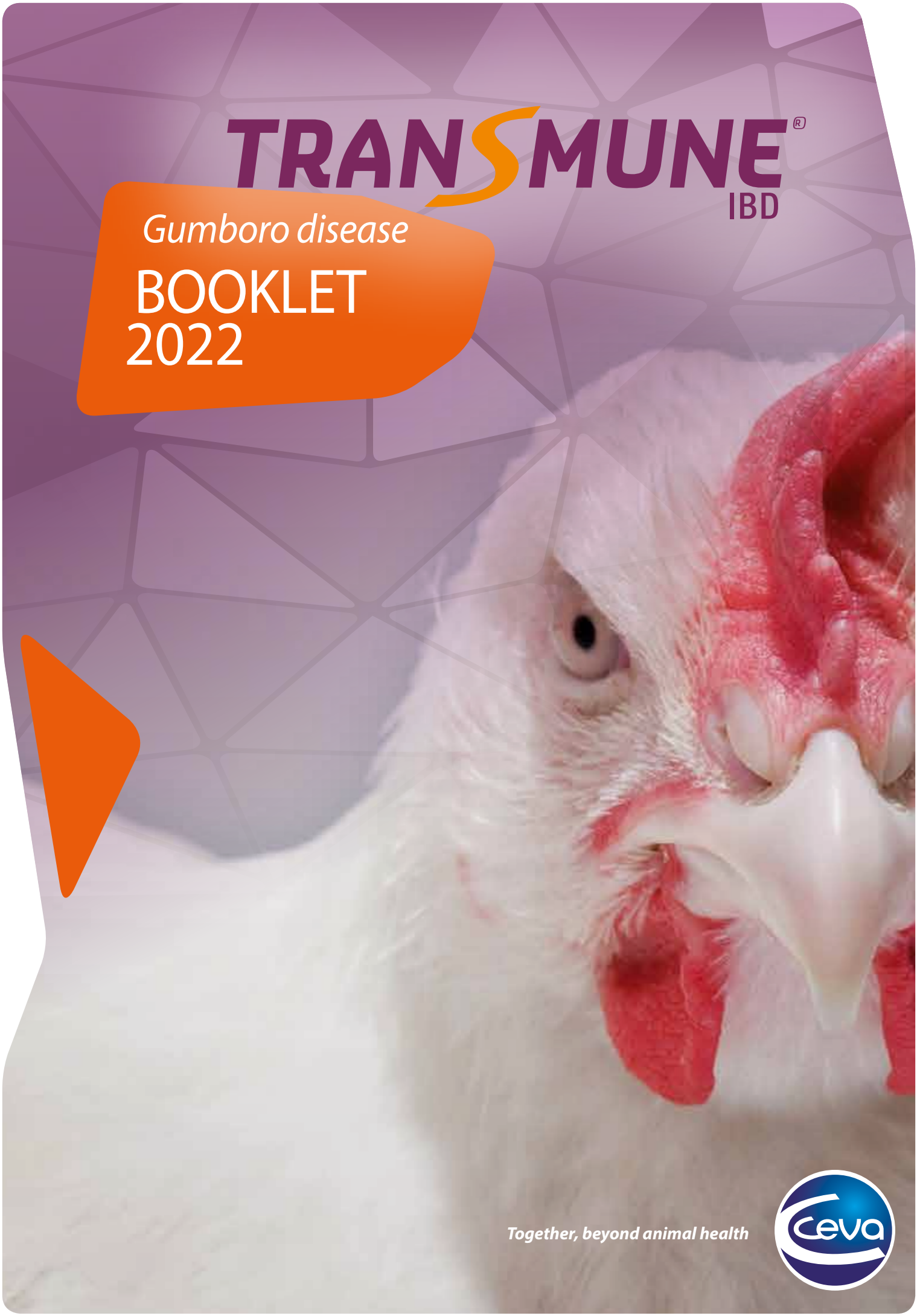
TRANSMUNE® IBD

Gumboro disease

BOOKLET 2022

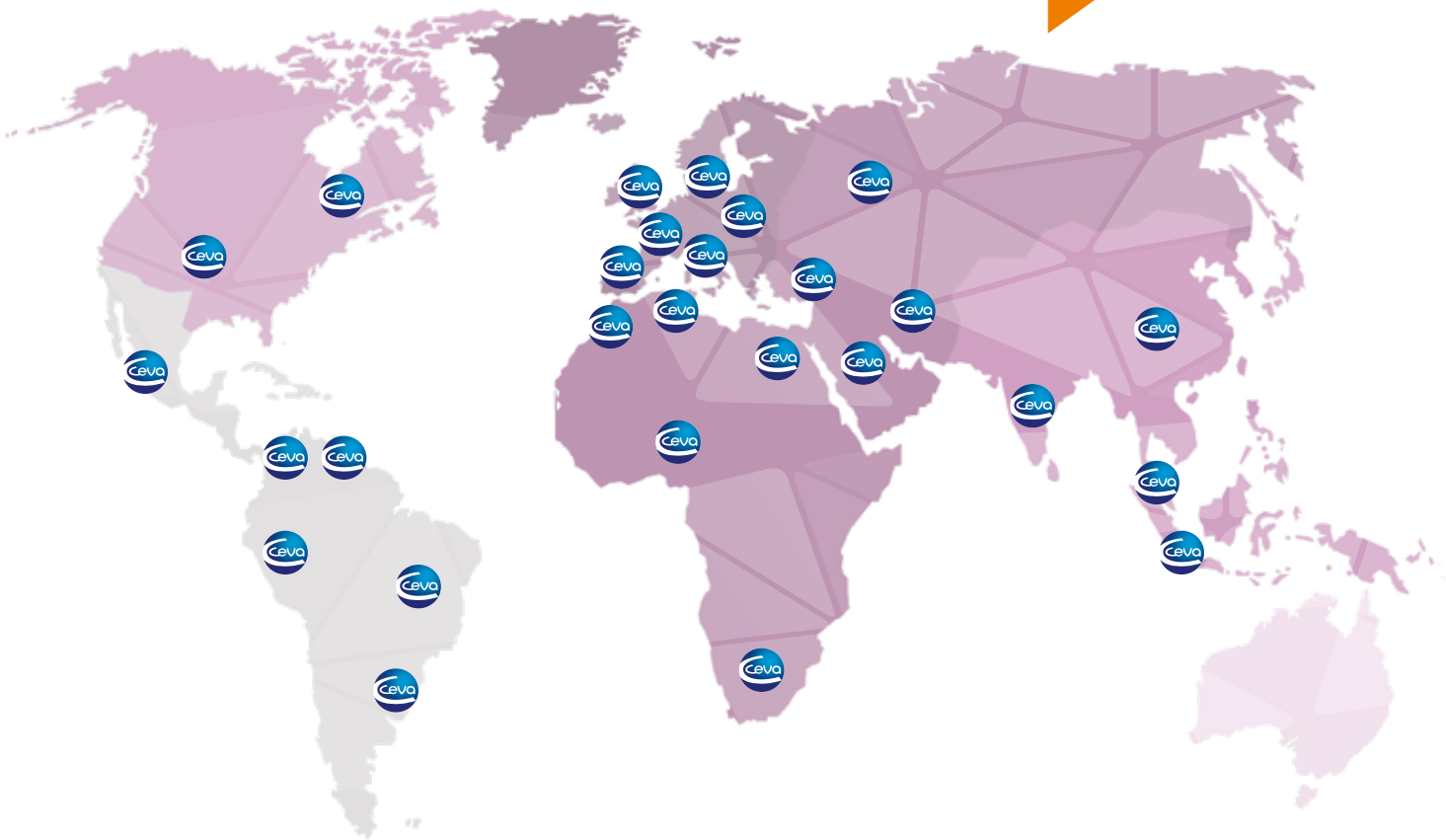


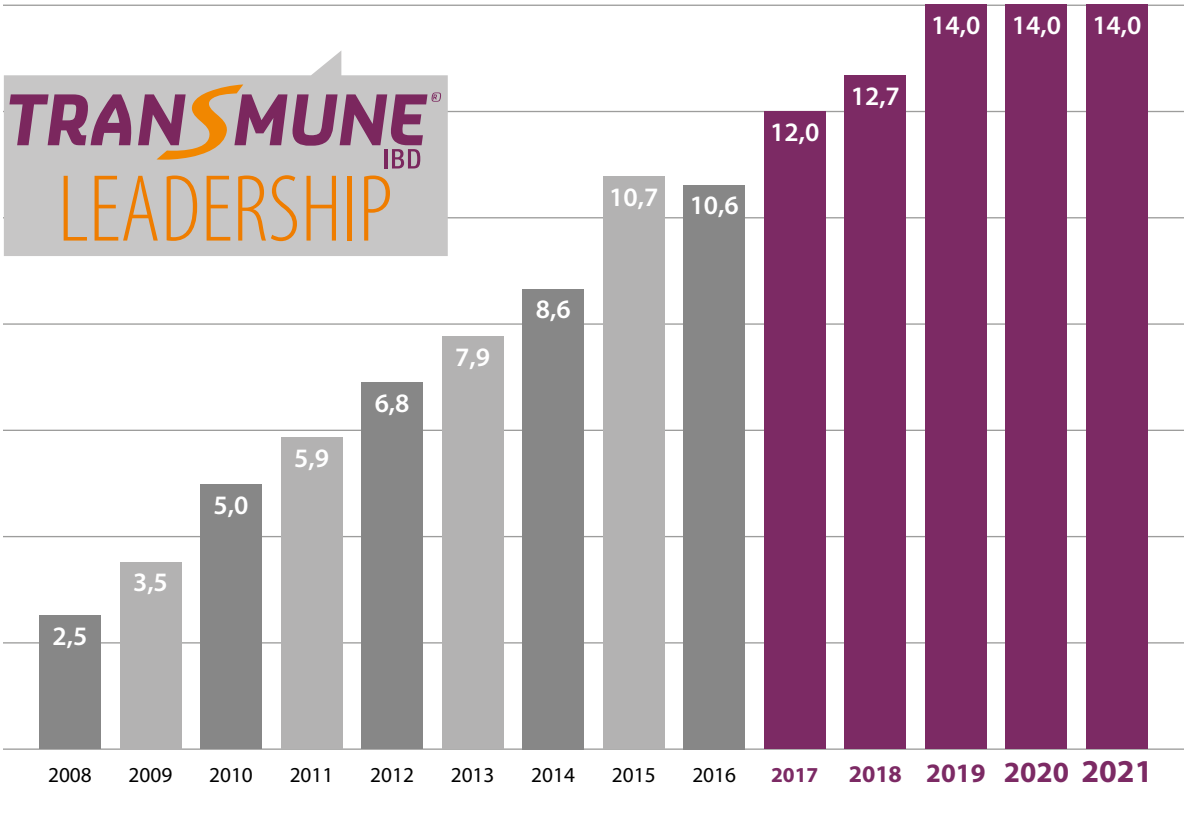
Together, beyond animal health

ceva

CEVA GLOBAL REFERENCE IN IBD CONTROL

220 BILLION
BIRDS PROTECTED AGAINST GUMBORO DISEASE WITH CEVA VACCINES





FOREWORD

Ceva Santé Animale has been contributing to the control of Gumboro disease (IBD) for several years, due the expertise of our teams, and the portfolio of products developed for the poultry industry, such as TRANSMUNE®.

Ceva has protected, since 2006, over 220 billion broilers against IBD, acquiring a large expertise and knowledge.

In this book you will find an updated technical-economical summary of TRANSMUNE®, containing all the concepts required to understand IBD control.

In a recent IBD Survey conducted during 2019-2021, independent researchers and Ceva Santé Animale Vet Specialists updated the epidemiology of the IBD virus around the world.

We obtained real world evidences in several countries worldwide, where Ceva Sante Animale has presence, representing South & Central America, Europe, Middle East, Europe, Africa and Asia.

Each experience includes an economic calculation, based on a specific and updated scale, which suggests the value of using TRANSMUNE®. These field cases compare TRANSMUNE® (administered either subcutaneously or in-ovo) versus different vaccination programs.

Ceva Santé Animale is committed to sharing information and updated scientific data with partners and customers.

Please contact us should you require further information or explanation.

Enjoy your reading.

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TRANSMUNE® IBD

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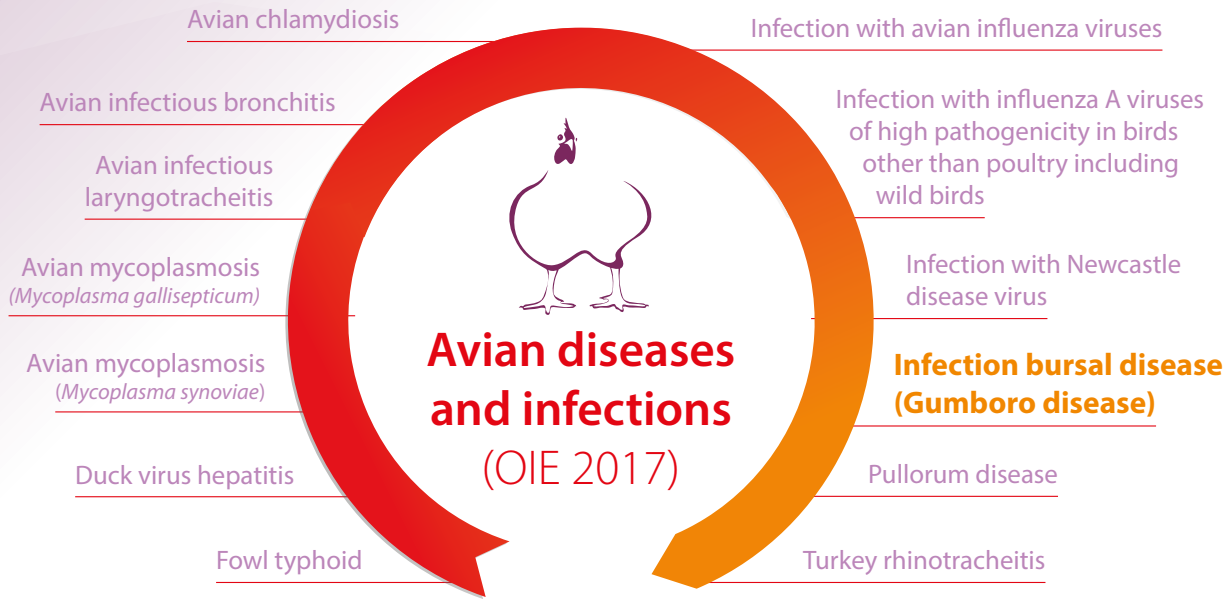
1 Infectious Bursal Disease:

A THREAT TO THE POULTRY INDUSTRY

Infectious Bursal Disease (IBD) or, most commonly known, Gumboro disease, despite the wide use of vaccines and increased biosecurity is, however, still very much present and ranks among the top five diseases in almost all countries globally. The World Organisation for Animal Health (OIE) listed IBD as a notifiable disease with importance in 2017.



One of the reasons for the worldwide distribution of the IBD virus is that it is very persistent, surviving in poultry houses in the absence of chickens during downtime periods. The industry is concerned about the immunosuppressive effects of IBD.

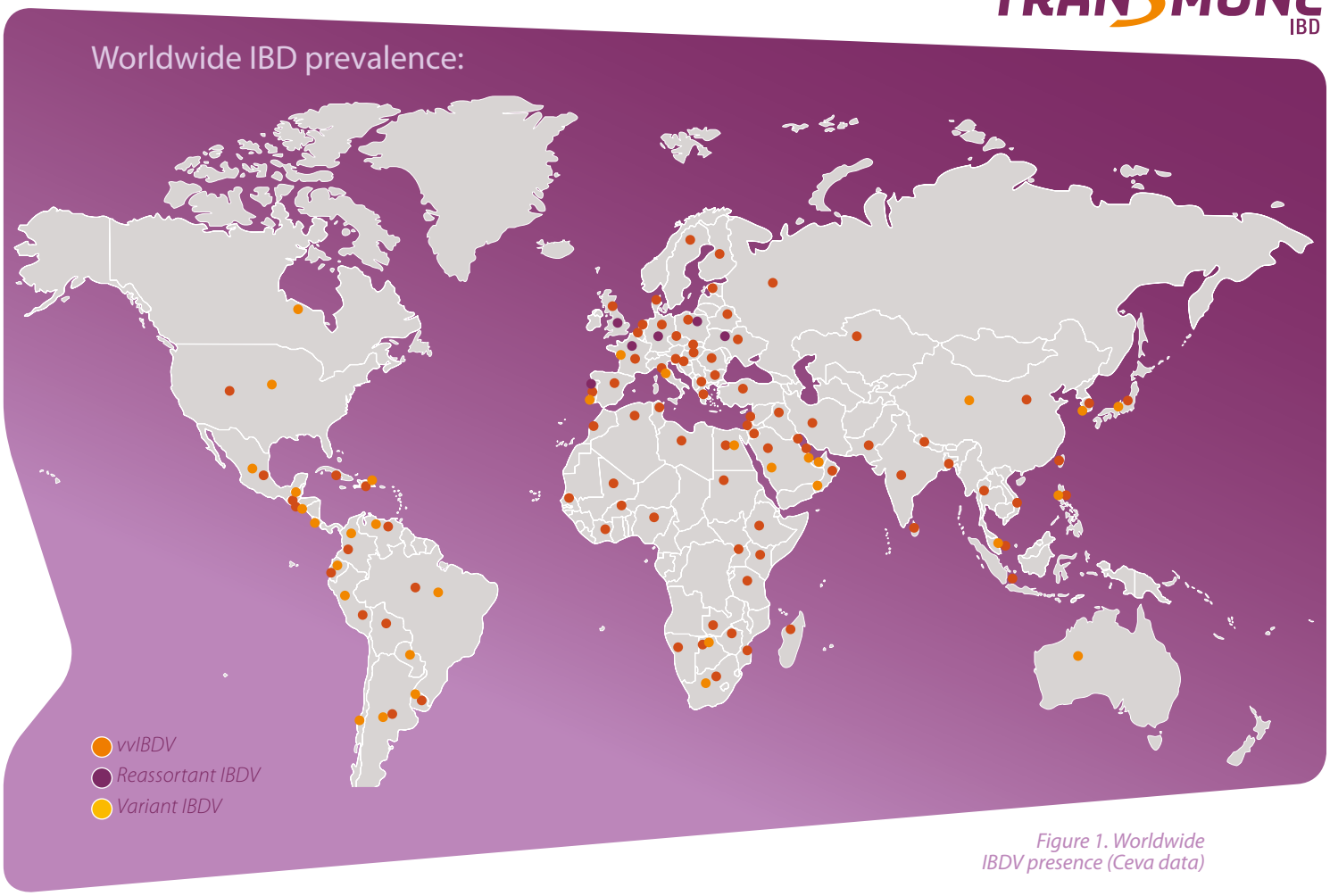


Figure 1. Worldwide IBDV presence (Ceva data)

After the initial outbreak in the US, clinical IBD was reported in many other countries in the 1960s and 1970s. More virulent forms were later reported around the same time with a very immunosuppressive form of IBD in the USA (starting around 1985), which then later spread to Central and South America (Figure 1). The very virulent (vvIBD) form of IBD spread around the same time to Western Europe, Nothern Africa, the Middle East and Asia. In the late 1990's and early 2000's, the very virulent form spread to Central, South America and California. Today, the very virulent form is predominant in most countries, and variant strains of IBD are present in several countries, leading to sub-clinical forms of the disease.

The cost of IBD has been very well described in different publications in the last decade. It has a direct impact on mortality, from 5% to 30%, depending on the degree of protection of the birds and the form of the disease (Rosenberger *et al.*, 1986; Van den Berg, 1991). In subclinical cases, it can reduce the income per flock up to 14%, with a 11% reduction in yield and 10% profit loss due to weight loss and increased FCR (McIlroy, 1992). In layers, it can reach mortality rates of 60%, as previously described (Nunoya, 1992).

Recently, interesting calculations have been performed in North America, especially focused on the subclinical variant IBD strains. The authors correlated positively the serological IBD titers with increased hepatic lesions and condemnations during processing.

Figure 2. Rejected livers with hepatitis in the processing plant (Ceva Animal Health)

Infectious bursal disease (IBD) is a viral disease that affects chickens worldwide and it has a major economic impact on the modern poultry industry.

- It is caused by a ***Avibirnavirus***, called infectious bursal disease virus (IBDV), which is a bi-segmented, double stranded RNA virus, highly resistant in the environment. The RNA encodes for five viral proteins (VP1 to VP5) of which VP2 contains hypervariable portions that enable classifying strains into various antigenic and genetic groups; in addition, VP2 contains the majority of neutralizing sites. Depending on the pathogenic type, IBDV strains are classified as very virulent, virulent, and subclinical.

Antigenically, two serotypes (serotype 1 and 2) of IBDV exist, although antigenic variants are described within serotype 1 strains,which are the ones that affect domestic poultry of the ***Gallus gallus*** species. There have been described, however, non-clinical cases of serotype 1 passages in turkeys, for example, making accidental carriers a determinant factor for the spread of the disease.

- Only the serotype 1 virus is pathogenic for chickens in which it can cause depression, diarrhoea, haemorrhages in muscles and proventriculus, and inflammation, necrosis and atrophy of the bursa of Fabricius depending on the virulence of the strain. Variant IBDV strains generally do not cause clinical signs or mortality, but can cause severe atrophy of the bursa without marked external pathological signs.

Depending on the age of the birds at infection and their immune status, IBDV can also induce immunosuppression. Recent reports confirmed IBD presence in various parts of the world, namely South America, North America, Africa, China, the Middle East, and Europe. Therefore, IBD is prevalent worldwide and its control is a global concern.

Clinical signs of deep depression are not always clear and present

Avibirnavirus replicates and damages the bursa of Fabricius in the domestic fowl. It is a disease which basically presents 3 different clinical forms: **immunosuppressive, clinical and subclinical.**

1 The **immunosuppressive form** is the consequence of the infection of chickens aged less than 2 weeks by any pathogenic IBD virus. During this time, the integrity of the bursa of Fabricius is critical since it is the organ where B-lymphocytes need to mature to become functional and provide the chickens with effective humoral immune response capabilities.

2 The **clinical form** is the consequence of infection of chickens with an IBD virus that replicates very rapidly and at a high level, increasing the mortality rate. Clinical signs may or may not be present. Post mortem examination generally shows a strong edema of the bursa with (or without) haemorrhages of variable intensity that can also be seen in the form of petechiae or suffusions in the thighs and breast muscles. The *'very virulent'* or *'hypervirulent'* cases of Gumboro disease that were reported in Western Europe in the late 1980s, and then in other parts of the world where they can still be observed, show this clinical form as well. The mortality rate varies a lot but is generally higher in slow growing chickens like layer pullets, layer/broiler breeder pullets or organic chickens (generally more than 25%) than in broilers (in general less than 15%).

3 The **sub-clinical (or economical)** form of the disease corresponds to infection of chickens after 2-3 weeks of age, by an IBD virus without occurrence of typical clinical signs (hence the term 'sub-clinical') or direct mortality. The bursa of Fabricius might show signs of variable intensity and persistence. Most of the time, only poor or sub-optimal performances are detected.

Irregular appearance of the bursae in a flock with sub-clinical IBD

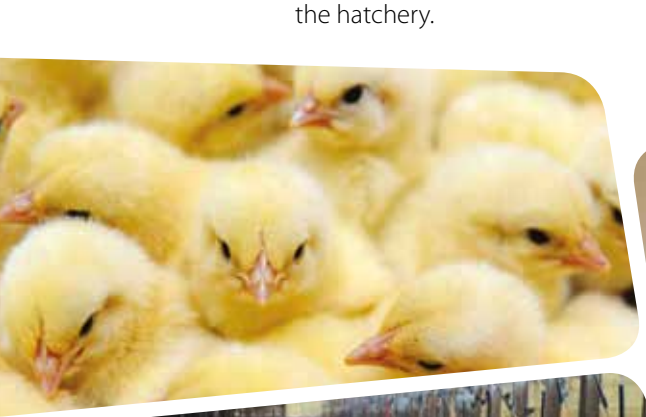
Biosecurity is key in preventing IBD. However, vaccination is regarded as an important tool to complement biosecurity efforts.

Parent stock vaccination is useful to elicit humoral immunity that will be transmitted to the progeny (passive immunity); it will protect the young chicks for the first few weeks of life. Live vaccination is applied in the progeny because passive immunity does not last long enough to ensure adequate protection for the whole broilers' lifespan. By doing so, chickens develop an active immunity. Several vaccines are commercially available for the control of IBD in broilers.

Historically, vaccination has been applied in the farm via drinking water using live attenuated vaccines of various residual pathogenicity (mild, intermediate, intermediate plus, hot). Hatchery vaccination is becoming a growing trend because of the increasing capacity of poultry producing companies, a higher degree of integration, and the willingness to better master the vaccine application using automated equipment, either by day-old injection via subcutaneous route, or in ovo route. High-throughput automated equipment is now available (in ovo or day-old injection) enabling a higher quality, consistency, and cost-effectiveness of vaccination. In addition, hatchery vaccination removes the risk of vaccination failure in the field (due to poor water quality, inappropriate timing, and insufficient flock coverage); it also prevents the stress of water withdrawal in the farm when using the classical drinking water method. As a consequence, moving vaccination in the hatchery improves the welfare of the birds in the farm. Altogether, it offers a significant improvement in terms of immunization success as recently demonstrated. Advances in technology have enabled the development of new vaccines that are able to escape the neutralizing effect of maternally derived antibodies (MDA) and hence are eligible for hatchery application.

Three types of IBD vaccines are currently available for hatchery application in several parts of the globe:

- An immune-complex vaccine in which a live attenuated IBD vaccine strain has been in vitro complexed with a high titre polyclonal serum in specific quantities;
- A vaccine using the herpesvirus of turkeys (HVT) vector technology as a carrier expressing IBDV's VP2 antigen.
- A third type of less attenuated, naked viruses or «hot strains», used as vaccines, which could be applied in the hatchery.



As the Gumboro virus is a very persistent virus, in many cases it is already present inside the farm, which can lead to a field challenge when new birds are placed.

The characteristics of this challenge in chickens (age of birds, severity, consequences, etc), will vary from house to house but the challenge will definitely occur. In this case vaccination should aim at both protecting the chickens and preventing the Gumboro challenge from getting out of control.

When considering a sound Gumboro vaccination program the main objectives must be:

- Ensure continuous protection of the chickens against farm infection of Gumboro disease, or "Prevention of Infection"
- Protect against the clinical signs of infection or "Clinical Protection",
- Prevent or significantly reduce the amount of virus shed after challenge or "Reduction of shedding of the Gumboro
- Prevent the build up of a higher virus pressure, production cycle after production cycle,
- Prevent the evolution of the farm Gumboro disease towards a virus that could escape the protection program.

The last two points are important for the reduction of the shedding of the Gumboro field virus, since the goal of a strong Gumboro vaccination program should be to stop the Gumboro cycle.

Over the last 50 years the economic development in many countries has increased the number of birds placed per farm and has led to stricter biosecurity and surveillance programs.

Despite the wide use of vaccines and increased biosecurity, still very much present and ranks among the top five diseases in almost all countries globally. One of the reasons for this dominance is that the **Gumboro disease virus** is a very persistent virus surviving in poultry houses in the absence of chickens during downtime periods.

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Samah M Mosad, Abdelfattah H Eladl, Mohamed El-Tholoth, Hanaa S Ali, Mohamed F Hamed.
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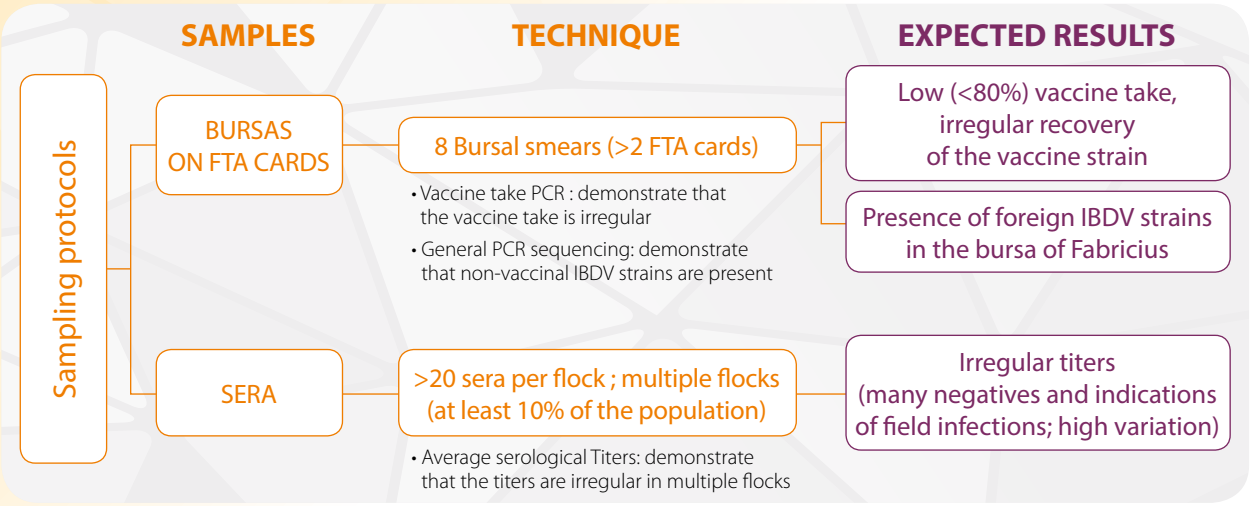
2 IBD surveys & global situation

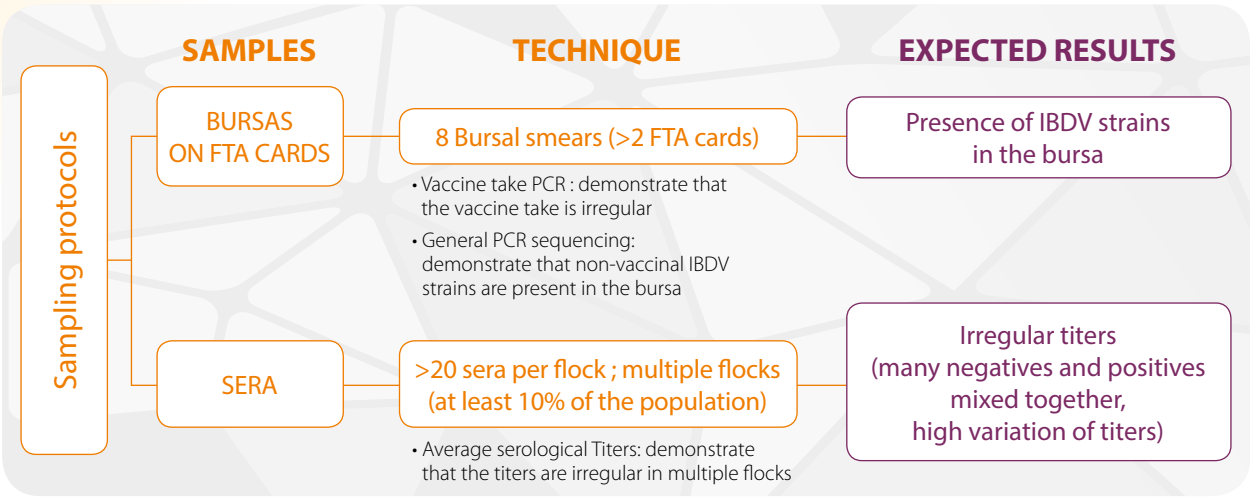
Conducting IBD surveys is key to understand the extension and disease challenge in poultry production.

In Ceva, we always conduct epidemiological IBD surveys in order to recognize the potential impact of the disease in the operations of our customers. First, we focus on the real problems of our customers in a specific setting and, once that they are correctly identified, we discuss different solutions to address them. This is how we believe that our solutions should be implemented. In order to accomplish this, we propose the following charts, which explain how to approach each situation.

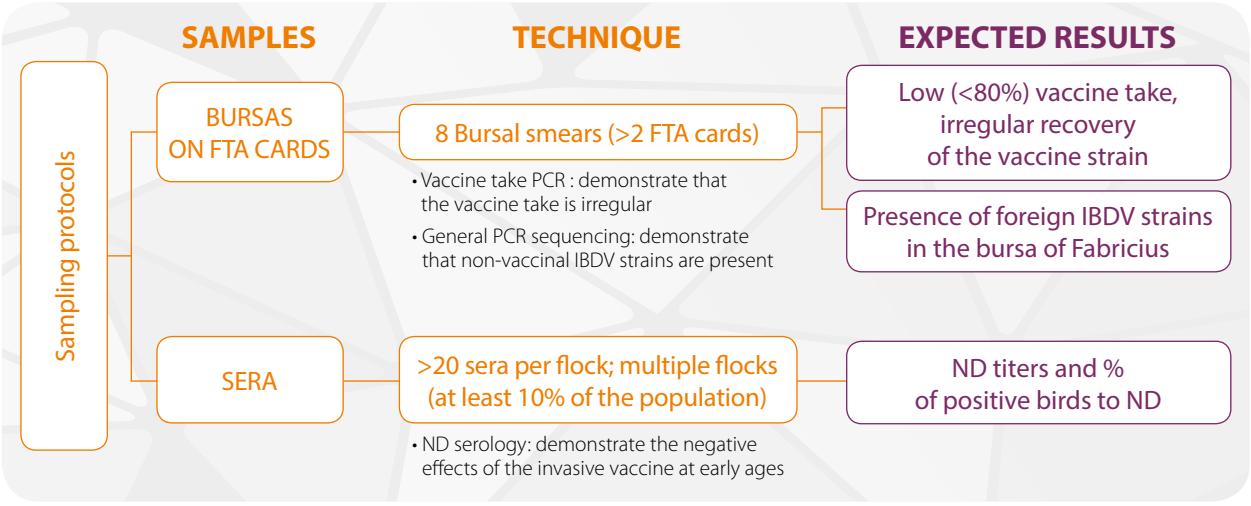
Presence of IBDV in flocks vaccinated with drinking water vaccines



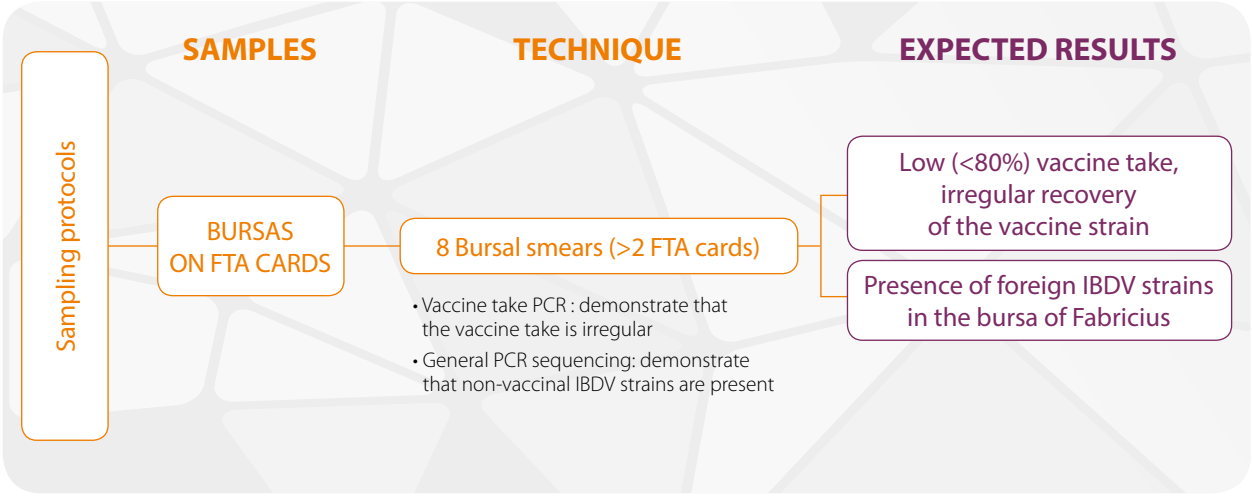
Presence of IBDV in flocks vaccinated with rHVT vaccines



Presence of IBDV in flocks vaccinated with very invasive vaccine strains



Presence of IBDV in flocks vaccinated with other immune-complex vaccines



Worldwide IBD surveys results

Ceva Santé Animale Vetarinary Services Specialists, in cooperation with independent researchers conducted an IBD Survey during 2019-2021 in order to update the epidemiology of the IBD virus around the world.

In the next pages, you will access result of several studies from this survey, demonstrating the presence of different field strains in Europe, Asia, Latin America and Africa.

United Kingdom

MATERIAL AND METHODS

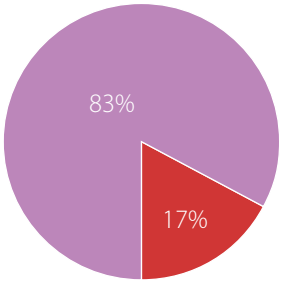
SAMPLING PERIOD	September 2020 to March 2021
TARGET	Broiler
SAMPLING AGE	30 to 49 days of age
NUMBER OF SAMPLES	148 bursas
TECHNIQUE	RT-PCR and Serology (Elisa Biochek)

VACCINATION PROGRAMS

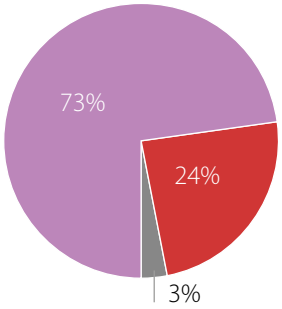
- TRANSMUNE® (First vaccination cycle)
- CEVAC® IBD L
- 228E
- GM-97
- S706

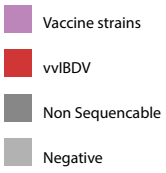
RESULTS

TRANSMUNE®

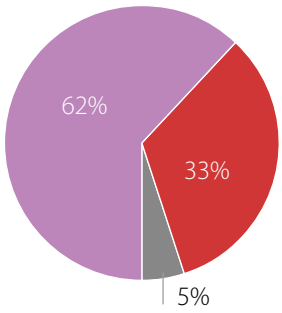


CEVAC® IBD L

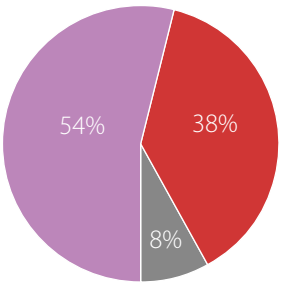




228E



GM-97



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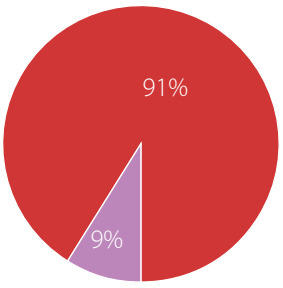
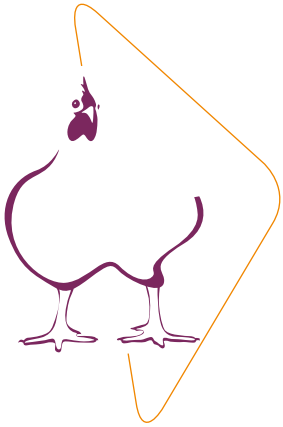




CONCLUSION

vvIBDVs were found, possibly associated to subclinical infections.
Compared to other drinking water vaccines, Transmune® demonstrated its superiority and STOPPED THE GUMBORO CYCLE.

The Netherlands

MATERIAL AND METHODS

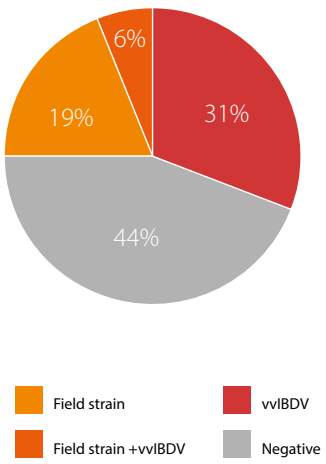
SAMPLING PERIOD	2019-2020
TARGET	Layers
SAMPLING AGE	6 and 8 weeks
NUMBER OF SAMPLES	Bursas from all 18 flocks
TECHNIQUE	Serology (Elisa Biochek) and RT-PCR (bursas)

VACCINATION PROGRAM

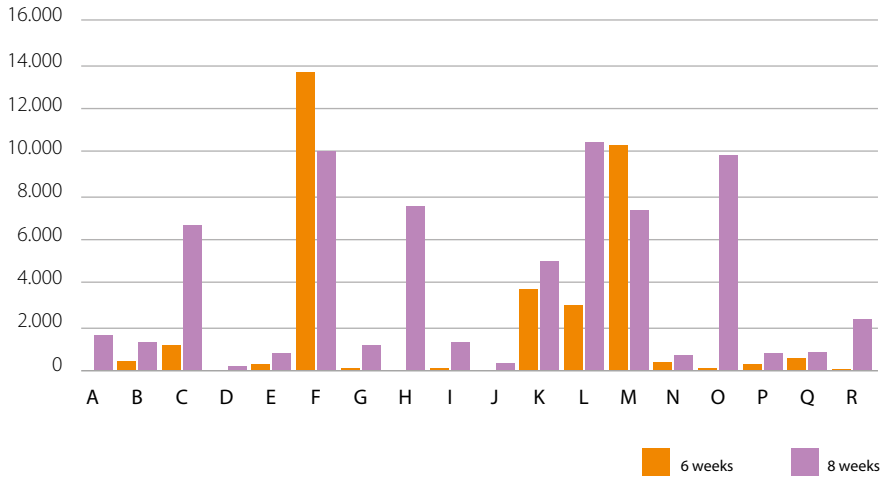
- rHVT-IBD

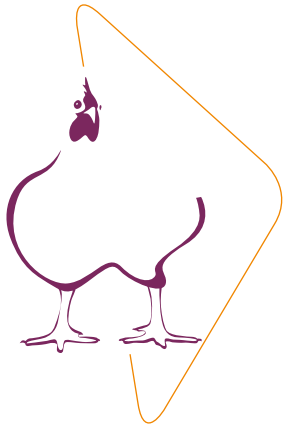
RESULTS

Virus detection rate



Serology IBD ELISA Biochek





CONCLUSION

Field and vvIBDV strains were detected in several rHVT-IBD vaccinated flocks. rHVT-IBD vaccine could not stop the Gumboro cycle.

Portugal

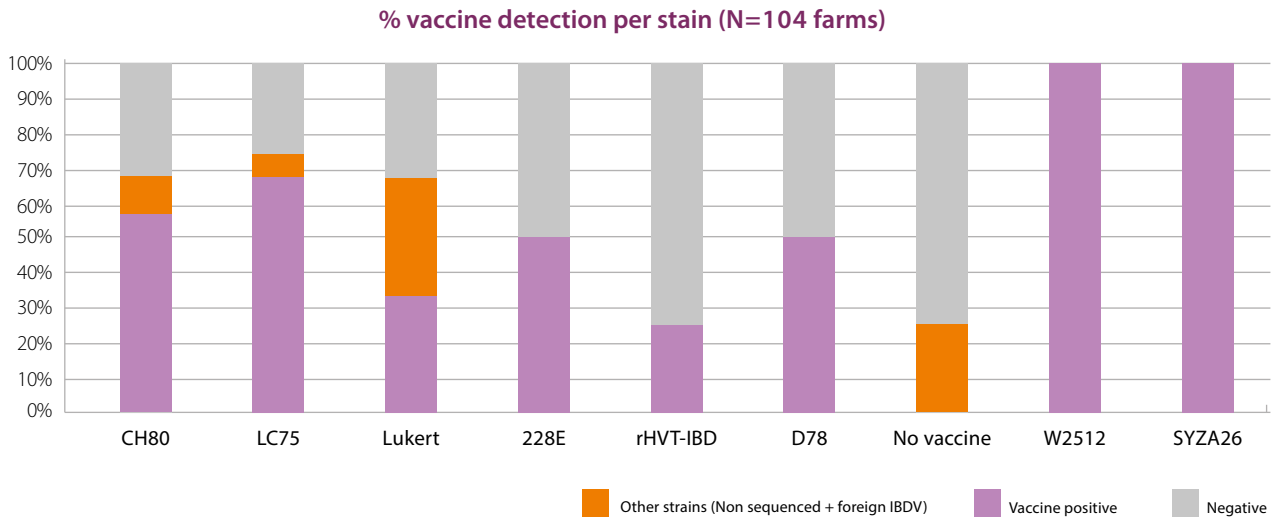
MATERIAL AND METHODS

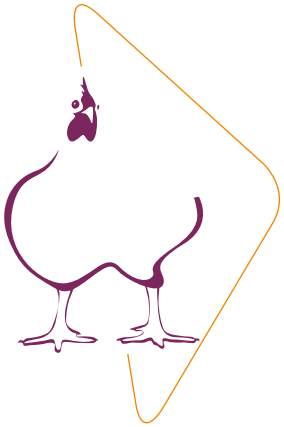
SAMPLING PERIOD	November 2020 - February 2021
TARGET	Broilers and Layers
SAMPLING AGE	> 35 days of age
NUMBER OF SAMPLES	104
TECHNIQUE	RT-PCR
LABORATORY USED	MAPS, Italy

VACCINATION PROGRAM

- Drinking water (various)

RESULTS





CONCLUSION

A potential new IBDV genogroup was discovered in Portugal.
Farm vaccination with other types of vaccines (not immune complex) could not protect the bursa of Fabricius.

Italy

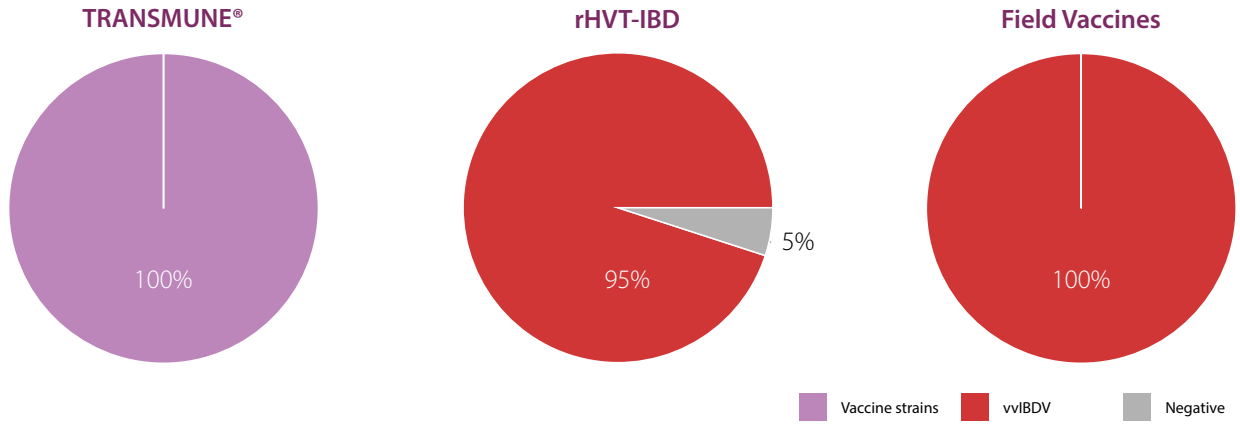
MATERIAL AND METHODS

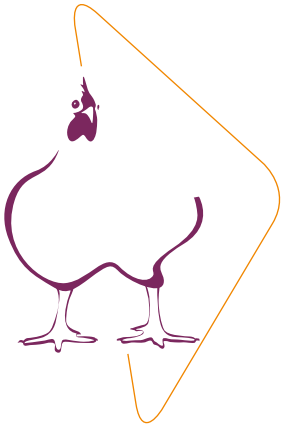
SAMPLING PERIOD	March 2020 to April 2021
TARGET	Broilers
SAMPLING AGE	28-42 days of age
NUMBER OF SAMPLES	25 bursas
TECHNIQUE	RT-PCR (bursas)

VACCINATION PROGRAM

- Transmune, rHVT-IBD vaccines or conventional field vaccines

RESULTS





CONCLUSION

There is a clear difference in vvIBDV prevalence in the flocks monitored. Transmune® was able to STOP THE GUMBORO CYCLE, when rHVT-IBD and conventional field vaccines did not.

China

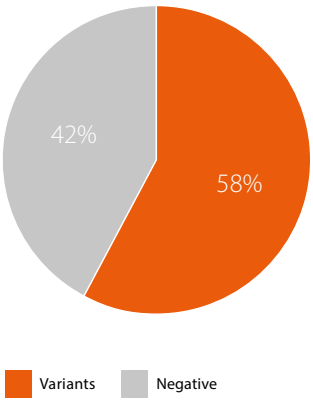
MATERIAL AND METHODS

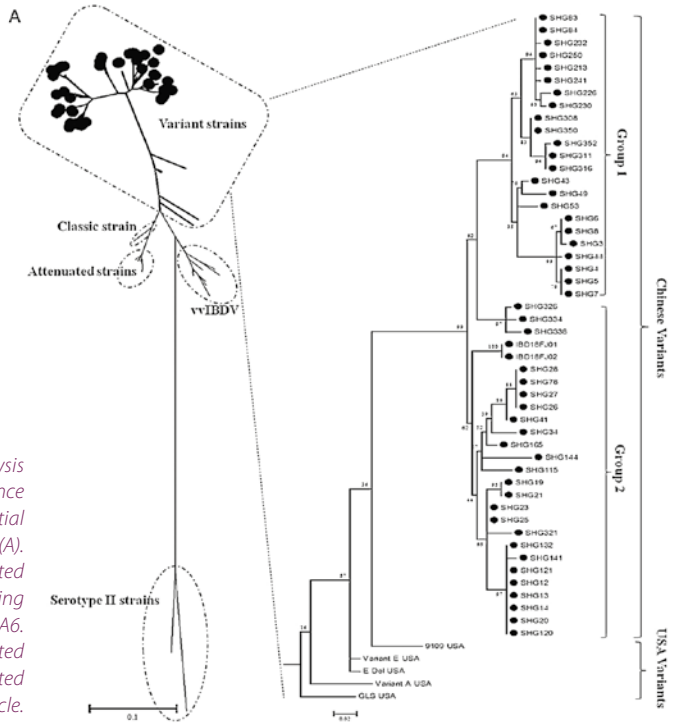
SAMPLING PERIOD	March 2019 - August 2019
TARGET	Broilers
SAMPLING AGE	35 days of age
NUMBER OF SAMPLES	249 BURSAS: Fresh (174); FTA Cards (75)
TECHNIQUE	Serology; RT-PCR;
LABORATORY USED	LAB – IND, Malaysia

VACCINATION PROGRAM

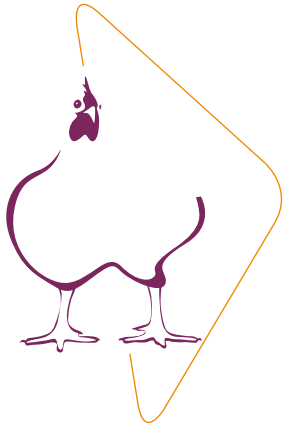
- **GROUP 1** (2 farms):
  - Cevac® IBD L + Cevac TRANSMUNE®
- **GROUP 2** (2 farms):
  - Chinese subunit ND-H9-IBD Inactivated

RESULTS





Phylogenetic tree analysis of the amino acid sequence of the representative partial fragments of VP2 (aa 183-441) (A). The trees were generated by the neighbor-joining method using MEGA6. The variant strains detected in this study are highlighted with a solid circle.



CONCLUSION

New IBDV variants were not perceived as a threat by the producers, despite their impact on performance. ND-H9-IBD vaccines could not stop the Gumboro Cycle.

India

MATERIAL AND METHODS

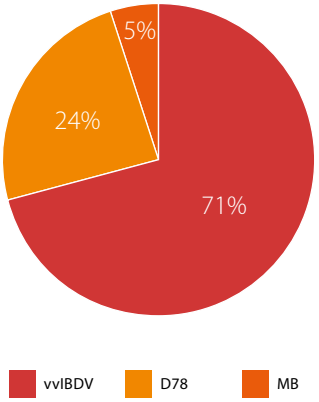
SAMPLING PERIOD	June - October 2018
TARGET	Broilers
SAMPLING AGE	1 day of age and 35-38 days of age
NUMBER OF SAMPLES	22 BURSAS on FTA Cards: 2500 sera
TECHNIQUE	Serology ELISA Biochek IBD; RT-PCR
LABORATORY USED	LAB – IND, Malaysia, Ceva SSIU Phylaxia

VACCINATION PROGRAM

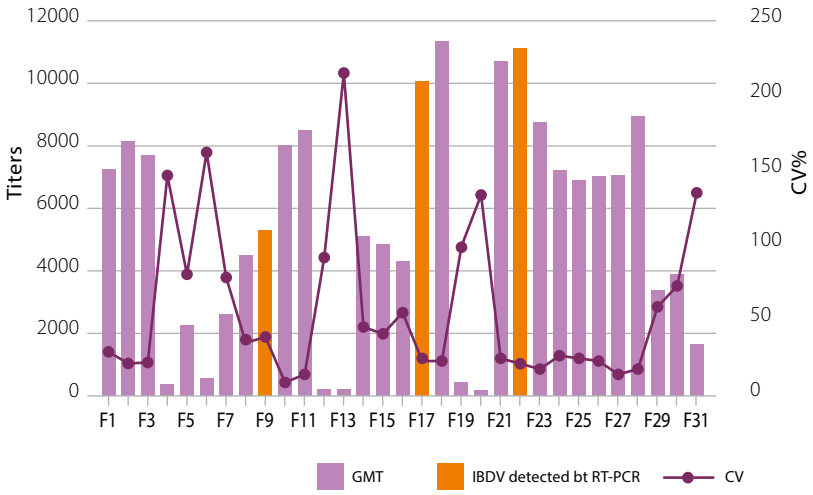
- Drinking water vaccination (D78 or MB group) at 12-13 days of age

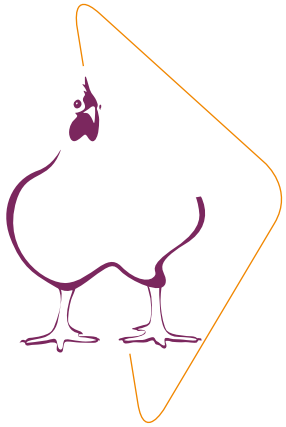
RESULTS

RT-PCR detection rate



Drinking Water IBD titers at slaughter age





CONCLUSION

Conventional Drinking Water IBD vaccines could not protect the Bursa of Fabricius and could not stop the Gumboro cycle.

Brazil

MATERIAL AND METHODS

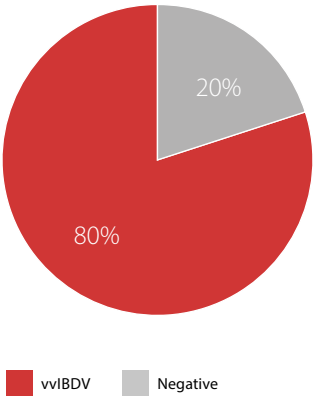
SAMPLING PERIOD	December 2020 – February 2021
TARGET	Broilers
SAMPLING AGE	34 days of age
NUMBER OF SAMPLES	50 Bursas in FTA Cards
TECHNIQUE	Histopathology

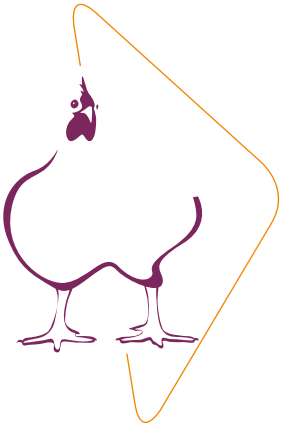
VACCINATION PROGRAM

- rHVT-ND-IBD

RESULTS

Histopathological results





CONCLUSION

The bursas from the flocks vaccinated by rHVT-ND-IBD vaccines showed lesions by field strains infection.

Peru

MATERIAL AND METHODS

SAMPLING PERIOD	March - May 2020
TARGET	Broilers
SAMPLING AGE	21-35 days of age
NUMBER OF SAMPLES	44 BURSAS in 11 FTA Cards
TECHNIQUE	RT-PCR
LABORATORY USED	SSIU Phylaxia, Hungary

VACCINATION PROGRAM

- Live Immune-Complex vaccine, strain 1052

RESULTS

CONCLUSION

Variant A IBDV was detected from the 24 days of age onwards despite a vaccination program which had been used for over a year. Competitor immune-complex vaccines could not stop the Gumboro Cycle.

Argentina

MATERIAL AND METHODS

SAMPLING PERIOD	January 2021 - March 2022
TARGET	Broilers
SAMPLING AGE	18-21 days of age
NUMBER OF SAMPLES	22 BURSAS in FTA Cards
TECHNIQUE	RT-PCR
LABORATORY USED	SSIU Phylaxia, Hungary; INTA Castelar (Argentina)

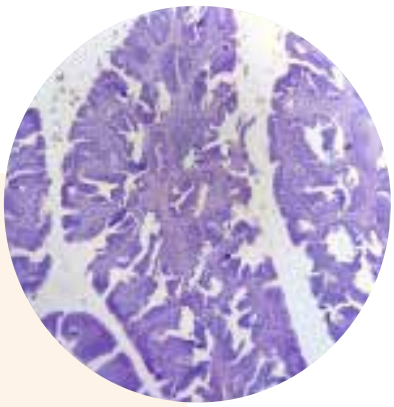
VACCINATION PROGRAM

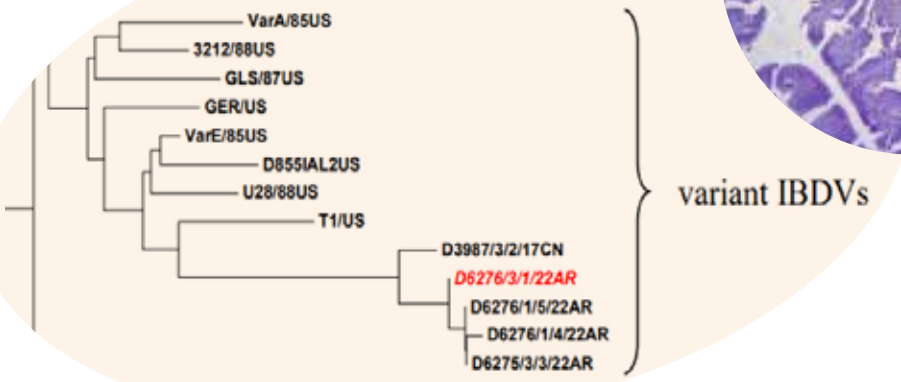
- rHVT-IBD

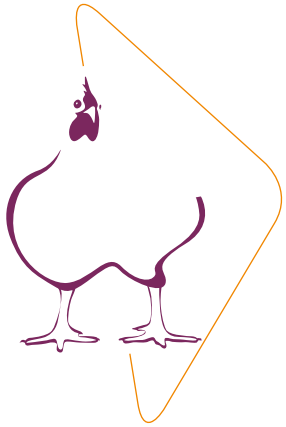
RESULTS

Broilers, 24 days of age

Broilers, 21 days of age







CONCLUSION

Early infection with a new genogroup 2 variant IBDV, was detected from 13 to 42 days of age.
New variant IBDVs are replacing vvIBDVs and were massively detected in rHVT-IBD flocks.

Mexico

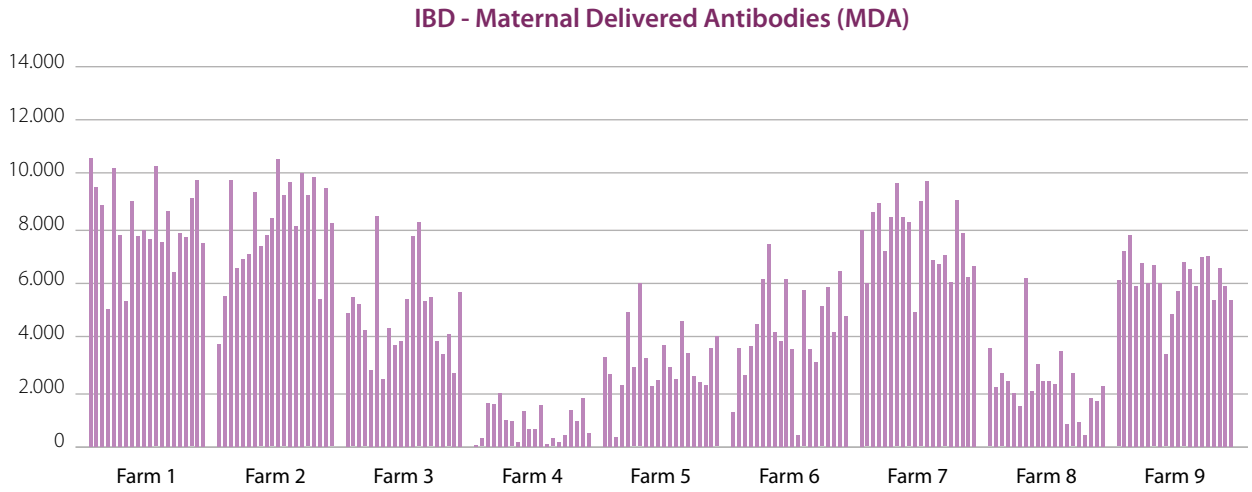
MATERIAL AND METHODS

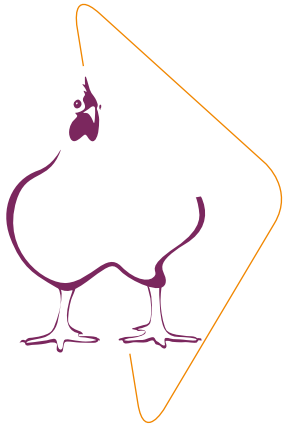
SAMPLING PERIOD	2020
TARGET	Broilers
SAMPLING AGE	1 day of age
NUMBER OF SAMPLES	180 blood samples
TECHNIQUE	Serology

VACCINATION PROGRAM

- Conventional field IBD vaccination

RESULTS





CONCLUSION

The MDA titers showed a high variation from farm to farm, and from chick to chick. This brings a strong challenge to define the correct date of field vaccination, and to protect all the chicks of the flock.

South Africa and Botswana

MATERIAL AND METHODS

SAMPLING PERIOD	Sept. 2019-December 2021
TARGET	Broilers
SAMPLING AGE	21-31 Days of age
NUMBER OF SAMPLES	1083 BURSAS
TECHNIQUE	RT-PCR

VACCINATION PROGRAM

- Live conventional DW IBD vaccines

RESULTS

AGE AT DIRECT INFECTION	7 DAYS OF AGE	10 DAYS OF AGE	
SAMPLING DAY	6 dpi (13 days of age)	4 dpi (14 days of age)	5 dpi (15 days of age)
BURSA GROSS LESIONS	9/9 positive (moderate- severe)	"5/5 positive (moderate- severe)"	4/5 positive (moderate- severe)
BURSA HISTOLOGICAL LESIONS	9/9 positive (4 at onset, 5 in acute-subacute phase)	4/4 positive (2 at onset, 2 in acute-subacute phase)	4/5 positive (in acute-subacute phase)

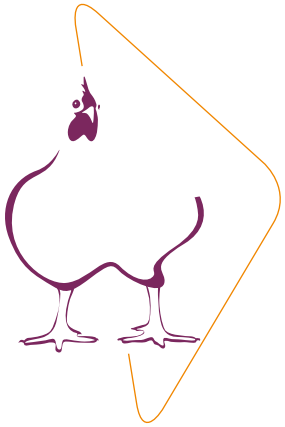
Ceva SSIU Phylaxia Study id. P126
Pathogenicity test of variant IBDV strain of South African origin in SPF and commercial broiler chickens. (2020)

No IBDV Infection

Infected at 7 days of age

Infected at 10 days of age

CONCLUSION



Poultry producers were not concerned about the pathogenicity of the south African family of variant IBD viruses. The behaviour of the virus in infected flocks was subclinical. New variant IBDVs produce subclinical signs and atrophy of the bursa of Fabricius.

3 Vaccination program

STOP
THE GUMBORO CYCLE

Since IBD is a very persistent virus, it is capable of prevailing for a long time in the farms. This can lead to a field outbreak if new birds are placed in the same houses. The characteristics of this challenge in chickens (age of birds, severity, consequences, etc.), might vary from house to house, but the challenge will definitely occur at some point in time. As a result, vaccination should succeed at protecting the chickens and preventing disease challenge.

THE MAIN PROPERTIES OF A SUCCESSFUL VACCINATION PROGRAM SHOULD BE:

- Ensuring continuous protection of the chickens against infection at farm level: 'Prevention of Infection'.
- Protecting against clinical signs of disease: 'Clinical Protection'.
- Preventing or significantly reducing the amount of virus shed to the environment after challenge: 'Reduction of shedding of the field IBD virus'.
- Avoiding the "elevator effect", or reaching a higher virus concentration cycle after cycle.
- Stopping the evolution of the IBD virus towards a form that could escape the prevention program.

The last two points are important for the reduction of the shedding of the field IBD virus, thus becoming the backbone of a quality IBD vaccination. The vvIBD virus is sometimes isolated where inefficient application and low vaccine take has been observed (Morla, 2016; Phylaxia, 2017).

Figure 3. 100% vvIBD virus PCR Isolation from FTA cards in a breeder flock vaccinated at 14 and 29 days of age intraocularly. SSIU Phylaxia, 2017

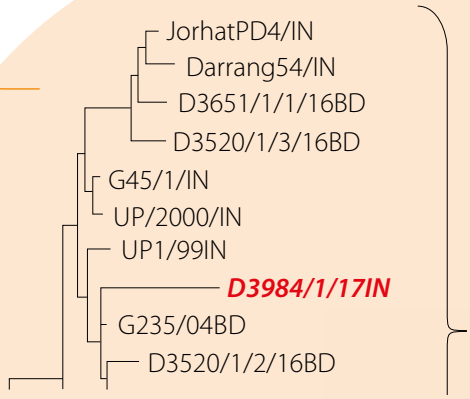
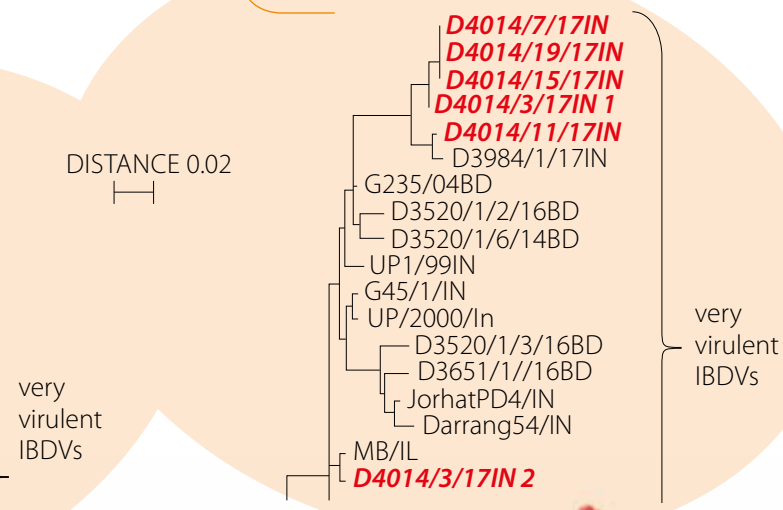


Figure 4. 100% vvIBD virus PCR Isolation from FTA cards in broilers vaccinated at 6 and 12 days of age intraocularly. SSIU Phylaxia, 2017

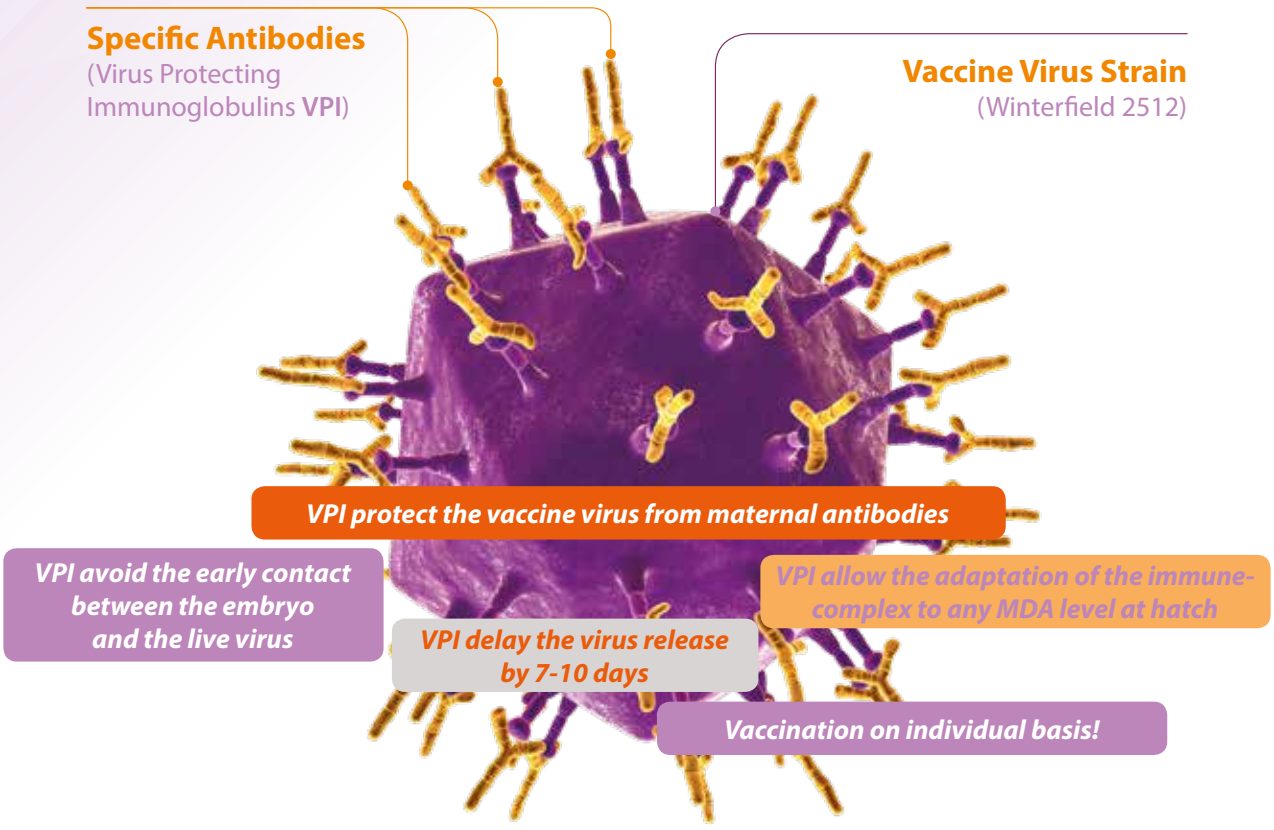


4 Transmune® vaccine

In broilers, the best option to control IBD is to use a live attenuated IBD vaccine of the Intermediate Plus type. Only this category of vaccine can bring a high level of protection against various types of IBD viruses and effectively prevent shedding, so that the virus pressure decreases cycle after cycle and the likelihood of emergence of variant IBDV can be strongly reduced. Since vaccination in the hatchery is the only method to ensure 100% vaccine coverage, then this vaccine should be presented under the immune-complex form.

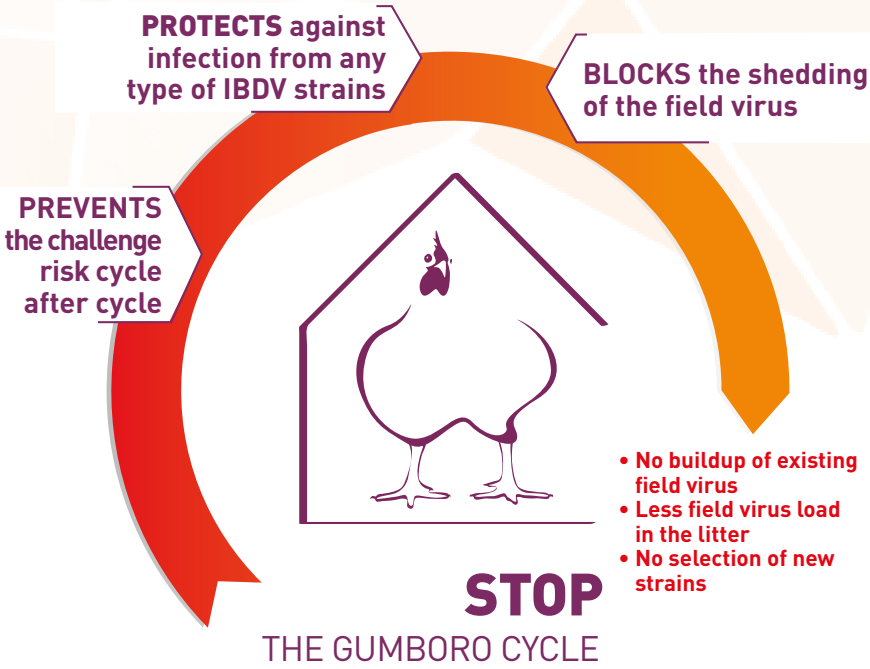
TRANSMUNE® is an IBD immune-complex vaccine containing the original Winterfield 2512 strain, which is blended with specific antibodies called Virus Protecting Immunoglobulins (see Figure 5). The product was developed in the early 2000´s, and quickly registered in many countries in Asia, Latin America and Europe. Currently, the vaccine is marketed in over 75 countries worldwide.

Figure 5. Schematic representation of TRANSMUNE®



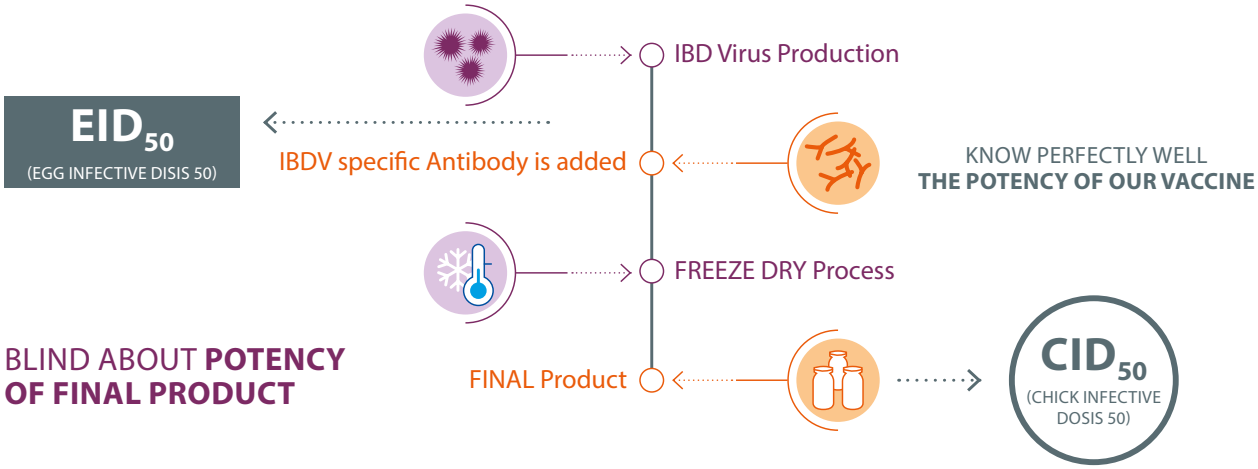
As the formulation between the attenuated vaccine virus and specific antibodies needs to be extensively tested, in order to have the optimum safety and efficacy balance of the product, more than 100 different formulations were tested before the introduction of TRANSMUNE® to the market.

It has been designed to be applied in the hatchery (in-ovo or subcutaneously) and it has been used in over 90 billion broilers worldwide, since its launch in 2006.



Since the vaccine is registered in Europe, an unique QC procedure was developed to safeguard the efficacy and safety of the vaccine. Every single production batch is thoroughly tested using a CID (Chick Infective Dose) 50 test. This test is performed with the aid of live birds and with the final blend of vaccine-antibodies, in order to guarantee the potency and safety of the vaccine.

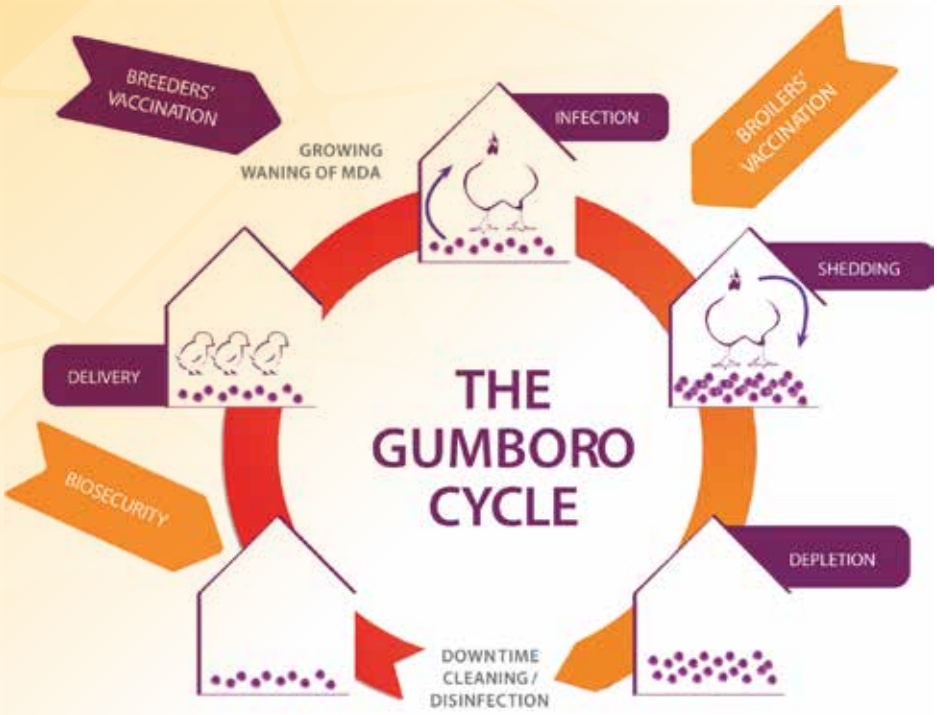
CONVENTIONAL PROCESS



5

STOP
THE GUMBORO CYCLE

Transmune® benefits



The take of the immune-complex vaccine (that corresponds to replication of the vaccine virus in the bursa) occurs when the MDA level has reached an optimum point that allows the vaccine to take and before the flock has become susceptible to infection, preventing the infection and shedding of the field virus. This is also known as «STOP The Gumboro Cycle».

- **Full protection against clinical signs, high degree of resistance against infection, independently of the challenge IBDV strain.**
- **High level of prevention against shedding, no selection pressure on the Farm IBDV population. The vaccine adapts individually to the immune status of each chicken and always replicates at the 'optimum' time.**
- **The vaccine can be administered in the presence of passive immunity, so it does not contradict and may even complement the breeders program.**
- **The vaccine can be injected in the hatchery, where reliability and consistency of application is at a maximum.**
- **Every chicken benefits from the properties of the vaccine.**

The use of TRANSMUNE® and the outstanding Ceva services team up for a perfect combination to stop the Gumboro cycle. Thanks to our long experience in collaborating with our customers, Ceva is proud to offer now an outsanding range of services from the hatchery to the further processing, namely:

- **Ceva Hatchery Immunisation Control Keys (C.H.I.C.K.) program**
- **Ceva Global Protection Services (GPS)**

In order to monitor the correct application of the vaccine, Ceva developed and implemented several years ago the C.H.I.C.K program. More recently, Ceva has introduced the Global Protection Services (GPS) to screen IBD pressure on farm and to monitor vaccine take and the serological response to IBD. These service programs are monitored by local and fully dedicated vaccination services managers and veterinary services experts. Several scientific papers and publications are available, which demonstrate the efficacy, safety and compatibility of the vaccine. A good example is the compatibility between TRANSMUNE® and Vectormune® ND providing protection against IBD, ND and MD in one application.(1)

Throughout the years, our customers have obtained very positive results with TRANSMUNE®, confirming the superiority of the immune-complex vaccination. These results can be described and organized, depending on the production phase where the improvements were observed

Improvements in vaccination control and immunization

Improvements in performance

Improvements in processing

(1) 24/07/2018 Vectormune ND - EMEA/V/C/003829 - IAIN/0010 - Annex I, page 3

Improvements in vaccination control and immunization

TRANSMUNE® can be injected in the hatchery, where reliability and consistency of application is at a maximum. Every chicken benefits from the properties of the vaccine. It requires an investment from the producer's side in "in-ovo" equipment or in extra staff, in case that the vaccination is performed subcutaneously. However, the investments are outperformed by the economic benefits of vaccinating and controlling the vaccination process in the hatchery.

eggject® IN OVO SYSTEM

desvac DOVAC

1 **The quality and strength of the protection** coming from replication of a complete Intermediate plus live attenuated IBDV are conserved: full protection against clinical signs, high degree of resistance against infection whatever the challenging IBDV strain, high level of shedding control, no IBDV strain selection at farm level (Ceva data, 2004-2017).

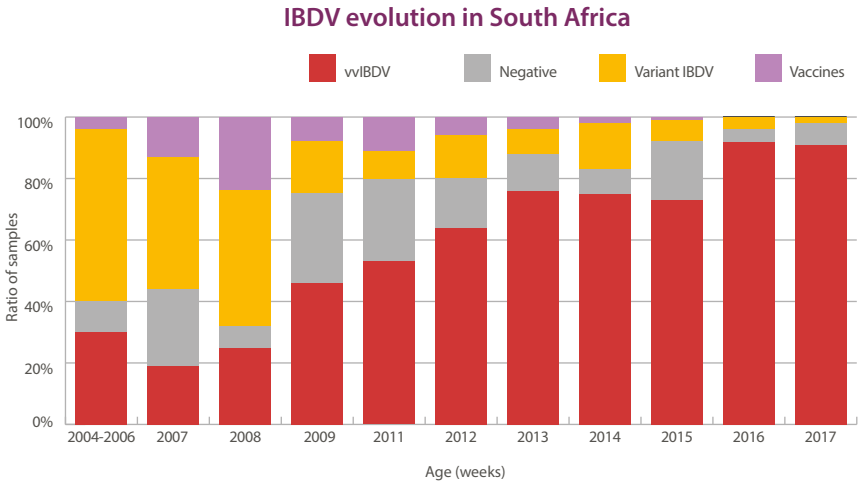


Figure 6. PCR field data, GPS South Africa 2004-2017 (Ceva, Data on file)

2 TRANSMUNE® achieves a more regular immunization when compared with drinking water vaccines:

- Absence of stress and thirst during application, thus compliance with welfare standards: *"Freedom from hunger or thirst by ready access to fresh water and a diet to maintain full health and vigour"* (Farm Animal Welfare Council, 2012).
- The vaccine can be administered in the presence of passive immunity, so it does not contradict the breeders' vaccination program. At least 25% better distribution of titers versus drinking water vaccination (GPS Spanish field data, 2009-2016, figures 7 & 8).

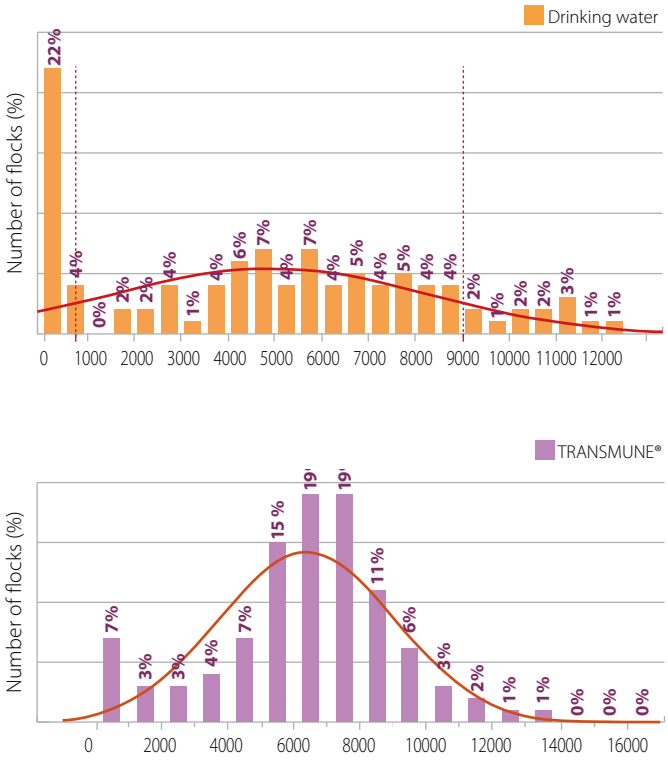


Figure 7 & 8: Distribution of titers in DW-Lukert (above) and TRANSMUNE® (below) vaccinated groups. Number of flocks (%) falling into each titer interval. A range of 4000-9000 ELISA BioChek units is considered an acceptable protection level (Ceva Data on file)

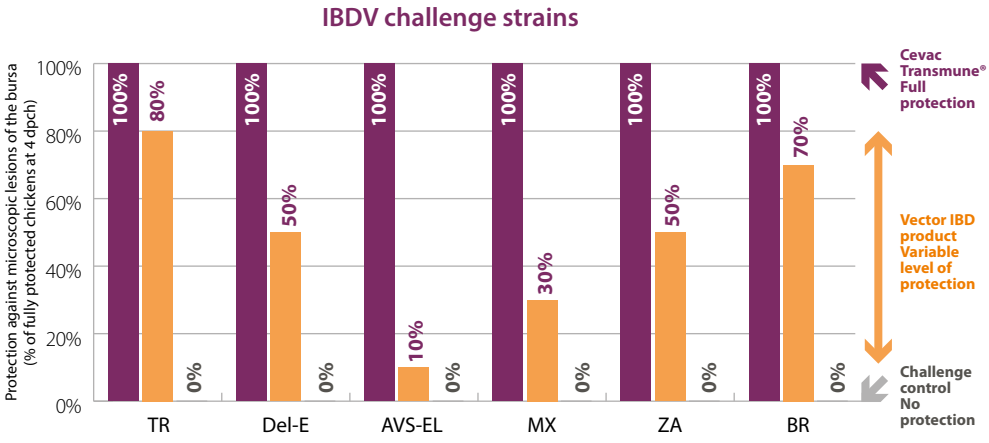


Figure 9: % of protected bursae of Fabricius in various TRANSMUNE® vs. rHVT IBD vaccine challenge models (Ceva, Data on file)

3 TRANSMUNE® blocks the bursa of Fabricius and the replication of field viruses, thus reducing undesired viral shedding. Additionally, by using the C.H.I.C.K. program and GPS, it can be ensured that all birds are well vaccinated and immunized.

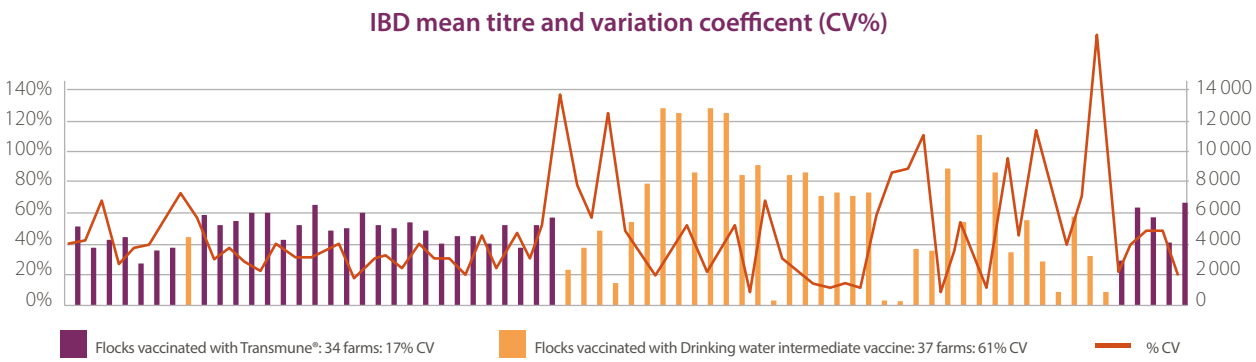


Figure 10. TRANSMUNE® and IBD-DW vaccine AMT and CV% 3-year-long field seromonitoring. GPS Spain 2012-2015 (Ceva, Data on file)

China

PREVIOUS SITUATION

Customer with high pressure of variants IBDV strains.

PREVIOUS VACCINATION PROGRAM

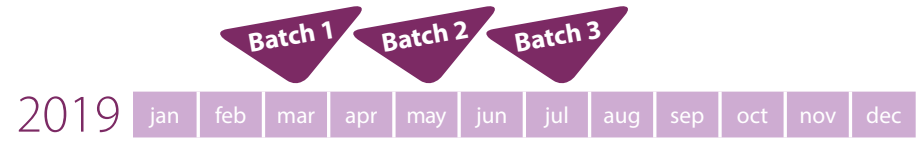
- IBD VP2 Killed vaccines

MATERIAL AND METHODS

Transmune® was introduced, and the flocks were monitored for 3 cycles.

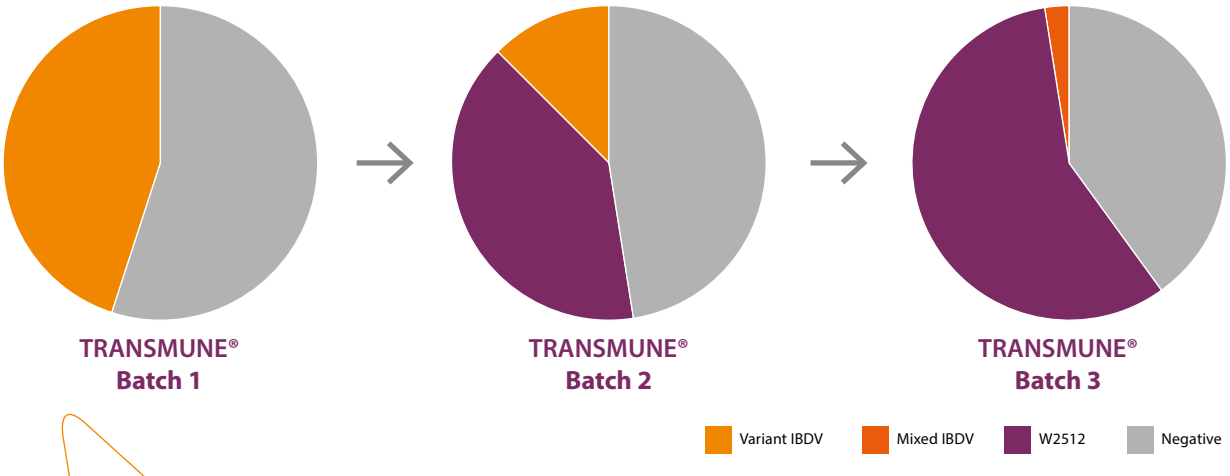
- 1,137,000 birds
- 17 Houses (21,000 - 23,750 birds/house)

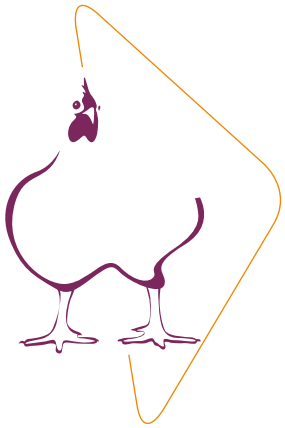
- Sampling :
  - 20 sera at 35 days of age
  - Performance data
  - Bursa sampling (5 bursae each) at 17, 21, 25, 28, 35 days of age



RESULTS

Displacement of variant IBDV





CONCLUSION

Displacing the variant strain, Transmune® was able to STOP THE GUMBORO CYCLE.

Arabic Peninsula

PREVIOUS SITUATION

Customer with high pressure of vvIBDV and variants IBDV strains.

VACCINATION PROGRAM

- Transmune®
- IBD Drinking Water conventional vaccines

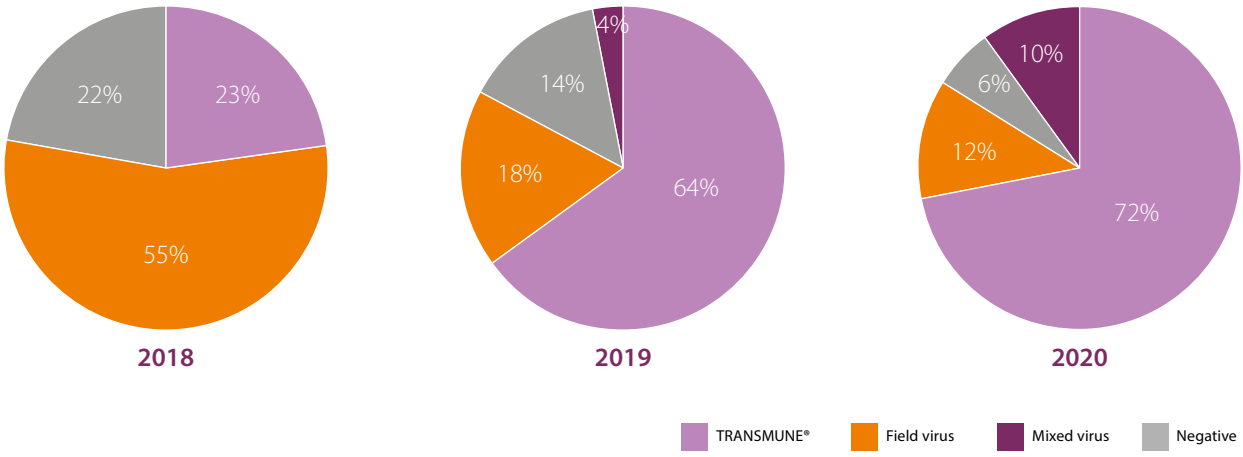
MATERIAL AND METHODS

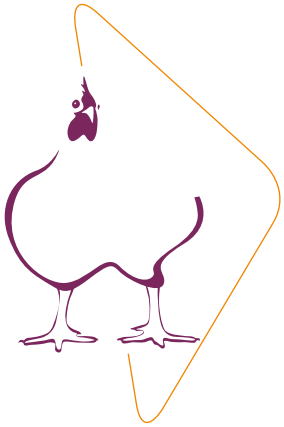
Transmune® was introduced to control.

600 Bursal samples were collected for PCR at 28 days of age.

RESULTS

IBDV detection by PCR : evolution of Transmune® year after year





CONCLUSION

Controlling the vvIBDV and variant strains challenges, Transmune® was able to STOP THE GUMBORO CYCLE.

United Kingdom

PREVIOUS SITUATION

Customer with presence of vvIBDV strains, and sub-clinical effects.

PREVIOUS VACCINATION PROGRAM

- IBD Drinking Water conventional vaccines

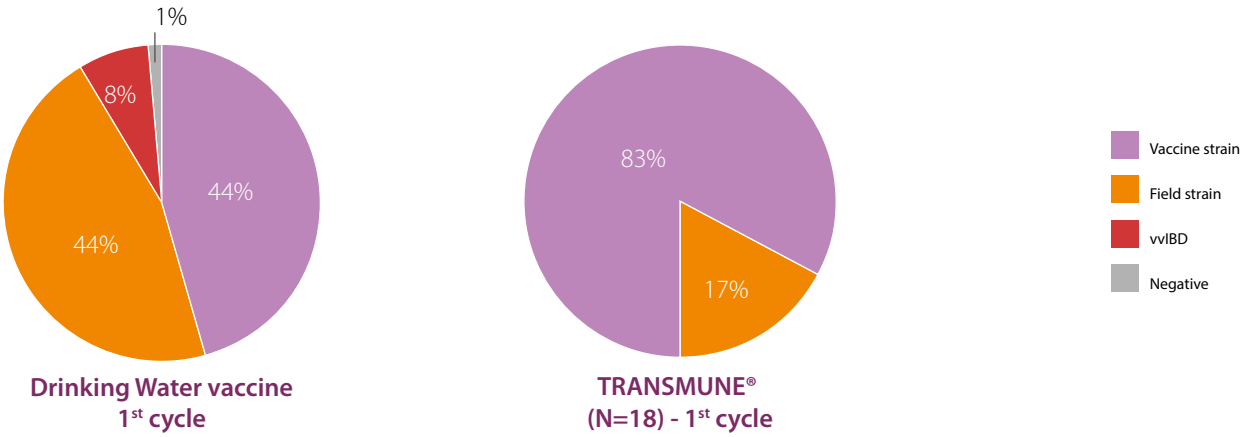
MATERIAL AND METHODS

Transmune® was introduced to control.

Bursal samples were collected for PCR at slaughter age and were compared after the first cycle.

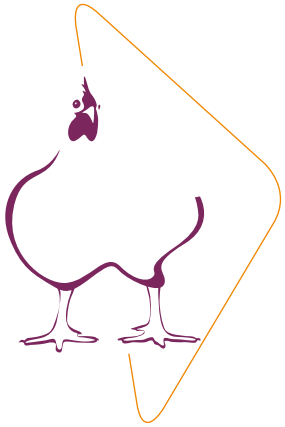
RESULTS

Comparison of PCR tests: Transmune® vs IBD Drinking Water conventional



Drinking Water vaccine 1st cycle

TRANSMUNE® (N=18) - 1st cycle



CONCLUSION

Transmune® controlled the vvIBDV challenge since the first cycle, and could STOP THE GUMBORO CYCLE.

Brazil

PREVIOUS SITUATION

Customer with low IBD pressure.

VACCINATION PROGRAM

- **Group 1:** Transmune®
- **Group 2:** rHVT IBD

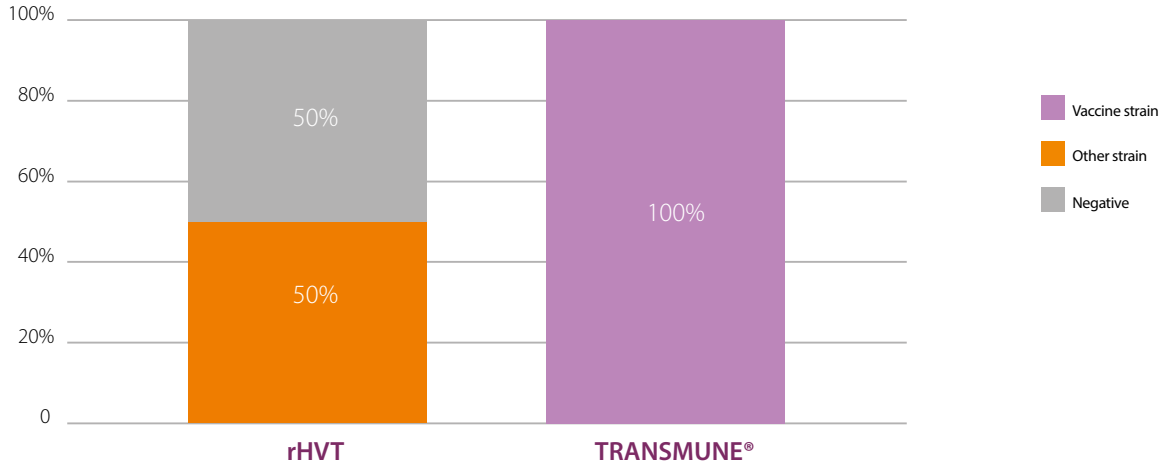
MATERIAL AND METHODS

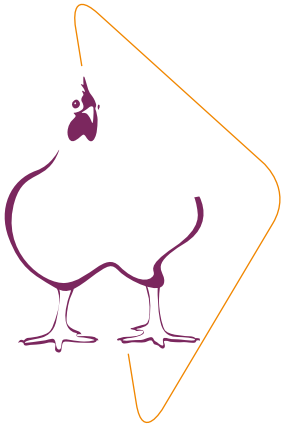
After the first cycle, bursal samples were collected at slaughter and tested by histopathology and RFLP-PCR in order to detect the presence of vaccine and field strains, or absence of virus.

- **Group 1:** Transmune® - 10 flocks (352,000 birds)
- **Group 2:** rHVT IBD - 10 flocks (340,000 birds)

RESULTS

Comparison of PCR tests: Transmune® vs rHVT-IBD vaccines





CONCLUSION

In the rHVT-IBD group, 50% of the bursae were positive to the IBDV (field strain). Transmune® had excellent recovery (100%) in the vaccinated flocks, and managed to STOP THE GUMBORO CYCLe.

6 Real world evidences

IMPORTANCE OF A PROPER ANALYSIS

Over the past 10 years, digitalization – along with the new technologies – has emerged and developed itself in all industries a llowing to get more and new relevant information. Valuable data helps in our constant decision-making process. The Poultry industry – globally integrated from the breeders to the slaughterhouses, passing by the hatcheries and farm – has therefore quickly adapt to this new environment, seeing the hidden value of the data.

In Ceva, we are collecting huge amounts of health data (serology data, broiler age, vaccination program…) thanks to our services, the GPS, and the hatchery C.H.I.C.K. program. Our customers are also collecting a lot of production parameters in order to follow the health and growth of their birds. Due the importance of combination of health and production parameters, in 2021, has been launched a Real World Evidence (RWE) project on top of the data activity already in place.

RWE is a recent wording commonly used in human medicine in order to demonstrate the benefits of a product through the analysis of real world data (RWD). Data in real life conditions, without control of the environment or some parameters, on chosen subjects. For us, it means analyses of field poultry data (vaccines or not involved). Even though, Ceva being an animal health company, the majority of our RWE analysis are focusing on the birds health

The objective of the RWE project is simple: enlarge the capability to work on poultry data, to do professional statistics for the Poultry Industry -using a statistical software called Python- thanks to key veterinarians located around the world. **The data analyse skill, associated with the veterinarian knowledges, is making a true difference for the interpretation of the results, as well as for the solution to put in place.**

A METHODOLOGY IN 3 MAIN STEPS HAS BEEN ESTABLISHED INTERNALLY :

1 - Challenge

Analysis of the individual serology titers to answer to the following question « Is there an IB / IBD / ND challenge in my farms ? if yes, how many farms were concerned ? ». According to the lab historic, the country, the vaccination program and the kit used, a threshold is defined by our experts. Then, if at least 20% of the birds are above that threshold, we consider the flock has « challenged »

2 - Performances

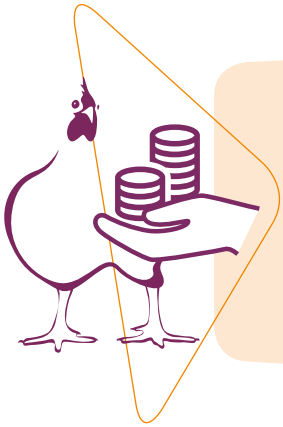
Analysis of the production parameters (slaughter age and weight, mortality percentage, feed conversion rate….). This analysis is done either per vaccination program, or following the previous classification « challenged vs non challenged »

3 - Economics

Analysis of a disease impact. The statistical differences observed at the previous step are converted into money, in order to evaluate the cost of an IB / IBD / ND challenge. In a few years, already 200 RWE studies have been done worldwide, demonstrating the strong enthusiasm and willingness of the Poultry Industry to learn from its data, to improve the production and raise healthy well protected birds.

Together with the clear benefits obtained in the hatchery and immune system, several trials have confirmed the superiority of TRANSMUNE® at field level. These are just a list of the clear economic benefits obtained throughout years of use of TRANSMUNE®. You will find below a sample of 12 field observations performed in different countries.

Based on our experience, the performance results obtained with a good application of a TRANSMUNE® vaccination program, compared to different vaccine program types, support clearly the application of TRANSMUNE® in the hatchery. The expected average improvement in performance corresponds to the following figures:



TRANSMUNE® IBD

AVERAGE RESULTS:

+72€/1000 birds

-6.6 points FCR

+1.61% livability

Extra +85g body weight

The return on investment has been calculated by assuming the following market prices:

Final body weight of 2kg • FCR 1.6 • Feed price: 0.30 €/kg • Live bird price: 0.80 €/kg

By doing so, it was possible to calculate an additional profit related to improvements in the major production performance parameters.

Technical Parameters	Value/000 Birds	Value/100 M. Birds
0.01 FCR	6€/000 birds*	600 K€*
10 g. BW	3.2€/000 birds*	320 K€*
1% Mortality	11€/000 birds*	1,100 K€*

France

STUDY DESIGN

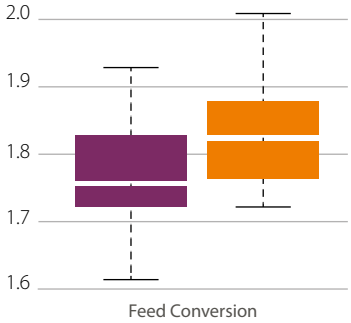
- *53 FLOCKS*
  1,590,000 DAY-OLD CHICKS,
  2 GROUPS
- ***GROUP1: 34 FLOCKS***
  (1,020,000 CHICKS)
  TRANSMUNE®
  SUBCUTANEOUSLY
- ***GROUP 2: 19 FLOCKS***
  (570,000 CHICKS)
  DRINKING WATER
  VACCINATION
- *SLAUGHTER AT*
  42 DAYS OF AGE

RESULTS & CONCLUSIONS

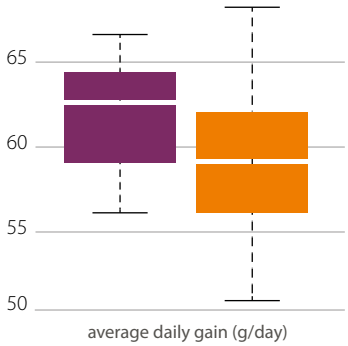
Vaccine	Feed conversion*	Slaughter weight (kg)	Mortality (%)	Average daily gain (g/day)*	EPEF*
TRANSMUNE®	1.77	2.600	2.01	63.15	329
Control Group	1.83	2.520	2.64	59.33	306

**Statistic difference*

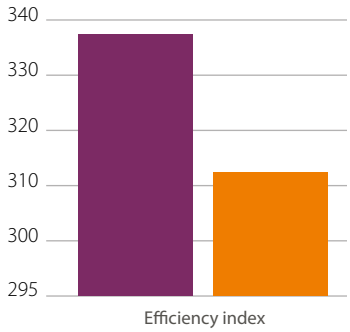
-8 points FCR



+3g and better uniformity



+23 points EPEF



ECONOMIC EVALUATION

Based on the cost benefits calculation (- 6 pts PCR, +80g of weight, +0.64% viability),

the extra revenues per 1,000 birds would be **+86€**

Ireland

STUDY DESIGN

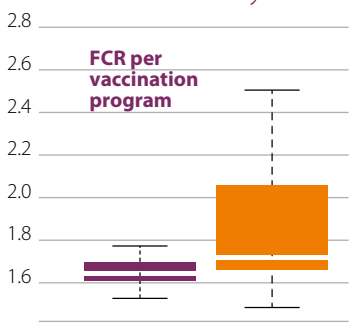
- *320 FLOCKS, 9,600,000 DAY-OLD CHICKS, 2 GROUPS*
- ***GROUP 1: 63 FLOCKS** (1,890,000 CHICKS) TRANSMUNE® SUBCUTANEOUSLY*
- ***GROUP 2: 257 FLOCKS** (7,710,000 CHICKS) DRINKING WATER VACCINATION*
- *SLAUGHTER AT 36 DAYS OF AGE*

RESULTS & CONCLUSIONS

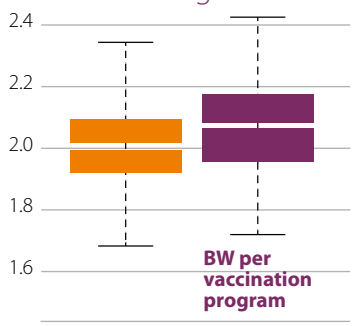
Vaccine	Feed conversion*	Slaughter weight (kg)*	Mortality (%)*	Average daily gain (g/day)	EPEF*
TRANSMUNE®	1.65	2.070	1.33	58.47	341
Control Group	1.73	1.970	3.51	54.12	310

**Statistic difference*

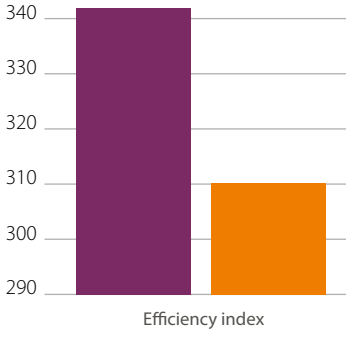
-6 points & better uniformity

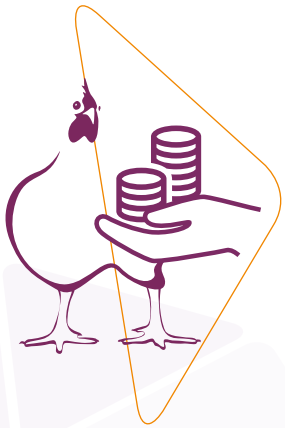


+100 g BW



+31 points EPEF





ECONOMIC EVALUATION

Based on the cost benefits calculation (-8 pts FCR, +100 g of weight, +2.18% viability),

the extra revenues per 1,000 birds would be +40€

Malaysia

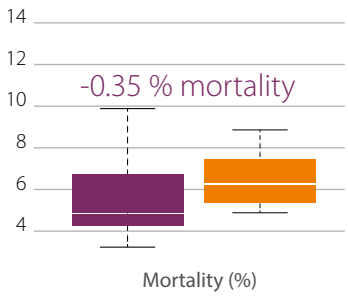
STUDY DESIGN

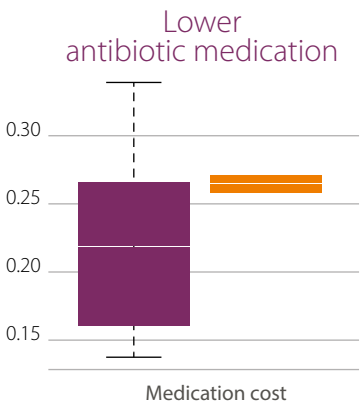
- *78 FLOCKS, 2,320,000 DAY-OLD CHICKS, 2 GROUPS*
- ***GROUP 1 : 64 FLOCKS** (1,900,000 CHICKS) TRANSMUNE® SUBCUTANEOUSLY*
- ***GROUP 2 : 14 FLOCKS** (420,000 CHICKS) DRINKING WATER VACCINATION*
- *SLAUGHTER AGE: GROUP 1: 36.2 DOA GROUP 2 : 35.9 DOA*

RESULTS & CONCLUSIONS

Vaccine	Feed conversion	Adjusted feed conversion	Slaughter weight (kg)	Mortality (%)*	Condem-nation (%)*	Antibiotic cost (RM/kg)*
TRANSMUNE®	1.54	1.54	2.100	6.14	0.61	0.22
Control Group	1.52	1.52	2.070	6.49	0.90	0.26

**Statistic difference*





TRANSMUNE®
Control

ECONOMIC EVALUATION

Based on the cost benefits calculation
(-0.35% mortality, -0.29% condemnations, lower medication),

the extra revenues per 1,000 birds would be +19,60€

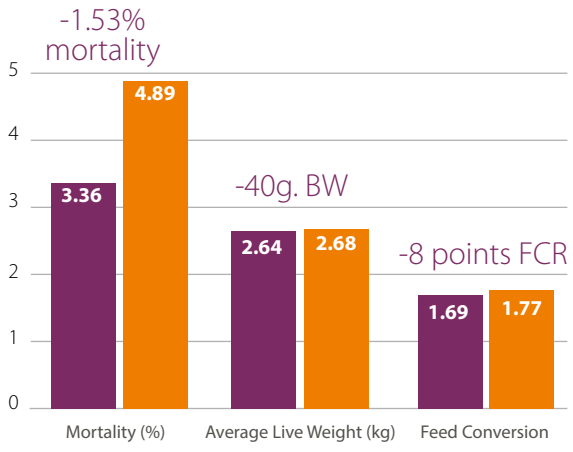
Brazil

STUDY DESIGN

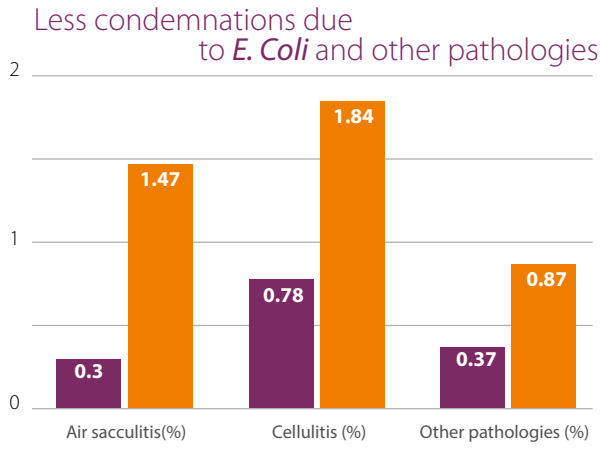
- *600,000 DAY-OLD CHICKS, 2 GROUPS (CONTEMPORANEOUS)*
- ***GROUP 1:*** *TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2:*** *INTERMEDIATE IBD IN DRINKING WATER AT 6 AND 15 DAYS OF AGE*
- *SLAUGHTER AT 45 DAYS OF AGE*

RESULTS & CONCLUSIONS

Vaccine	Broilers	Days	Mortality (%)	Average Live Weight (Kg)	FCR	Efficiency Index
TRANSMUNE®	188.000	45	3.36	2.64	1.69	335
Intermediate IBD	388.000	45	4.89	2.68	1.77	320

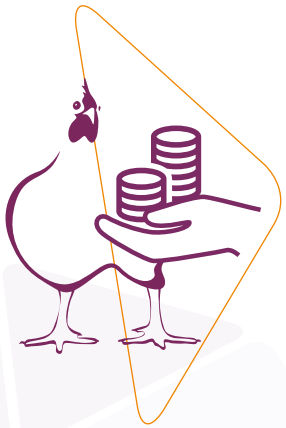


Performance Results



Condemnation Results

TRANSMUNE®
Intermediate IBD



ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

the extra revenues per 1,000 birds would be +48€

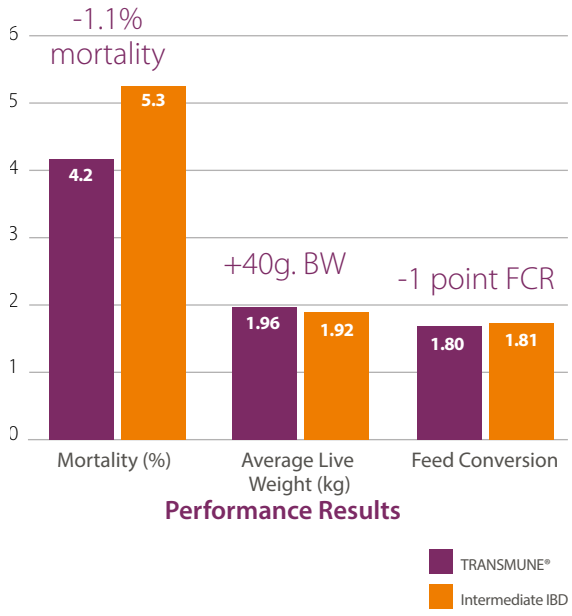
Portugal

STUDY DESIGN

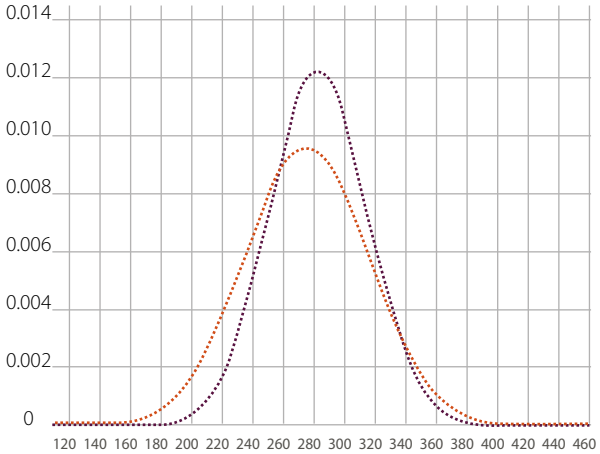
- ***GROUP 1:***
  4,868,205 BROILERS
  TRANSMUNE®
  SUBCUTANEOUSLY
  AT DAY 1

- ***GROUP 2:***
  10,238,709 BROILERS
  INTERMEDIATE IBD
  IN DRINKING WATER
  AT 10 AND 15 DAYS OF AGE

RESULTS & CONCLUSIONS



The Efficiency Index was more homogeneous in the TRANSMUNE® group



ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

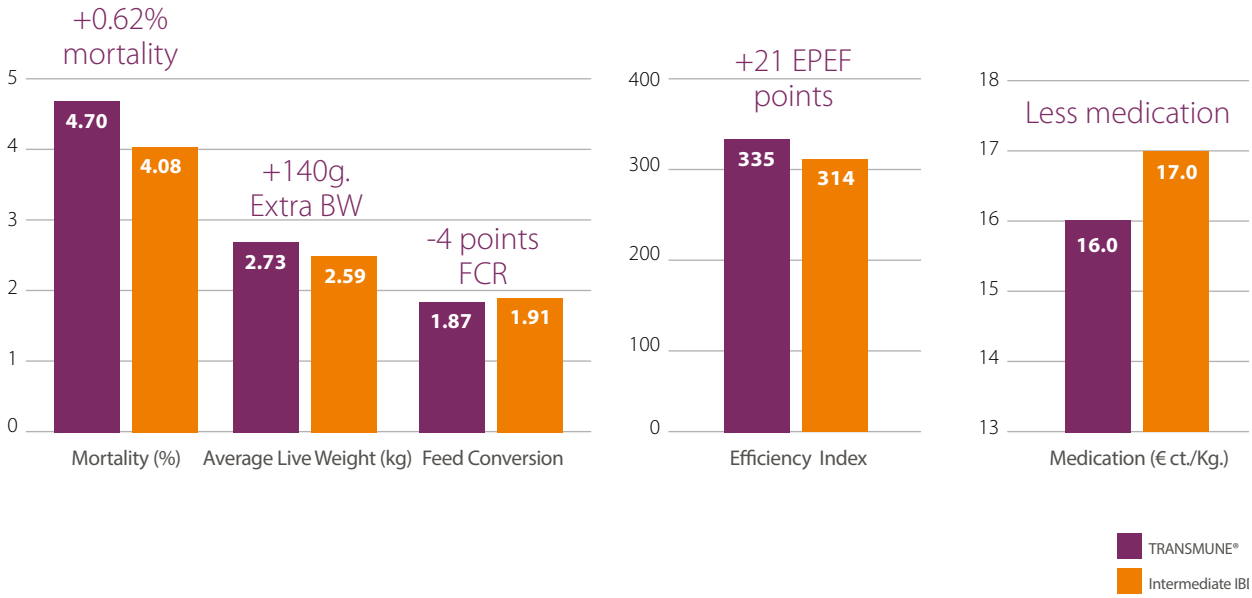
the extra revenues per 1,000 birds would be +31€

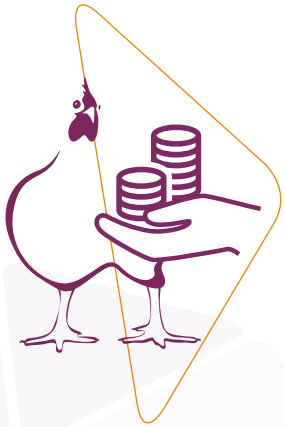
Spain

STUDY DESIGN

- ***GROUP 1:***
  TRANSMUNE®
  SUBCUTANEOUSLY
  AT DAY 1
- ***GROUP 2:***
  INTERMEDIATE IBD
  IN DRINKING WATER
  AT 10 AND 15 DAYS OF AGE
- *300,000 DAY-OLD CHICKS PER WEEK,*
  2 GROUPS, 4 FARMS EACH.
  ROSS 308 AND COBB 500 BREEDS

RESULTS & CONCLUSIONS





ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

the extra revenues per 1,000 birds would be +72€

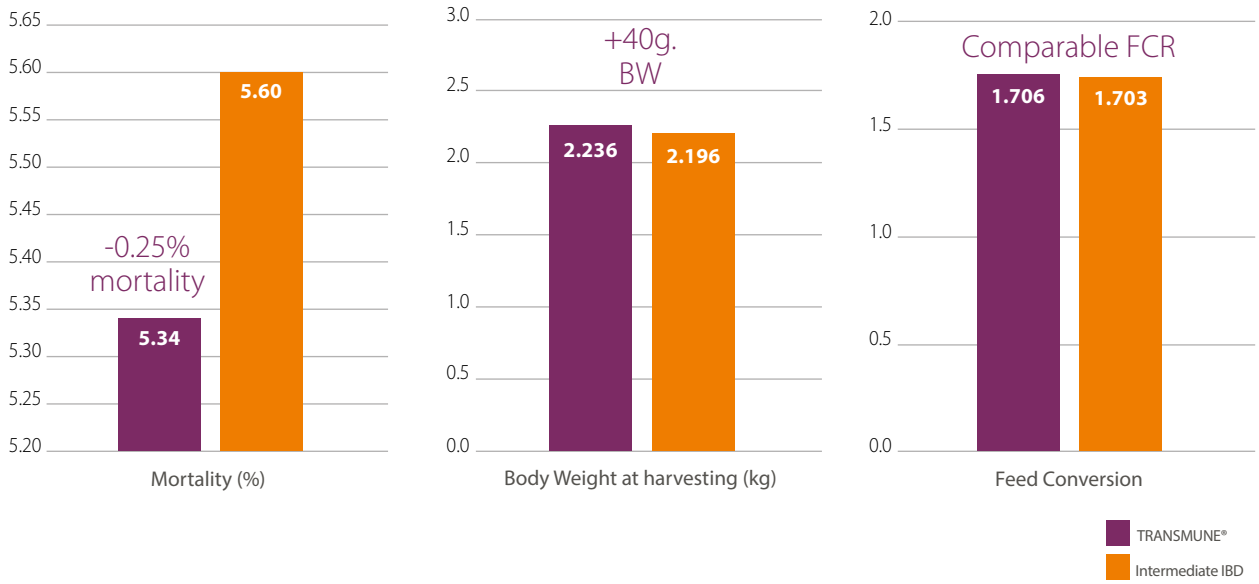
India

STUDY DESIGN

- ***GROUP 1:***
  386,000 BIRDS
  TRANSMUNE® SUBCUTANEOUSLY
  AT DAY 1

- ***GROUP 2:***
  1,580,000 BIRDS
  INTERMEDIATE PLUS VACCINE STRAIN
  INTRAOCULAR VACCINATION
  AT 12 DAYS OF AGE

RESULTS & CONCLUSIONS



ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

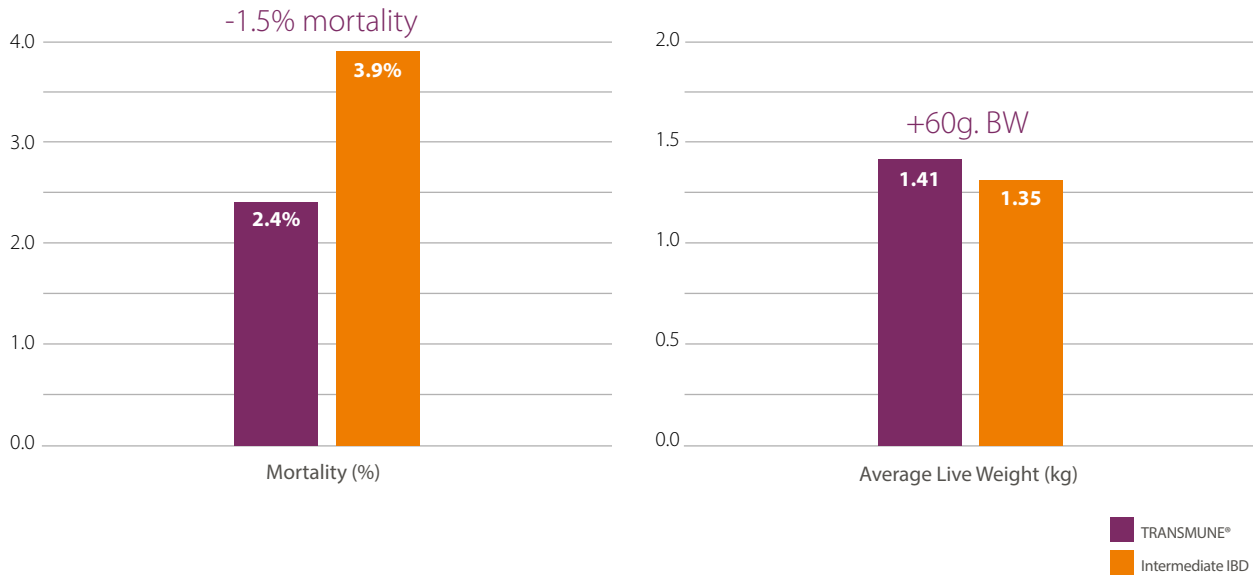
the extra revenues per 1,000 birds would be +17€

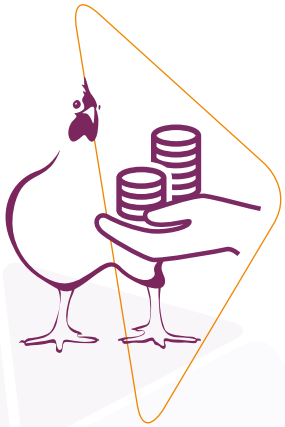
Indonesia

STUDY DESIGN

- *42,000 DAY-OLD CHICKS*
  2 GROUPS
- ***GROUP 1:***
  21,000 BIRDS
  TRANSMUNE® SUBCUTANEOUSLY
  AT DAY 1
- ***GROUP 2:***
  21,000 BIRDS
  INTERMEDIATE PLUS VACCINE STRAIN
  IN DRINKING WATER
  AT 12 DAYS OF AGE

RESULTS & CONCLUSIONS





ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, and body weight),

the extra revenues per 1,000 birds would be +36€

Brazil

STUDY DESIGN

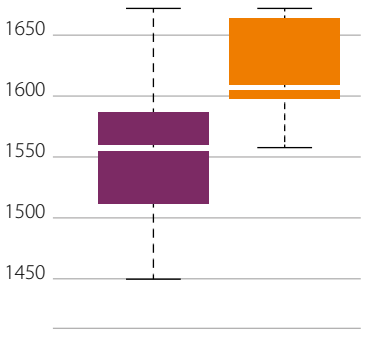
- *22 FLOCKS*
  660,000 DAY-OLD CHICKS,
  2 GROUPS
- ***GROUP 1: 17 FLOCKS***
  (510,000 CHICKS)
  TRANSMUNE®
  SUBCUTANEOUSLY
  AT DAY 1
- ***GROUP 2: 5 FLOCKS***
  (150,000 CHICKS)
  rHVT-IBD
  VACCINATION
- *SLAUGHTER AT*
  47 DAYS OF AGE

RESULTS & CONCLUSIONS

Vaccine	Feed conversion*	Adjusted feed conversion*	Slaughter weight (kg)	Mortality (%)	Average Daily gain	Condem-nation (%)*	Airsac-culatis (%)*	EPEF*
TRANSMUNE®	1.625	1.555	3.130	2.55	66.65	0.17	0.35	400
Control Group	1.692	1.621	3.136	3.4	66.01	0.37	1.47	380

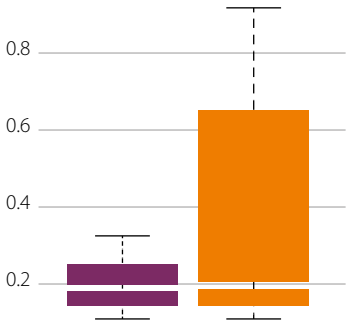
**Statistic difference*

-7 pts FCR



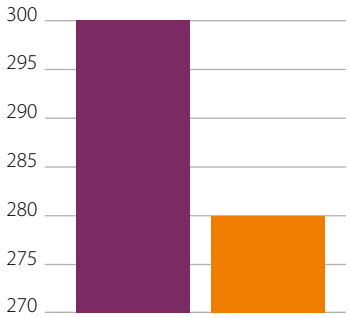
Feed conversion

Decrease of condemnation & airsacculatis



Condemnation rate and airsacculatis (%)

+20 points EPEF



Efficiency index

TRANSMUNE®
Control

ECONOMIC EVALUATION

Based on the cost benefits calculation
(-7 pts FCR, +0.85% viability, less condemnations),

the extra revenues per 1,000 birds would be +71€

Egypt

STUDY DESIGN

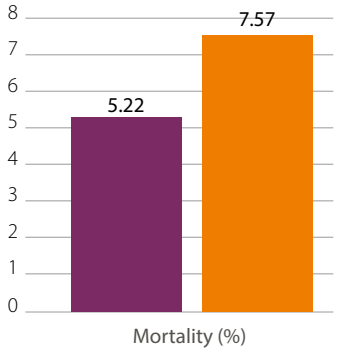
- *448,850 DAY-OLD CHICKS, 2 GROUPS*
- ***GROUP 1:*** *(224,500 CHICKS) TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2:*** *(224,350CHICKS) CONTROL GROUP rHVT-IBD*
- *SLAUGHTER AT GROUP 1: 29,6 DOA GROUP 2: 31,1 DOA*

RESULTS & CONCLUSIONS

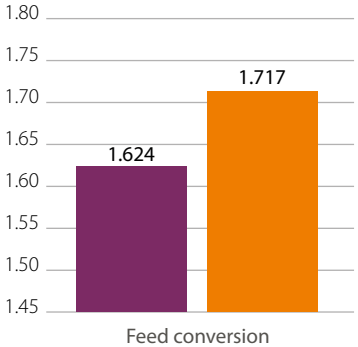
Vaccine	Slaughter weight (kg)*	Mortality (%)*	Feed conversion*	EPEF*
TRANSMUNE®	1.839	5.22	1.624	360
Control Group	1.705	7.57	1.717	295

**Statistic difference*

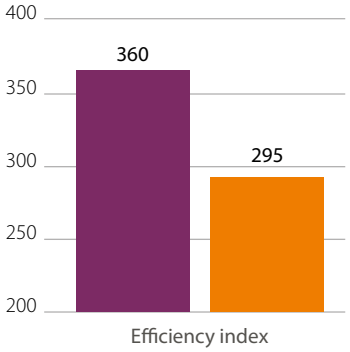
+2.35% viability

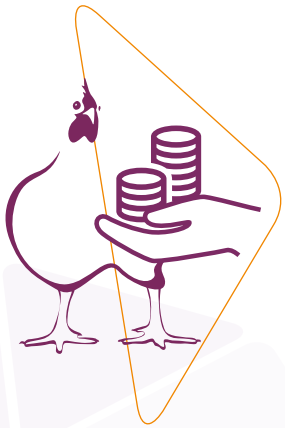


+9 points FCR



Improvement of EPEF





ECONOMIC EVALUATION

Based on the cost benefits calculation
(-2.35% mortalituy, +134g of body weight, -9 pts FCR)

the extra revenues per 1,000 birds would be +90€

TRANSMUNE® vs HVT IBD vaccines

Brazil

STUDY DESIGN

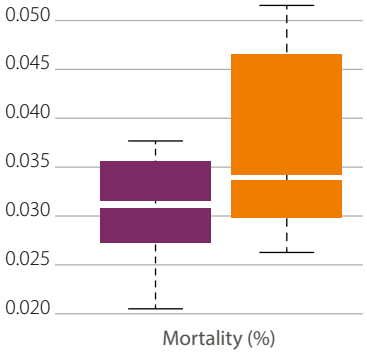
- *18 FLOCKS 950,000 BROILERS, 2 GROUPS*
- ***GROUP 1: 11 FLOCKS** (816,000 CHICKS) TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2: 7 FLOCKS** (134,000 CHICKS) rHVT IBD VACCINATION*
- *SLAUGHTER AT GROUP 1 : 43 DOA GROUP 2: 42 DOA*

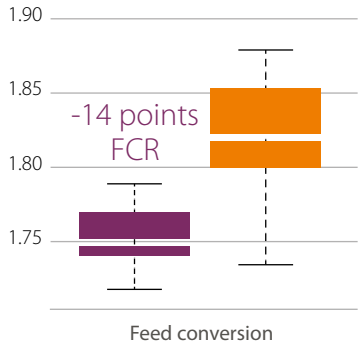
RESULTS & CONCLUSIONS

Vaccine	Feed conversion*	Adjusted feed conversion*	Slaughter weight (kg)*	Mortality (%)	Average daily gain*	EPEF*
TRANSMUNE®	1.766	1.707	2.431	2.20	55.58	305
Control Group	1.922	1.849	2,180	3.77	51.90	274

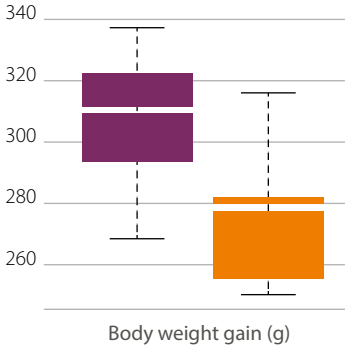
**Statistic difference*

+0.57% livability





+251g higher



TRANSMUNE®
HVT IBD group

ECONOMIC EVALUATION

Based on the cost benefits calculation
(-7 pts FCR +0.85% viability, less condemnations),

the extra revenues per 1,000 birds would be +171€

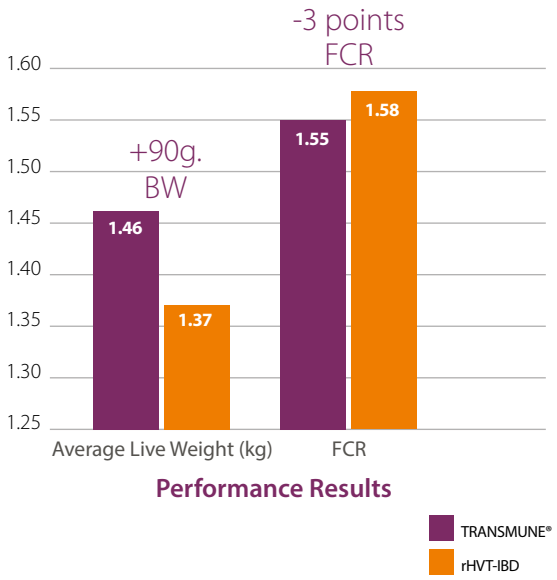
TRANSMUNE® IBD

Arabic Peninsula

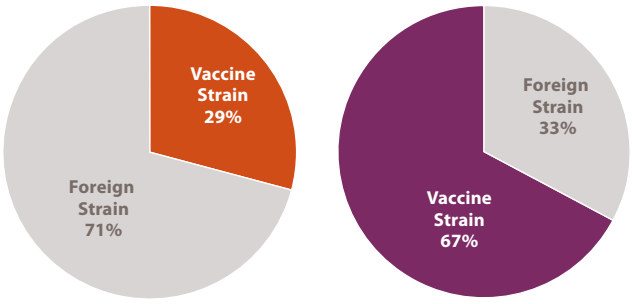
STUDY DESIGN

- ***GROUP 1:*** *COMPETITOR VECTOR IBD PRODUCT, SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2:*** *TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- *8 SAMPLES PER HOUSE AT 21, 28 AND 35 DAYS OF AGE (BLOOD, BURSA, SPLEEN)*
- *SLAUGHTER AT 30-32 DAYS*

RESULTS & CONCLUSIONS



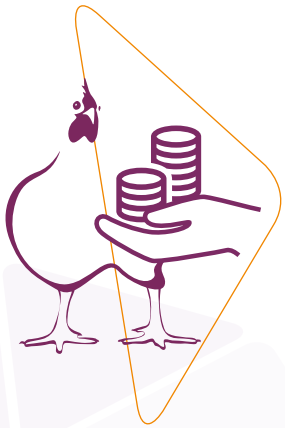
Performance Results



Protection against IBDV colonization

The rHVT-IBD group could not protect against IBDV colonization in the bursa of Fabricius in 71% of the bursas investigated. On the opposite, TRANSMUNE® could block colonization in 67% of the bursas in just 1 cycle of application.

Applying TRANSMUNE® for more than 1 cycle will increase the rate of reisolation of the Winterfield 2512 strain in the bursas. Having a unique quality control and balance of antigen-antibodies, the Winterfield 2512 strain is expected, after some cycles, to colonize the bursae and STOP the Gumboro cycle.



ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

the extra revenues per 1,000 birds would be +45€

TRANSMUNE® vs VP2 killed vaccines

China

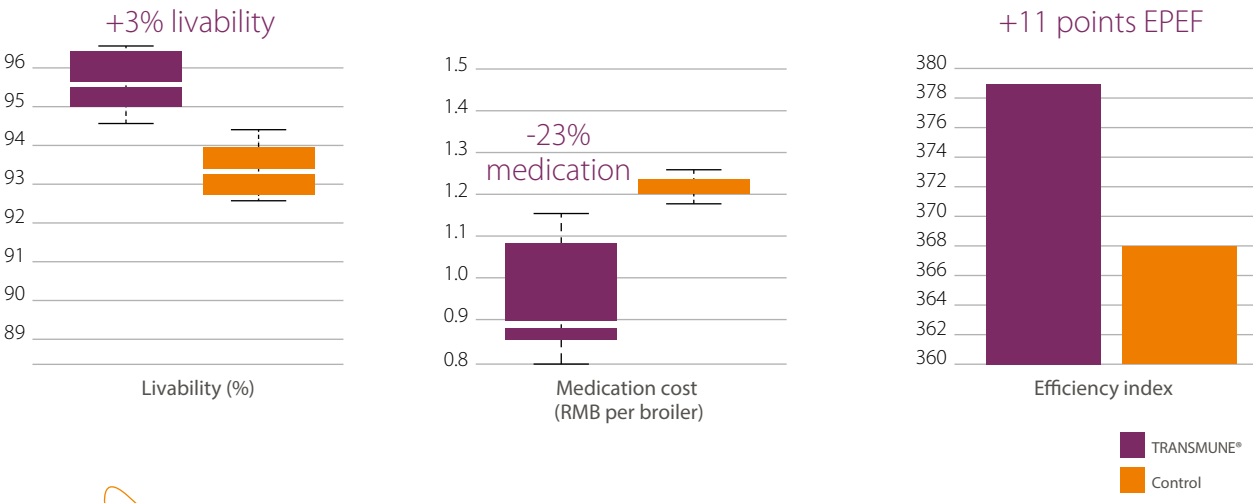
STUDY DESIGN

- *12 FLOCKS, 360,000 BROILERS, 2 GROUPS*
- ***GROUP 1: 6 FLOCKS*** *(180,000CHICKS) TRANSMUNE® SUBCUTANEOUSLY*
- ***GROUP 2: 6 FLOCKS*** *CONTROL GROUP (180,000 CHICKS) VP2 killed*
- *SLAUGHTER AT 44. DAYS OF AGE*

RESULTS & CONCLUSIONS

Vaccine	Slaughter weight (kg)	Livability (%)*	Average daily gain (g/day)	Medication cos (RMB per broiler)*	EPEF
TRANSMUNE®	2.74	95.6	63.7	0.95	379
Control Group	2.82	92.6	62.7	1.24	368

**Statistic difference*



ECONOMIC EVALUATION

Based on the cost benefits calculation +3% livability, -23% medication, +11pts EPEF),

the extra revenues per 1,000 birds would be **+83,70€**

TRANSMUNE® IBD

Egypt

STUDY DESIGN

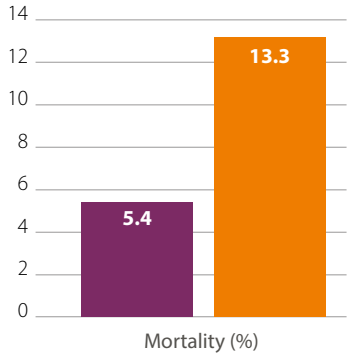
- *18 FLOCKS 332,900 BROILERS, 2 GROUPS*
- ***GROUP 1: 9 FLOCKS** (1 900 000 CHICKS) TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2: 9 FLOCKS** (420 000 CHICKS) OTHER IMMUNE COMPLEX VACCINATION*
- *SLAUGHTER AT 26 DAYS OF AGE*

RESULTS & CONCLUSIONS

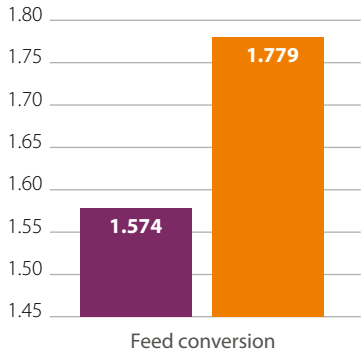
Vaccine	Slaughter weight (kg)*	Mortality (%)*	Feed conversion*	EPEF*
TRANSMUNE®	1.935	5.43	1.571	354
Control Group	1.385	13.27	1.779	240

**Statistic difference*

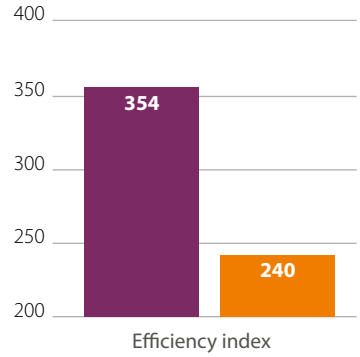
+7,9% livability

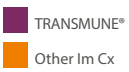


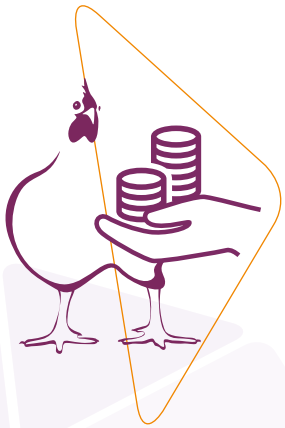
-20 points FCR



+114 points EPEF







ECONOMIC EVALUATION

Based on the cost benefits calculation
(-7.9% mortality, -20 pts feed conversion, +114 pts EPEF)

the extra revenues per 1,000 birds would be +382€

Venezuela

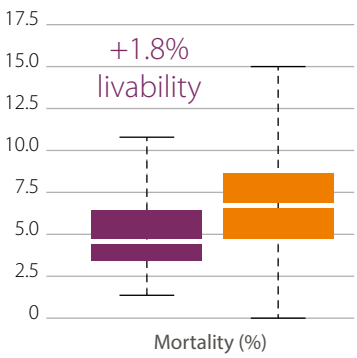
STUDY DESIGN

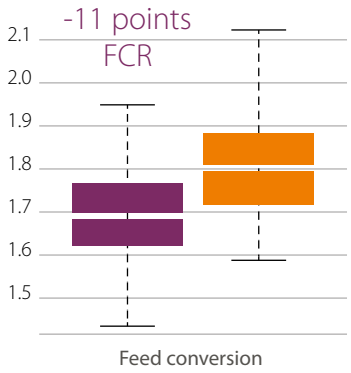
- *2122 FLOCKS, 3,660,0000 BROILERS, 2 GROUPS*
- ***GROUP 1: 61 FLOCKS*** *(1,830,000 CHICKS) TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2: 61 FLOCKS*** *(41,830,000 CHICKS) OTHER IMMUNE-COMPLEX VACCINATION*
- *SLAUGHTER AGE: GROUP 1: 37 DOA GROUP 2: 39,5 DOA*

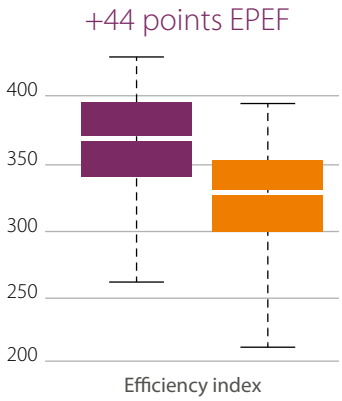
RESULTS & CONCLUSIONS

Vaccine	Feed conversion*	Adjusted feed conversion*	Slaughter weight (kg)	Mortality (%)*	Average daily gain (g/day)*	EPEF*
TRANSMUNE®	1.661	1.702	2.369	5.17	63.9	366
Control Group	1.74	1.81	2.368	6.97	59.98	322

**Statistic difference*







TRANSMUNE®
Other immune Complex

ECONOMIC EVALUATION

Based on the cost benefits calculation
(-1.8% mortality, -11 pts food conversion, +44 pts EPEF)

the extra revenues per 1,000 birds would be +90€

Brazil

STUDY DESIGN

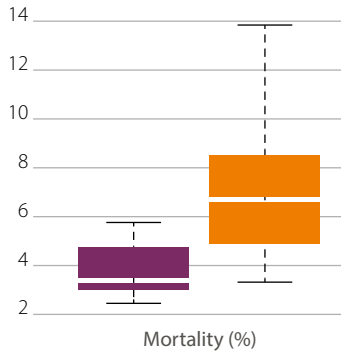
- *84 FLOCKS, 2,520,000 BROIILERS, 2 GROUPS*
- ***GROUP 1: 12 FLOCKS** (360,000 CHICKS) TRANSMUNE® SUBCUTANEOUSLY AT DAY 1*
- ***GROUP 2: 72 FLOCKS** (2,1160,000 CHICKS) OTHER IMMUNE-COMPLEX VACCINATION*
- *SLAUGHTER AT 42 DAYS OF AGE*

RESULTS & CONCLUSIONS

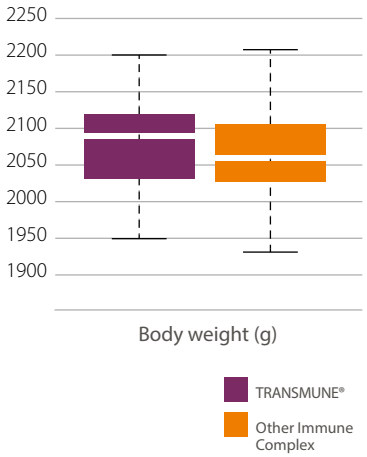
Vaccine	Slaughter weight (kg)	Mortality (%)*	AVERAGE DAILY GAIN
TRANSMUNE®	2.082	4.06	49.57
Control Group	2.064	6.89	49.14

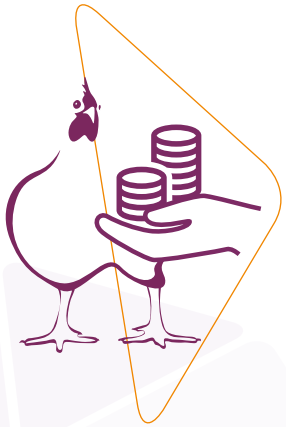
**Statistic difference*

+2.83% livability



+18% BW





ECONOMIC EVALUATION

Based on the cost benefits calculation (-2.83% mortality, +18g body weight),

the extra revenues per 1,000 birds would be +32€

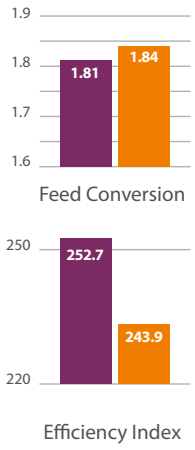
Colombia

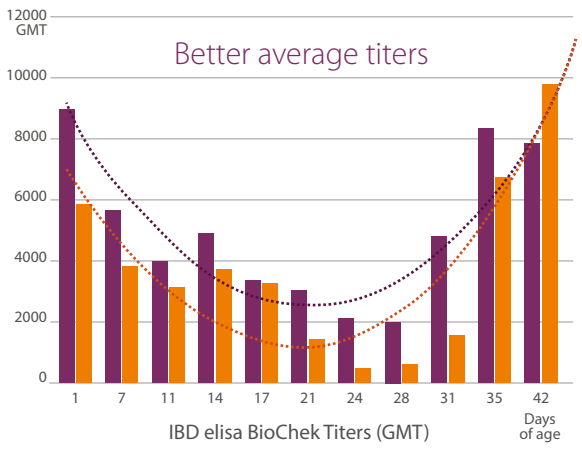
STUDY DESIGN

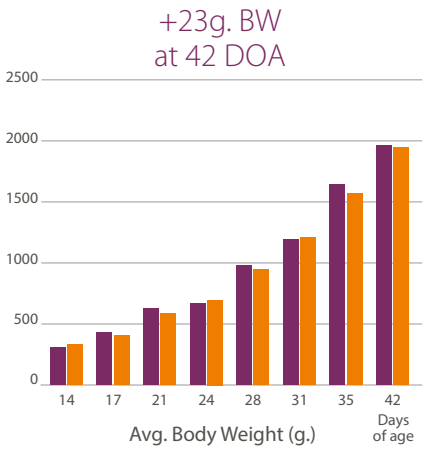
- ***2 GROUPS:***
  TRANSMUNE® VS.
  IMMUNE-COMPLEX A
  (CONTEMPORANEOUS)
- *VACCINATION*
  SUBCUTANEOUSLY
  AT DAY 1

RESULTS & CONCLUSIONS

Vaccine	BW (g)	Mortality (%)	Age of slaughter (days)	FCR	Efficiency Index
TRANSMUNE®	1.913	3.17	40.5	1.81	252.7
Immune-complex A	1.894	3.09	40.9	1.84	243.9







ECONOMIC EVALUATION:

Based on the cost benefits calculations (mortality, body weight and FCR),

the extra revenues per 1,000 birds would be +20€

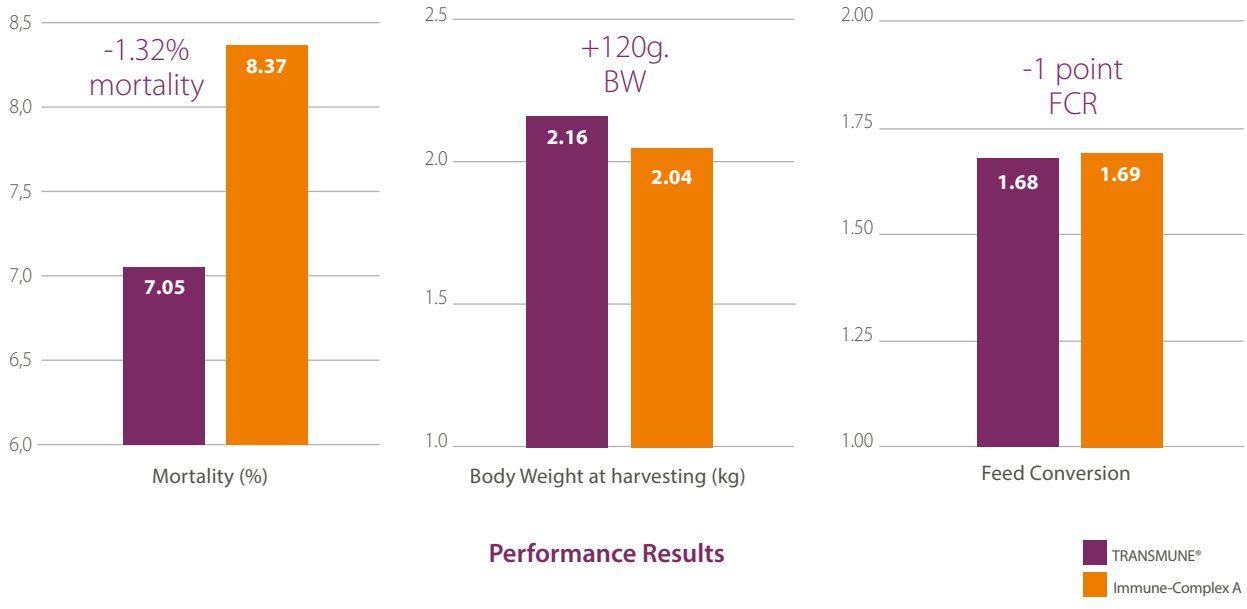
India

STUDY DESIGN

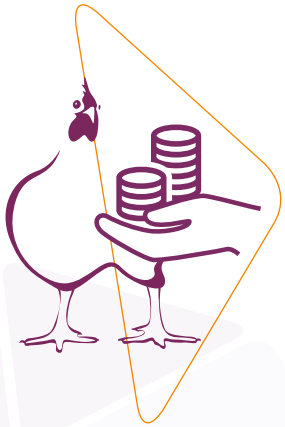
- ***GROUP 1:***
  287,000 BIRDS
  TRANSMUNE® SUBCUTANEOUSLY
  AT DAY 1

- ***GROUP 2:***
  358,000 BIRDS
  OTHER IMMUNE-COMPLEX VACCINE
  SUBCUTANEOUSLY
  AT DAY 1

RESULTS & CONCLUSIONS



Performance Results



ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

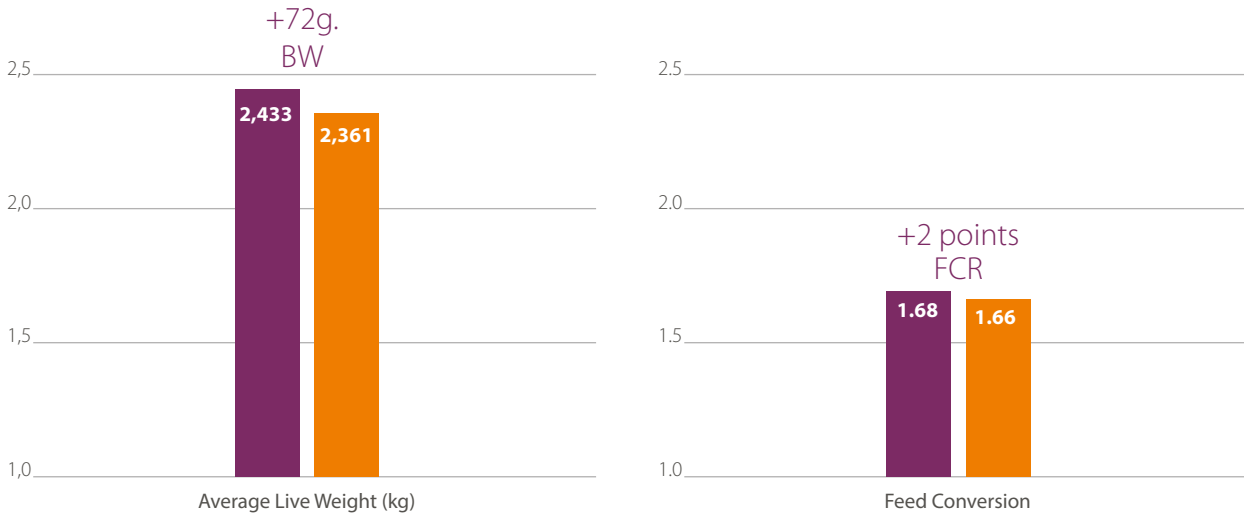
the extra revenues per 1,000 birds would be +59€

Russia

STUDY DESIGN

- ***GROUP 1:***
  133,708 BIRDS
  TRANSMUNE® SUBCUTANEOUSLY
  AT DAY 1
- ***GROUP 2:***
  159,597 BIRDS
  HOT LIVE VACCINE IN DRINKING WATER
  AT 16 DAYS OF AGE

RESULTS & CONCLUSIONS



Performance Results

TRANSMUNE®
Hot live strain

ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

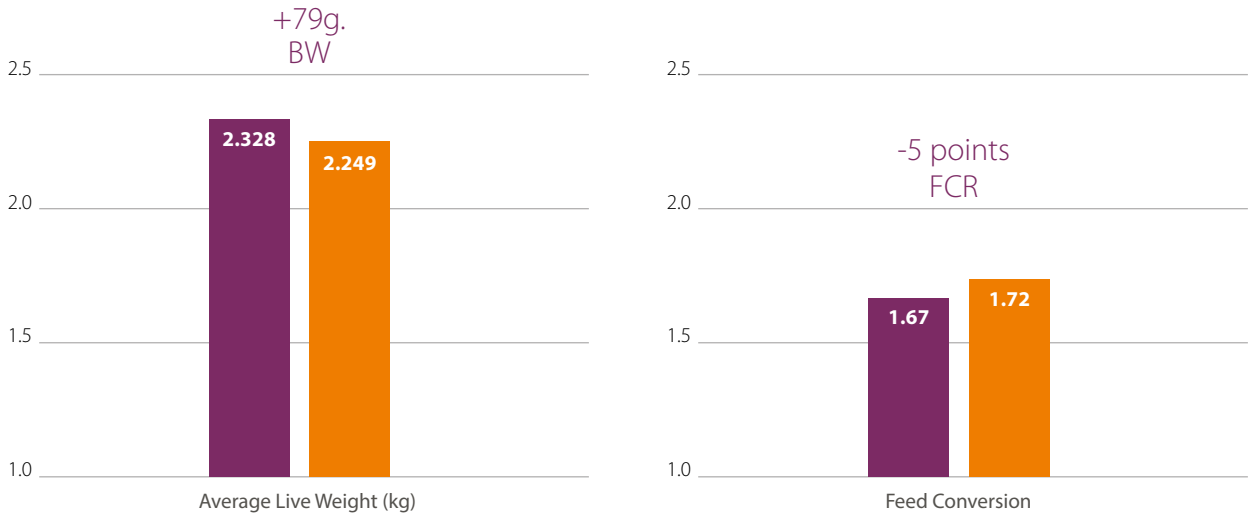
the extra revenues per 1,000 birds would be +1€

Russia

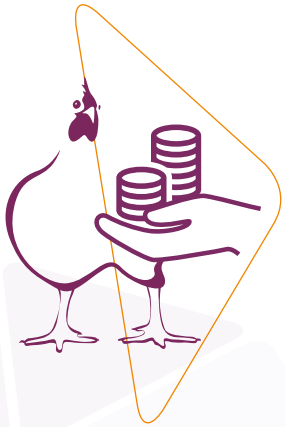
STUDY DESIGN

- ***GROUP 1:***
  110,624 BIRDS
  TRANSMUNE® SUBCUTANEOUSLY
  AT DAY 1
- ***GROUP 2:***
  164,723 BIRDS
  HOT LIVE VACCINE IN DRINKING WATER
  AT 9 AND 16 DAYS OF AGE

RESULTS & CONCLUSIONS



Performance Results



ECONOMIC EVALUATION

Based on the cost benefits calculations (mortality, body weight and FCR),

the extra revenues per 1,000 birds would be +52€

Summary of profitability

To summarize, advanced technology like the Egginject in-ovo equipment and new technology vaccines, like TRANSMUNE®, are becoming more popular among hatcheries, since they enable fast, safe and welfare friendly vaccination of chicken embryos. The time between hatch and delivery to the farms is reduced, and less handling is needed in the field due to extra vaccinations. This vaccination application needs specific high quality equipment, close support, maintenance and monitoring of correct vaccine application. It also needs specific vaccines which are able to overcome the presence of MDA, while inducing an active immunity. TRANSMUNE® is able to do this. At the same time, profitability is the lead driver for change in the industry nowadays.

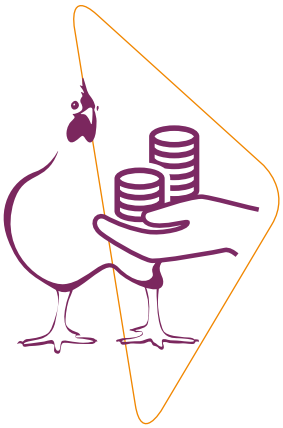
TRANSMUNE® has demonstrated in several countries that it reduces disease pressure, profitability loss and condemnations, linked to clinical or subclinical IBD, to a value range of 41€/1,000 birds . An estimated amount of 13 billion broiler chickens were vaccinated with TRANSMUNE® in 2018, thus confirming the economic advantages of hatchery vaccination with TRANSMUNE®.

Technical Parameters	Value/000 Birds	Value/100 M. Birds
0.01 FCR	6 €/000 birds*	600 K€*
10 g. BW	3.20 €/000 birds*	320 K€*
1% Mortality	11 €/000 birds*	1100 K€*

Table 1. Summary of the economic results in the field cases previously described.

* This value has been calculated from Ceva field data and might vary depending on IBD disease pressure and region

Disclaimer: Study results disclosed through the present document are intended to report the results that have been obtained in the specific conditions of performance of the Study and were known at the time of the Study's completion. Ceva does not make any warranty, expressed or implied, with respect to results herein disclosed and assume no liability for any party's use, or the results of such use, of any information contained in this document.



IMPACT IN PERFORMANCE RESULTS

Country	Mortality (%)	BW (extra g./bird)	FCR (points)	Results (€/1000 birds)
France	-0.63	+80	-6	+86
Ireland	-2.18	+100	-6	+40
Malaysia	-0.35	+30	-2	+19.60
Brazil (1)	-1.56	-40	-8	+48
Portugal	-1.1	+40	_	+31
Spain	+0.62	+140	_	+72
India (1)	-0.25	+40	-3	+17
Indonesia	-1.5	+60	_	+36
Brazil (2)	-0.85	-6	-7	+71
Egypt (1)	-2.35	+134	-9	+90
Brazil (3)	-0.57	+251	-14	+171
Arabic Peninsula	_	+90	-3	+45
China	-3	-80	_	+83.70
Egypt (2)	-7.9	+550	-20	+382
Venezuela	-1.8	+1	-11	+90
Brazil (4)	-2.83	+18	_	+32
Colombia	+0.08	+23	-3	+20
India (2)	-1.32	+120	-1	+59
Russia (1)	_	+72	-2	+1
Russia (2)	_	+79	-5	+52

*Table 2. Values used to evaluate the economic return of the field cases previously described: BW: 2Kg. ; F.C.R.: 1.6 ; Feed price: 0,3€/Kg. Live Bird Price: 0.8€/Kg. ; *Additional profit.*

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TRANSMUNE® IBD

of peace of mind:
stops the Gumboro cycle

of consistency:
flocks with uniform results

of trust: strong partnership between producers & Ceva year after year

TRANSMUNE® IBD

STOP THE GUMBORO CYCLE

Transmune® stops reinfection and protects against all IBD virus strains

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