAL SAFETY

In a controlled internal study, chickens vaccinated with PREVEXXION® RN had no mortality and no gross lesions of Marek's disease. There were also no significant differences in body weights compared to the unvaccinated chickens.⁶

Clinical safety results of PREVEXXION® RN on SPF chickens

Treatment	Mortality		Body weight at 120 days post vaccination
	0-14 days	14-120 days	
PREVEXXION® RN (10x dose)	0/48	0/48	1728 g*
Sham-vaccinated controls	0/50	0/50	1751 g*
Sham-vaccinated contact controls for vaccinated birds	0/49	0/49	1749 g*

*no significant differences (alpha risk at 5%)

BIOLOGICAL PROPERTIES - VIRUS TROPISM

PREVEXXION® RN *in vivo* dissemination pattern was similar to the reference CVI988 Rispens serotype 1 vaccine with a trend to lower persistence⁸ in vaccinates. The safety of the PREVEXXION® RN was confirmed using that criterion.

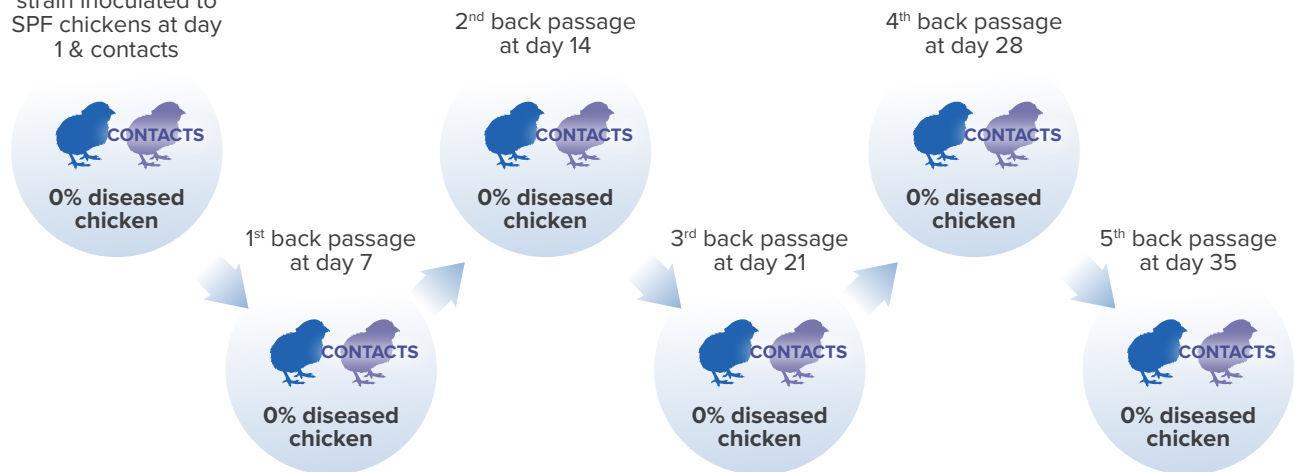
Virus tropism

Vaccination at day-old	Chicken positive for virus detection in at least one target organ		
	D7	D14	D49
PREVEXXION® RN	3/3	2/5	0/5
Reference CVI988 Rispens vaccine	5/5	5/5	2/5
Negative control – diluent only	0/3	0/3	0/3

NO REVERSION TO VIRULENCE

PREVEXXION® RN remains safe, stable and does not revert to virulence after 5 back passages in SPF chickens.⁹

Master seed vaccine strain inoculated to SPF chickens at day 1 & contacts



EFFICACY

Clinical studies conducted by Boehringer Ingelheim demonstrated the efficacy of PREVEXXION® RN:

- ▶ **Protective** when challenged^{7,10}
- ▶ **Onset of immunity** from four days of age⁷
- ▶ **Long-lasting immunity**¹⁰ like classic serotype 1 vaccines even for long-lived birds
- ▶ Efficacious for chickens vaccinated *in ovo*¹¹

≡ Clinical protection against RB1B provided by PREVEXXION® RN¹⁰ ≡

Vaccine regimen	% of birds with no tumor lesions – D49
PREVEXXION® RN – batch 1	96.7%
PREVEXXION® RN – batch 2	100%
Positive controls – no vaccination, MDV challenge	3.3%
Negative controls – no vaccination, no MDV challenge	100%

COMBINATION OF PREVEXXION® RN WITH OTHER VACCINES

PREVEXXION® RN was efficacious when used in combination with HVT vectored vaccines such as VAXXITEK® HVT+IBD^{12,13} and NEWXXITEK™ HVT+ND.^{14,15} In both cases, the protection is high against Marek's disease RB1B challenge at four days of age.

≡ Compatibility of PREVEXXION® RN with HVT vector vaccines ≡

Vaccine regimen	% of protection against MDV challenge	% of protection against velogenic NDV challenge	% of protection against IBDV challenge
PREVEXXION® RN alone	93%*	-	-
PREVEXXION® RN & VAXXITEK HVT+IBD	100%*	-	100%**
PREVEXXION® RN & NEWXXITEK HVT+ND	93%*	95%***	-
Non vaccinated - challenged	0%	0%	0%

* Higher than the requested level of protection as stated by 9 CFR 113.330

** Higher than the requested level of protection as stated by 9 CFR 113.331

*** Higher than the requested level of protection as stated by 9 CFR 113.329

PREVEXXION® RN is suitable for a customized vaccination program involving other advanced vaccines.

CONVENIENCE

MAREK'S DISEASE VACCINATION PROGRAMS

PREVEXXION® RN was shown to be compatible with other Marek's vaccine serotypes such as SB-1 and HVT.¹⁶ Using those vaccines in combination improves protection against very virulent pathotypes of the MDV.

Recommended Marek's disease vaccination

Type of birds	Needed protection against very virulent virus strains of Marek's disease	Marek's vaccination program
Broilers	Basic protection	HVT*
Broilers	Protection	HVT* & SB-1**
Long-lived birds, like future layers and breeders	Protection	PREVEXXION® RN & HVT*
Long-lived birds, like future high value breeders	Protection	PREVEXXION® RN & HVT* & SB-1

* Vector vaccines such as VAXXITEK® HVT+IBD or NEWXXITEK™ HVT+ND also apply

** Long-lived meat producing chickens may be vaccinated with PREVEXXION® RN

PREVEXXION® RN IN A NUTSHELL

- ▶ Next generation Marek's disease vaccine strain effective against very virulent MDV
- ▶ Innovative and controlled attenuation process for a Marek's disease strain that results from different MD virus and LTR gene sequence insertions
- ▶ Administration in-ovo or at day-old
- ▶ Correct balance between safety and efficacy
- ▶ Application as convenient as for classic MDV vaccines

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