Edema Disease – prevalence, diagnostics and control

Short review on *Escherichia coli*

Characteristics of *Escherichia coli* I

Family: *Enterobacteriacae*

Rod-shaped, gram-negative, facultative anaerobe

Are found everywhere and can survive well in the environment

Can be zoonotic

Classification is based on

- Adhesion factors such as fimbriae
- Other surface proteins
- Toxins produced such as LT

Characteristics of *Escherichia coli* II

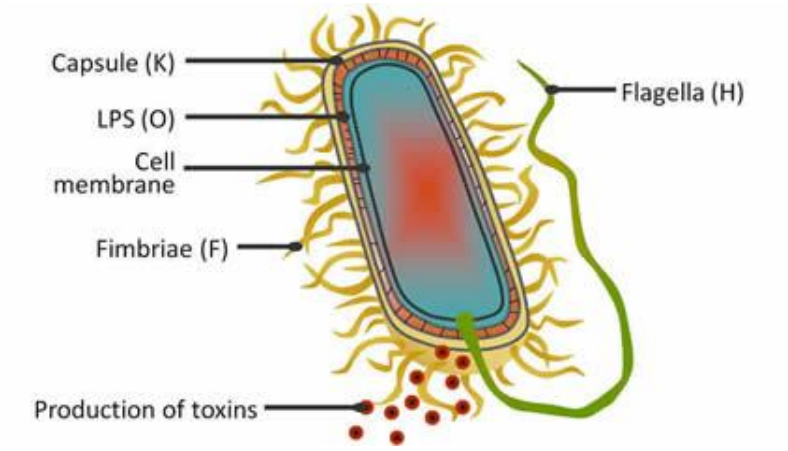
Historically: O:K:H-Seroformula

Based on: Slide agglutination with antisera

What can be detected:

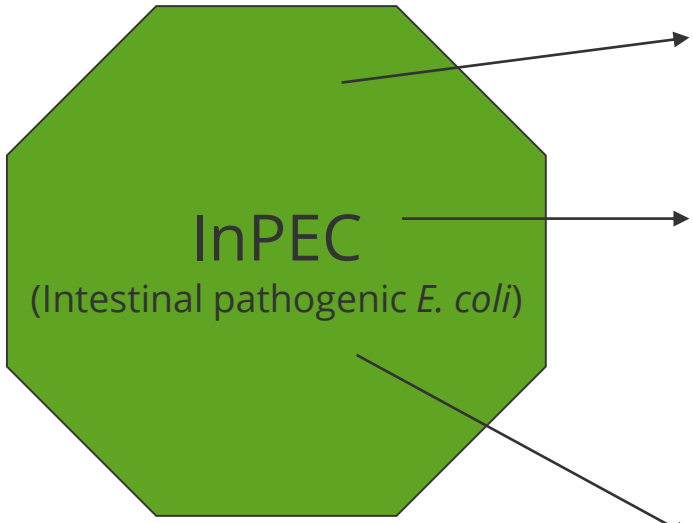
O-Antigens: somatic proteins
H-Antigens: flagellar proteins
K-Antigens: (micro-)capsular proteins
F-Antigens: fimbrial proteins

Toxins: Endo-, Entero- and Cytotoxins



http://www.ecl-lab.com/en/ecoli/index.asp

Escherichia coli –Infections in weaned pigs



ETEC

EPEC

STEC
(shigatoxin encoding *E. coli*)

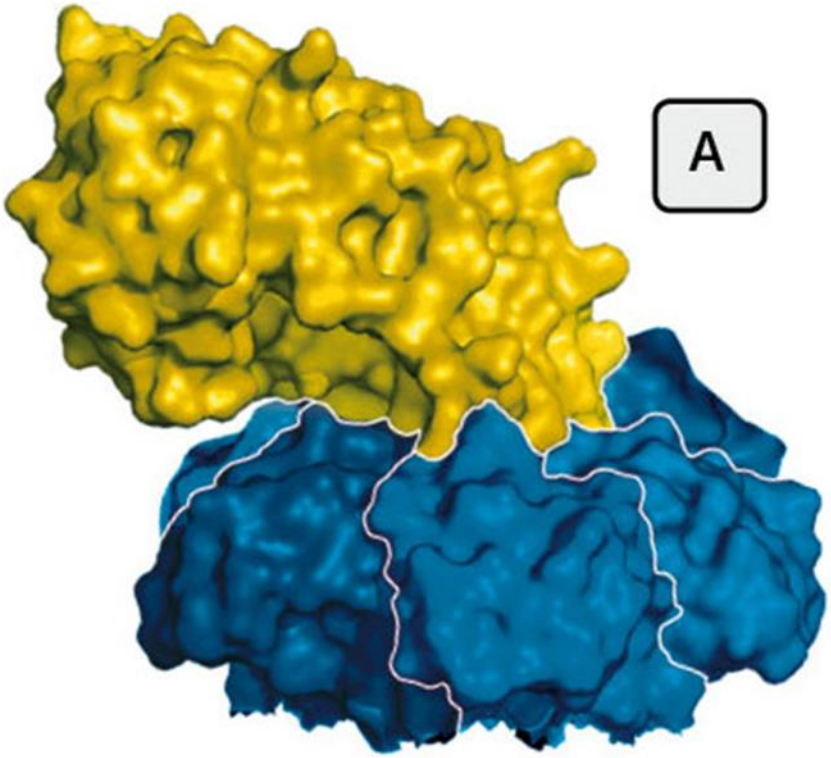
post-weaning diarrhoea (PWD)

Edema Disease

Adhesion factors: F18 fimbriae, AIDA-I
Toxin: **Stx2e**
O-Antigens (examples): 138, 139, 141

IDT

Shigatoxin 2e



A subunit is responsible for the cytotoxic effect
➞ damage of capillaries

B subunit is responsible for binding to the receptor and uptake in target cell

Pathogenesis of Edema Disease

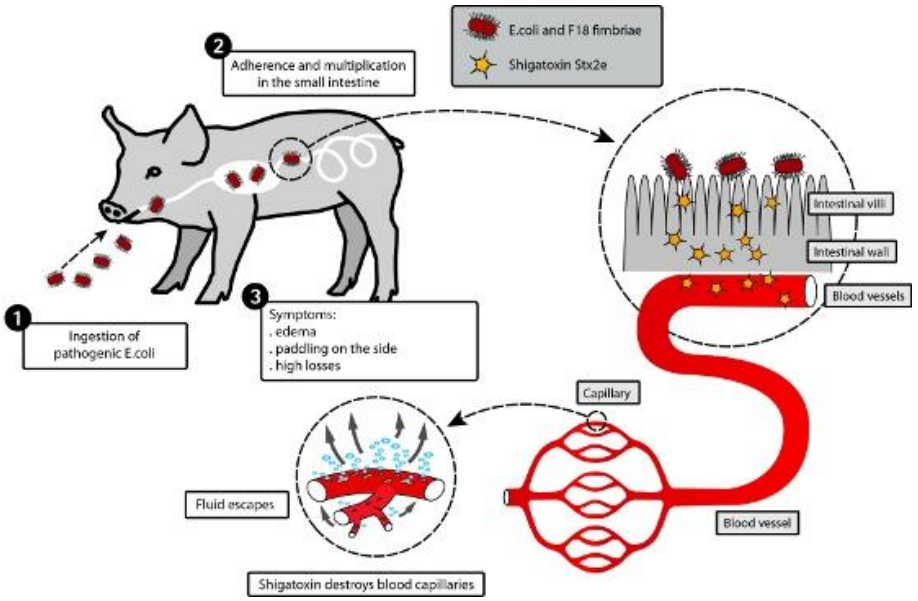
Occurrence: worldwide

Pathogen: certain strains of *E. coli* of the pig (STEC)

Effected animals (mainly): piglets at 1 – 3 weeks after weaning, but also later!

Virulence factors:

(F18 fimbriae)
Shigatoxin 2e (Stx2e)



Damage of the capillary vessels ⟶ Edema

Prevalence of STEC in Germany 2013-2017

Year	No. of farms	No. of positives	% positives
2013	138	54	39.1
2014	121	47	38.8
2015	140	43	30.7
2016	158	66	41.8
2017	71	26	36.6
Sum	628	236	37.6

Prevalence STEC worldwide

Country	Source	Prevalence in %
France	Leneveu et al. 2017	65.0
Denmark	Frydendahl et al. 2002	16.4
Germany	Barth et al. 2007	11.1
Germany	Sting and Stermann 2008	19.0
Portugal	VETDIAGNOS 2014	54.0
USA	Zhang et al. 2007	20.0
USA	Torrison et al. 2011	24.0
Korea	Choi et al. 2002	40.7
Japan	Fukuyama et al. 2003	10.7
China	Cheng et al. 2006	35.0
Vietnam	Cu Huu Phu et al. 2006	75.5

Diagnostics: how to find STEC?

Clinical signs

Sources: Field Station for Epidemiology Bakum (University of Veterinary Medicine Hannover); IDT Biologika GmbH

How to select pigs for sampling:

1. Weaners in the 2nd week after weaning (but may depend on the farm > when will it occur most likely)
2. Not treated with antimicrobials
3. Make the impression, that they have eaten well after a period of „starvation“
4. Have one or several of the clinical signs mentioned above
5. If no obvious clinical signs are present, then those that do not seem “fit”, but also do not have fever

Okay, the pigs are selected – now what?

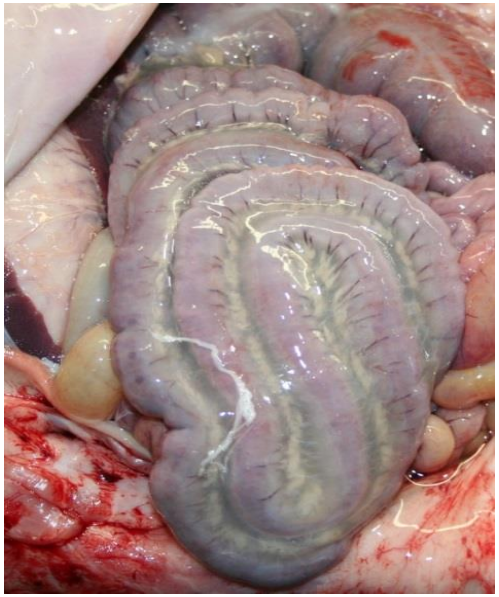
We prefer/recommend samples to be taken from necropsies.

Why?

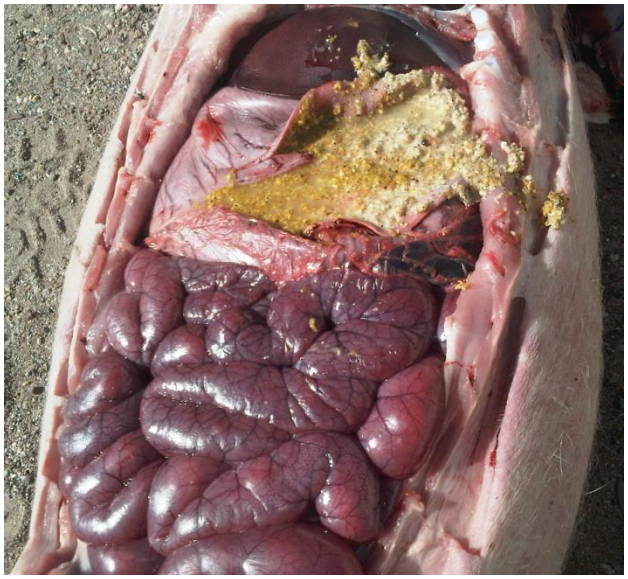
- The gut seems to be the best sample to detect STEC
- You have the „complete picture“ in gross pathology
- Samples for differential diagnostics (*S. suis*, *H. parasuis*) can be taken at the same time

Of course, fecal samples are also possible!

Gross pathology

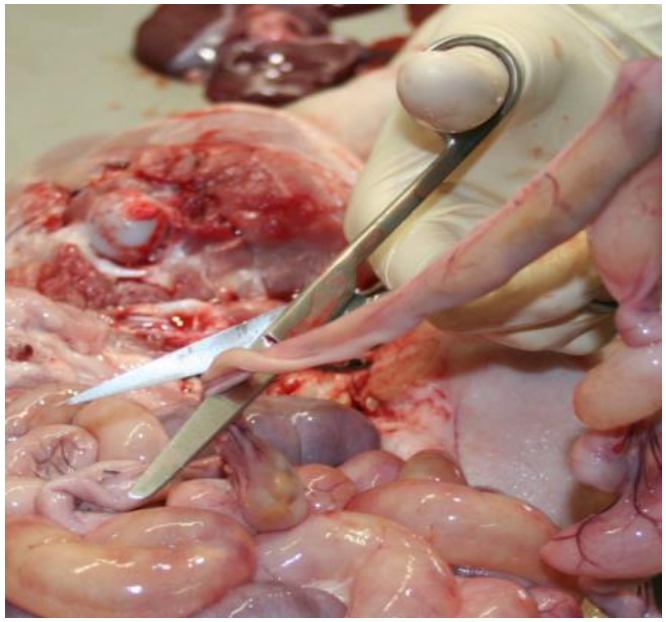


Source: Field Station for Epidemiology Bakum (University of Veterinary Medicine Hannover)



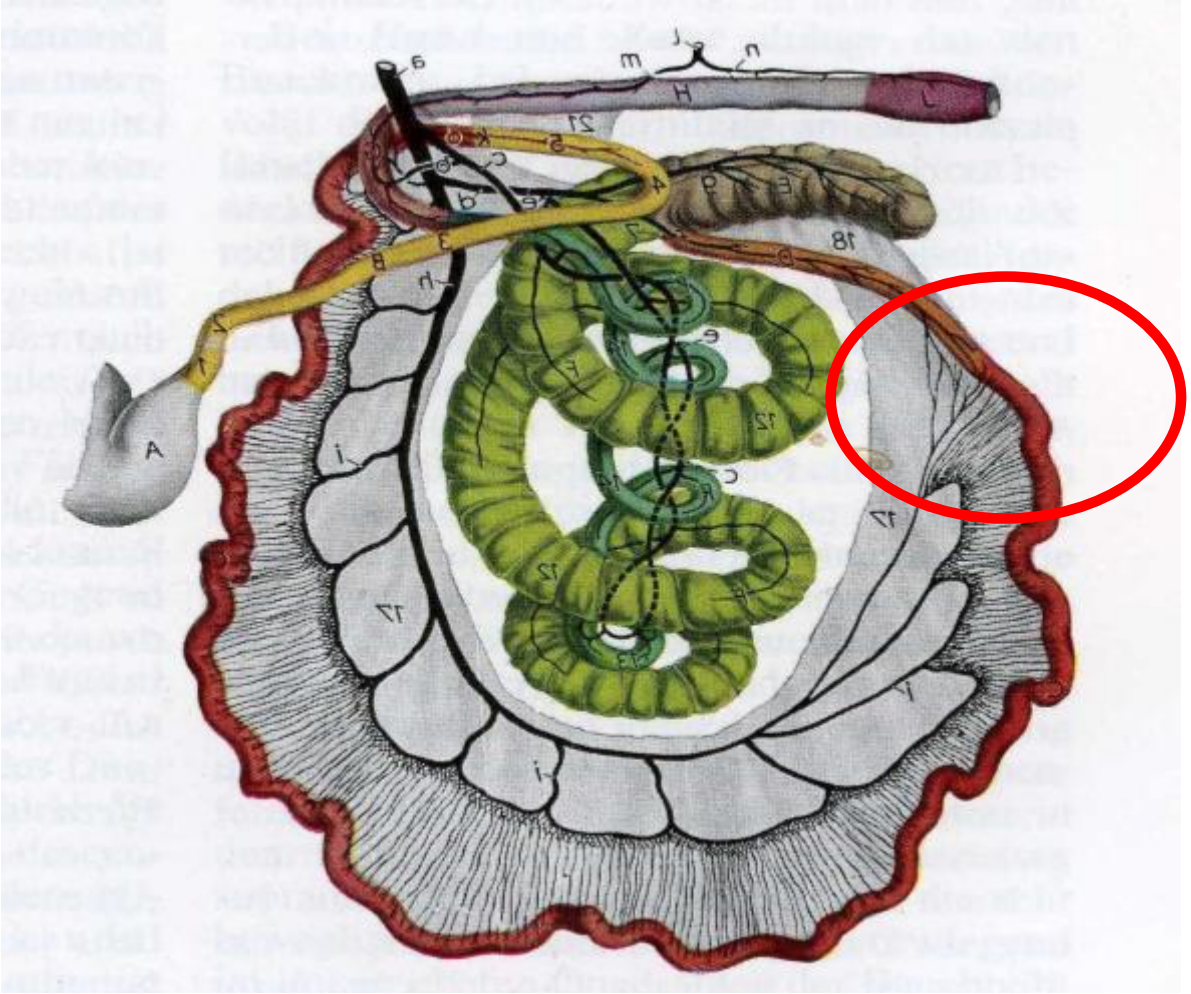
Source: Jose Joaquìn Sanchez, JYSAPS

Sampling for STEC



Source: Field Station for Epidemiology Bakum
(University of Veterinary Medicine Hannover)

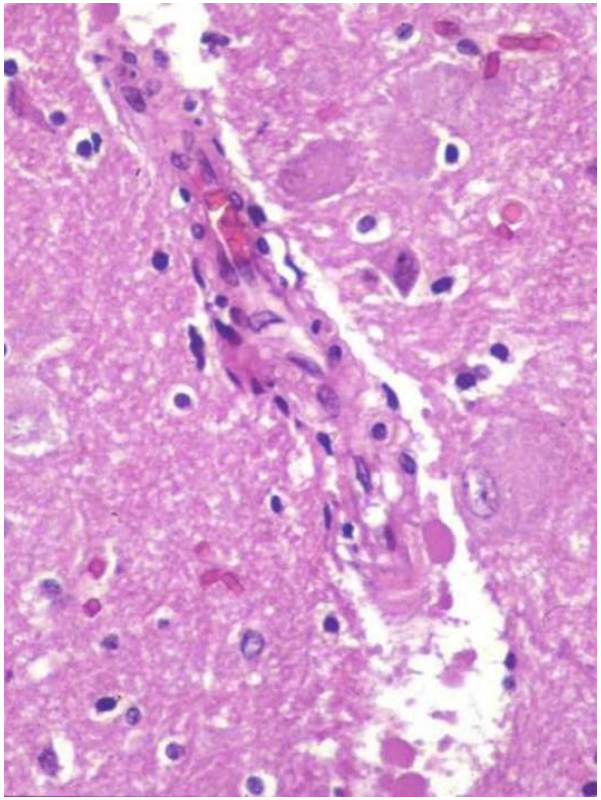
Where to sample:



Source:
Nickel, Schummer, Seiferle
Lehrbuch der Anatomie der Haussäugetiere, Band II s. 124.

Histopathology

Polioencephalomalacia of the brain stem



Perivascular oedema

Source: CReSA

The STEC Check-Kit

- 5 Amies Swabs/Vials
- Packaging material
- Cool pack

Remember – (Sample) size matters!

	Percentage of infected animals in the group					
	5 %		10 %		20 %	
	Confidence-Level					
Group size	90 %	95 %	90 %	95 %	90 %	95 %
100	36	44	20	25	10	13
200	40	50	21	26	10	13
300	42	53	21	27	10	13
750	44	57	22	28	10	13
3000	45	58	22	29	10	13

Modified after Canon and Roe, 1982

IDT

Our laboratory partner:

Justus-Liebig Universität
Institut für Hygiene
und
Infektionskrankheiten der
Tiere
Frankfurter Strasse 85-89
35392 Giessen
Germany

Methods for the analysis of Edema Disease

Bacterial culture: the basis

- Reason: identification of *Enterobacteriacae*
- Pro: simple, cheap
- Con: possible inhibition of growth due to antimicrobials, overgrowth with other bacteria if samples are not taken and/or stored correctly

Serotyping: the “old” method

- Reason: identify what type of *E. coli* there are
- Pro: simple, cheap
- Con: cannot identify all types of *E. coli*; culture may influence what factors are expressed; toxins not detected

Virulence factor analysis via Polymerase Chain Reaction (PCR): the “new” method

- Reason: identify what type of *E. coli* there are
- Pro: can identify more *E. coli* than the serotyping, looks for toxins as well
- Con: difficult, costly

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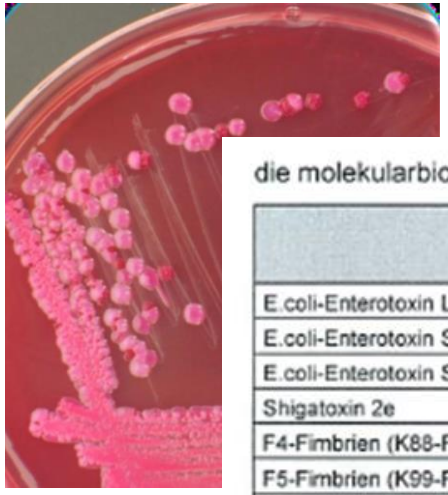
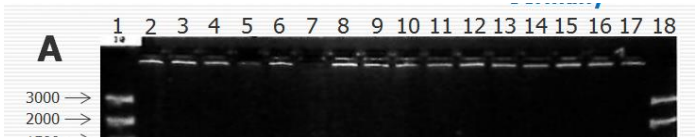
Microbiology and Molecular biology



Cultiv



Fax. : 04641-920320

Email: hygiene@vetmed.uni-giessen.de
www.vetmed.uni-giessen.de/hygiene

Gießen, 27.01.2014

Tgb.Nr.: P 288 + 289/14

Untersuchung von Darmproben von 2 Ferkeln **(15.10.2013STEC-CHECK Nr.: STECG682)**
Bestand: T. Asmussen, Gelting

die molekularbiologische Charakterisierung erbrachte mittels PCR folgende Ergebnisse:

	P 288 – Darm 1 E. coli Isolate 1 – 6	P 289 – Darm 2 E. coli var. haem. Isolate 1 – 4	P 289 – Darm 2 E. coli var. haem. Isolate 5 + 6
E.coli-Enterotoxin LT-1	negativ	negativ	negativ
E.coli-Enterotoxin ST-IP	negativ	negativ	negativ
E.coli-Enterotoxin ST-II	negativ	negativ	negativ
Shigatoxin 2e	negativ	**positiv**	negativ
F4-Fimbrien (K88-Fimbrien)	negativ	negativ	negativ
F5-Fimbrien (K99-Fimbrien)	negativ	negativ	negativ
F6-Fimbrien (987P-Fimbrien)	negativ	negativ	negativ
F18-Fimbrien	negativ	**positiv**	negativ
F41-Fimbrien	negativ	negativ	negativ
E.coli-Anheftungsfaktor Intimin	negativ	negativ	negativ

Results

Source: Institute for Hygiene and Infectious Diseases of Animals, Justus-Liebig University, Gießen, Germany

Prevention of Edema Disease

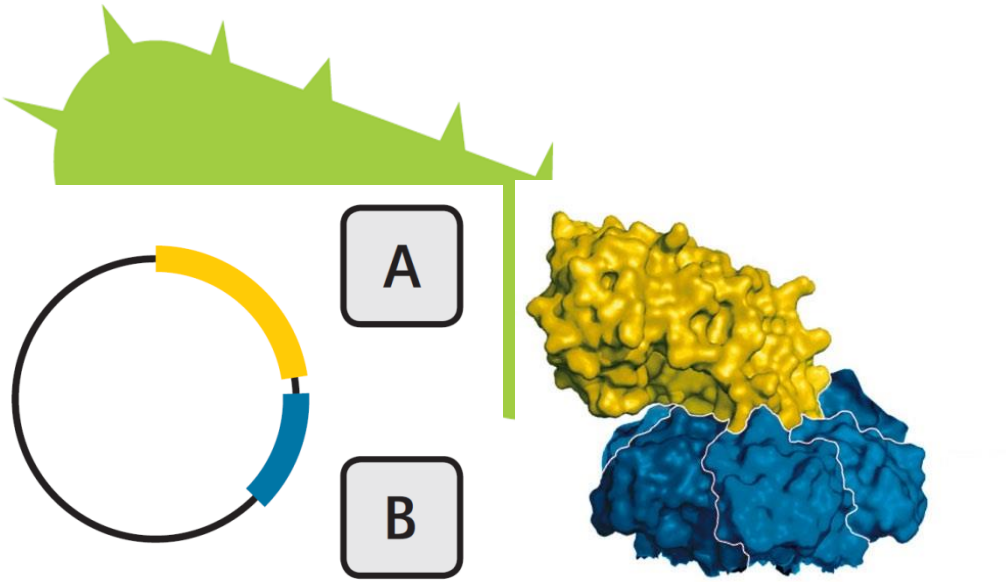
Ecoporc SHIGA

- Vaccine with genetically modified Stx2e, active immunization of piglets
- One shot, 1 ml *i.m.*, from the age of 4 days
- Onset of immunity 3 weeks after vaccination
- At least 15 weeks duration of immunity

„To **reduce** the **mortality** and **clinical signs** due to Edema Disease“

Vaccine Development

- Development of a suitable *E. coli* K12 strain
- Construction of a Stx2e encoding plasmid
- Genetic attenuation of the A subunit



Production of a genetically modified Stx2e antigen with highly reduced toxicity

IDT

Gathering success: User Experience Trials (UETs)

User Experience Trial (UET)

Goal: gathering data to evaluate the success of vaccination

Two main possibilities:

- Protocol Alpha: before & after
- Protocol Beta: side-by-side

Data assessed:

- Morbidity rate
- Mortality rate
- Average Daily Weight gain
- Usage of antimicrobials

All these can be used to assess the **return on investment (ROI)**

User Experience Trial (UET)

Protocol Alpha:

- Evaluation of 5-6 batches **before and after** vaccination

Advantage:

- Easy to conduct, all piglets in a batch can be vaccinated

Disadvantage:

- Comparison depends on historical data, not considered scientific state-of-the-art

User Experience Trial (UET)

Protocol Beta:

- Evaluation of 5-6 batches **side-by-side**

Advantage:

- Protocol is more scientific

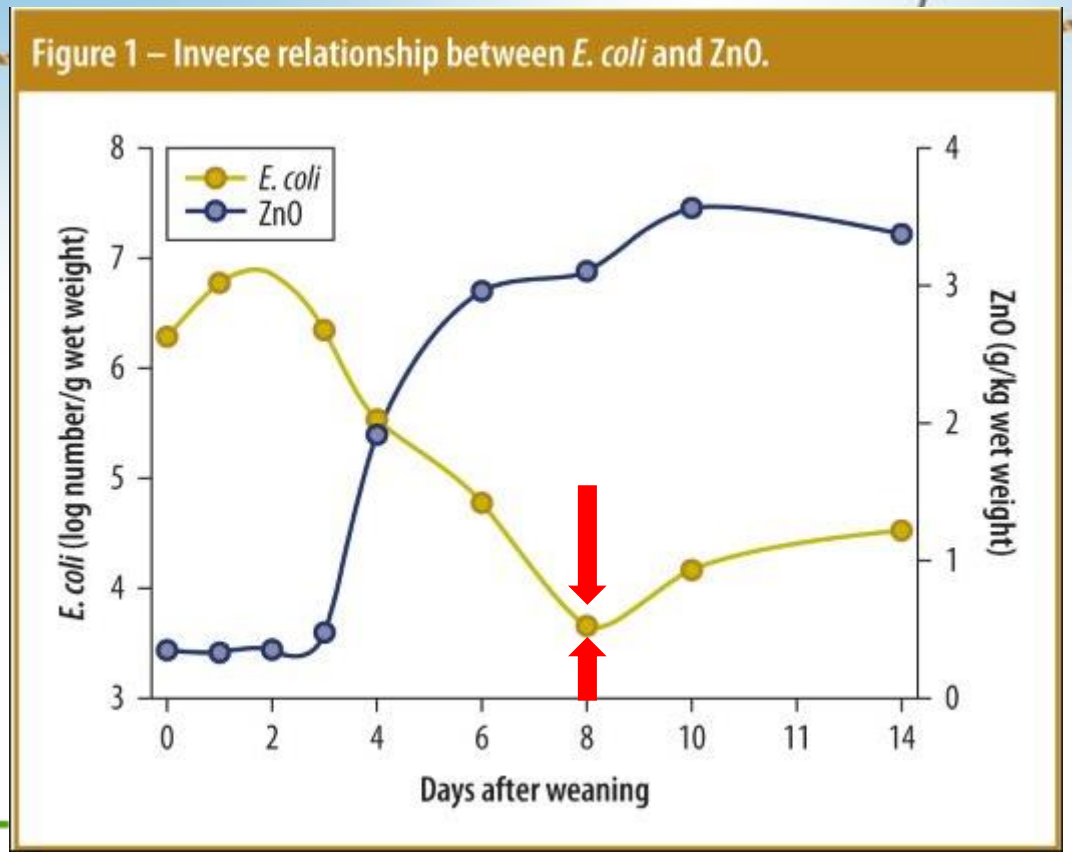
Disadvantage:

- Animals must be eartagged, so it is clear which group is which
- Trial may not be allowed due to animal welfare legislation

Ecoporc SHIGA –what is in for me?
-results from UETs-

IDT Biologika

Changing environment in the EU



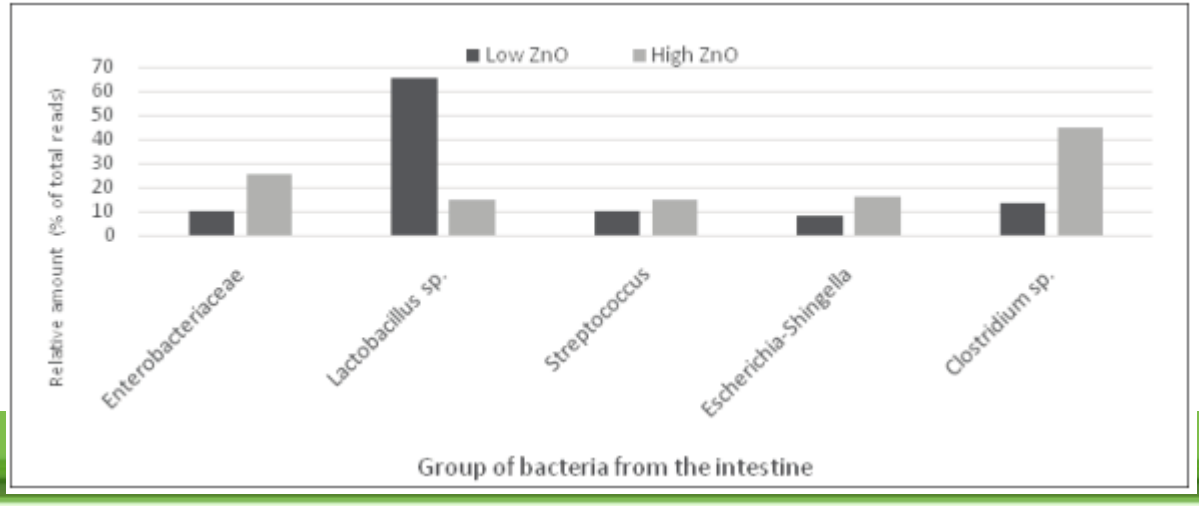
Dr Wilfried Vahjen & Prof Dr Jürgen Zentek

Changing environment in the EU

EMA, 16 March 2017: "CVMP concluded that the overall benefit-risk balance for veterinary medicinal products containing zinc oxide to be administered orally to pigs is negative, as the benefits of zinc oxide for the prevention of diarrhoea in pigs do not outweigh the risks for the environment. "

-> ban of the use of ZnO by 2022

"The most pronounced impact of high dietary zinc was found in 32d old piglets, while changes in older piglets were more moderate. The increased diversity of the *Enterobacteriales* may act beneficial during the first week after weaning to combat *E. coli* induced diarrhea, but a continuous reduction of lactobacilli in the small intestine may lead to unfavorable effects later in life. Due to concerns regarding environmental pollution and possible development of antibiotic resistant enterobacteria, it is proposed that the application of pharmacological doses of zinc oxide should be restricted to the first week after weaning." *Starke IC, Pieper R, Vahjen W, Zentek J,* FEMS Microbiol Ecol. *2014*

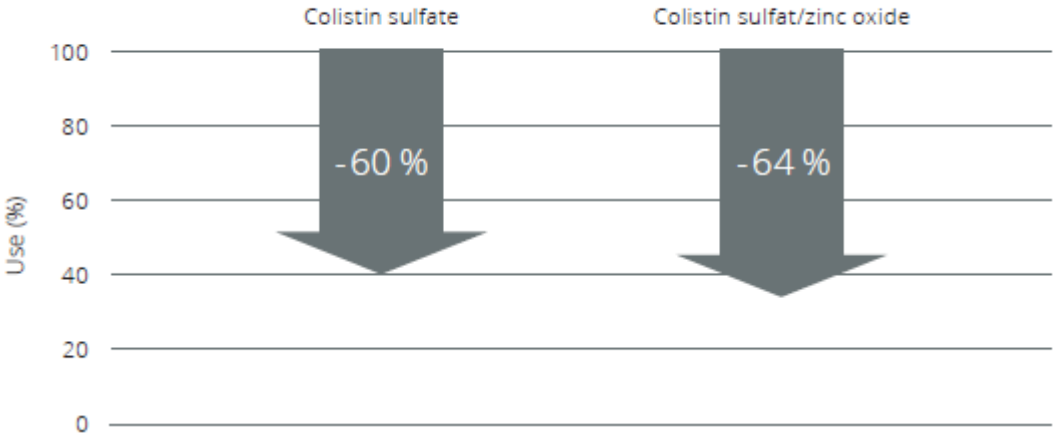


Potential of reduction of antibiotics/ ZnO - I

Germany – a nationwide field study (UET 6 months before and after vacc.)

In 179 farms the impact of the vaccination with Ecoporc SHIGA with respect to the use of oral antimicrobials (colistin sulfate and zinc oxide) was calculated. [1]

Total use of antimicrobials



[1] K. Lillie-Jaschniski, M. Köchling, T. Lindner: Erste Erfahrungen mit dem Einsatz von ECOPORC SHIGA, der neuen Vakzine gegen Ödemkrankheit – Auswertungen aus Feldversuchen in Deutschland; Tierärztl. Umschau, 68, 377-382 (2013)

Longitudinal Study in The Netherlands

- Farrowing and nursery farm with 600 sows
- 28-30 sows with 12 piglets every week
- Weaning after 25 – 26 days
- Nursery unit: 2600 piglets → 10-12 / pen
- Edema disease as sporadic outbreaks shortly after weaning
- Overall mortality of 7.7% in 2012
- Metaphylaxis Colistin for 10 days
- Feed crude protein reduced to 16%

Fricke et al. 2015 *Porcine Health Management*

Fricke et al. : Material and Methods

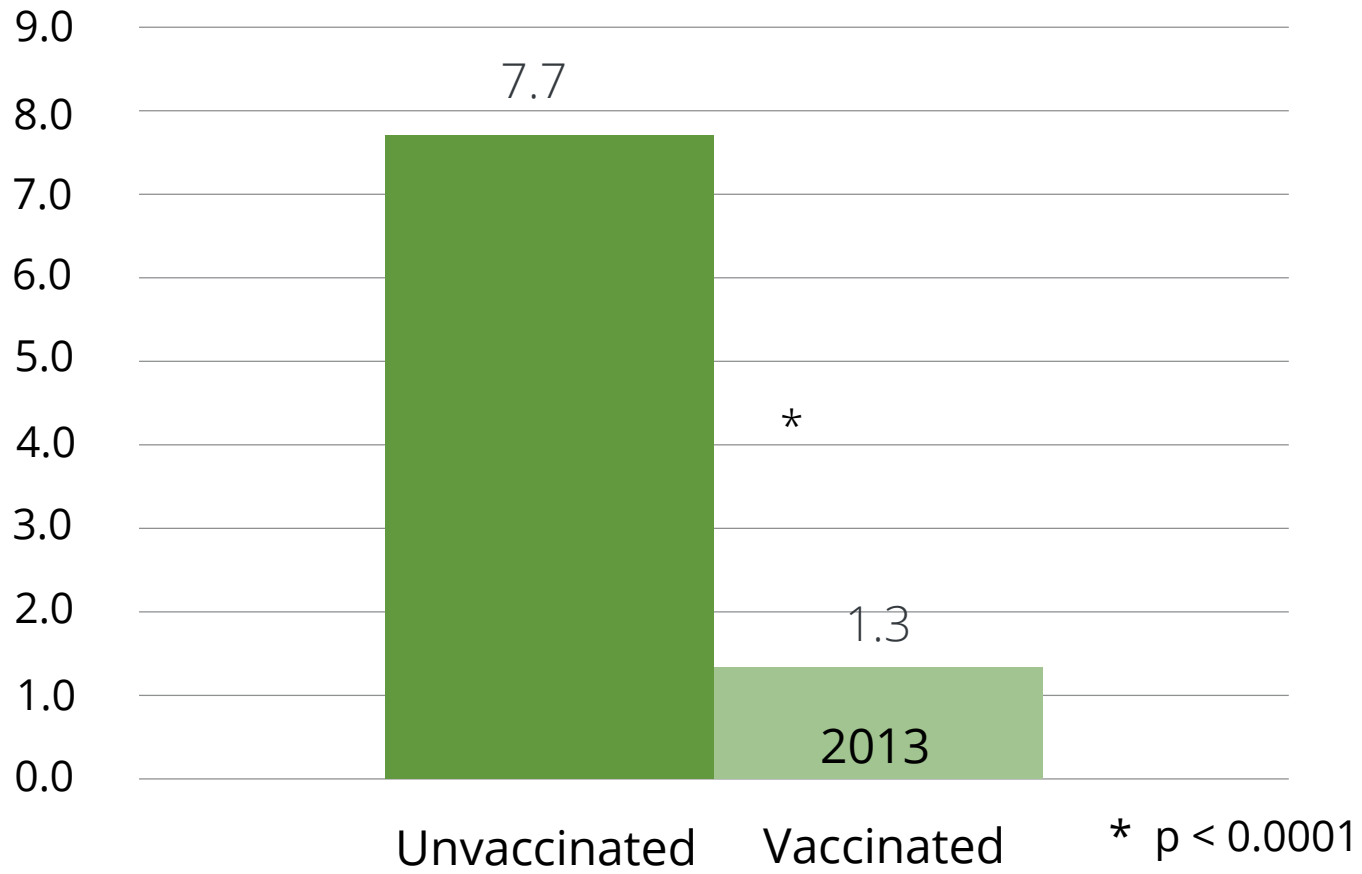
Comparison:

2012 52 week groups metaphylactic treatment with **Colistin**	2013 52 week groups vaccination with **Ecoporc SHIGA**

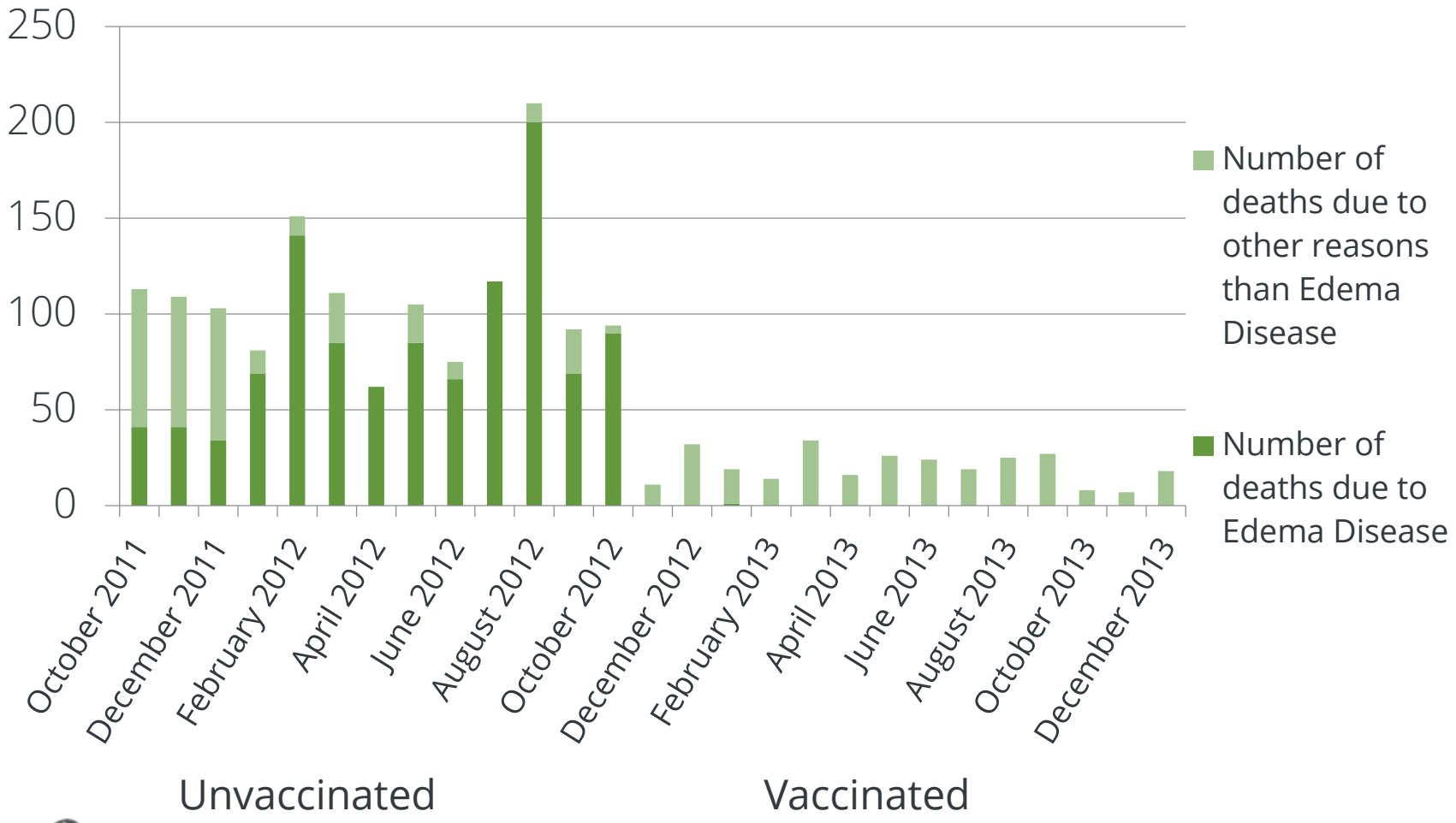
Observed parameters:

- Mortality in nursery period
- Antibiotic use in nursery
- Body weight at sale

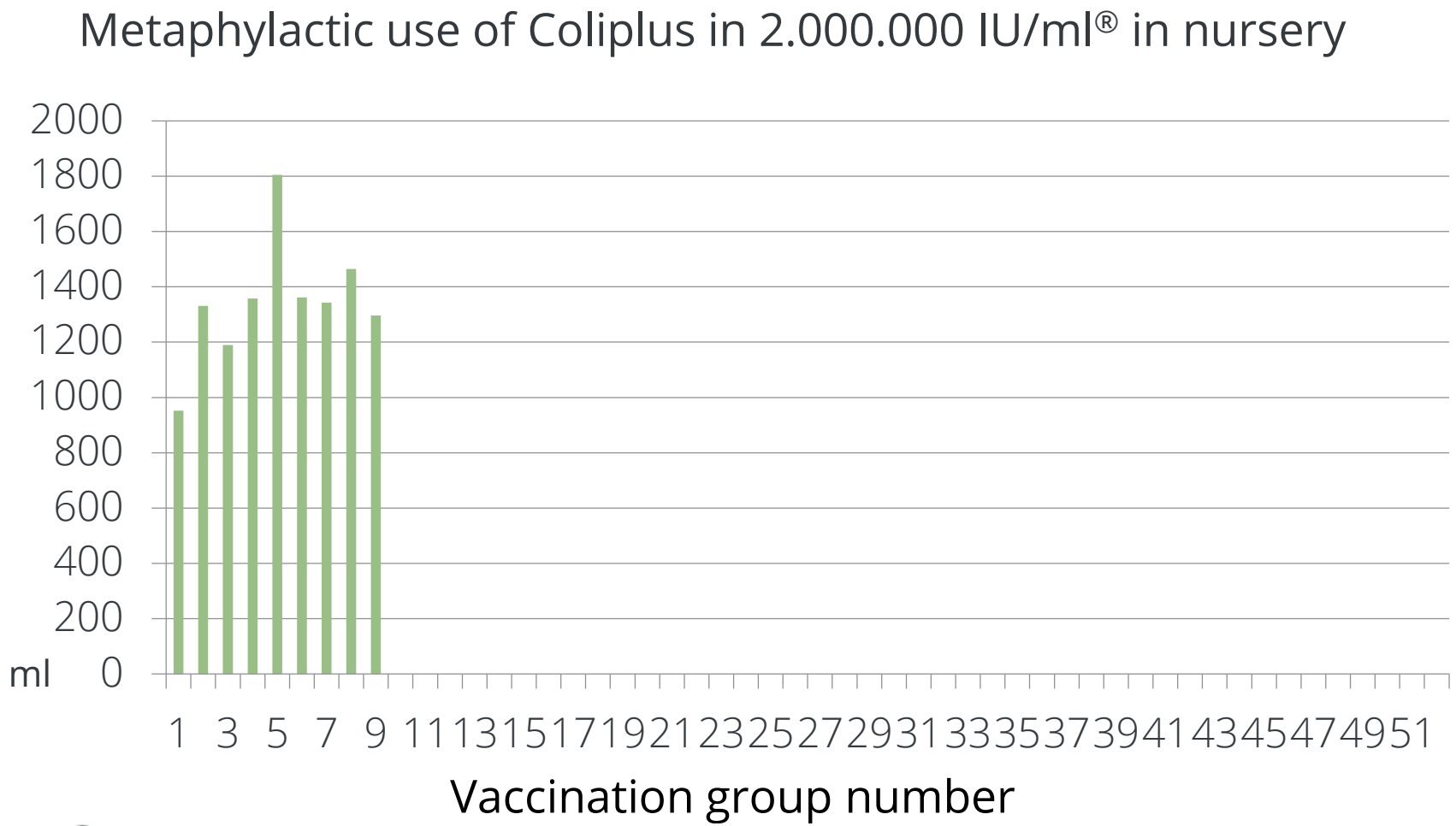
Fricke et al.: overall mortality rate %



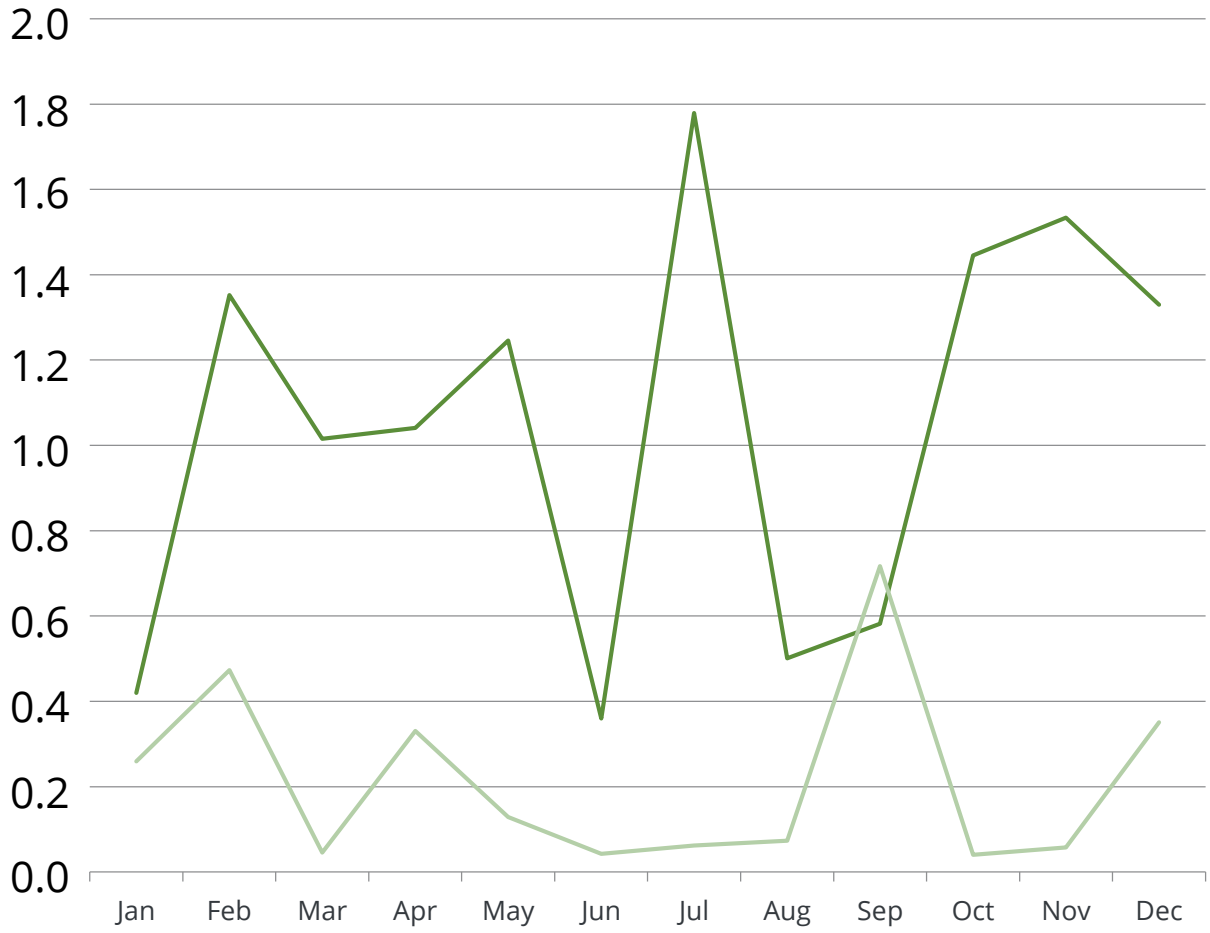
Fricke et al.: causes of mortality



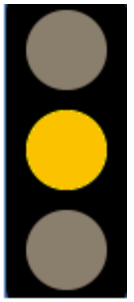
Fricke et al.: antimicrobial use



Fricke et al.: antimicrobial use

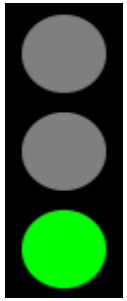


Year 2012



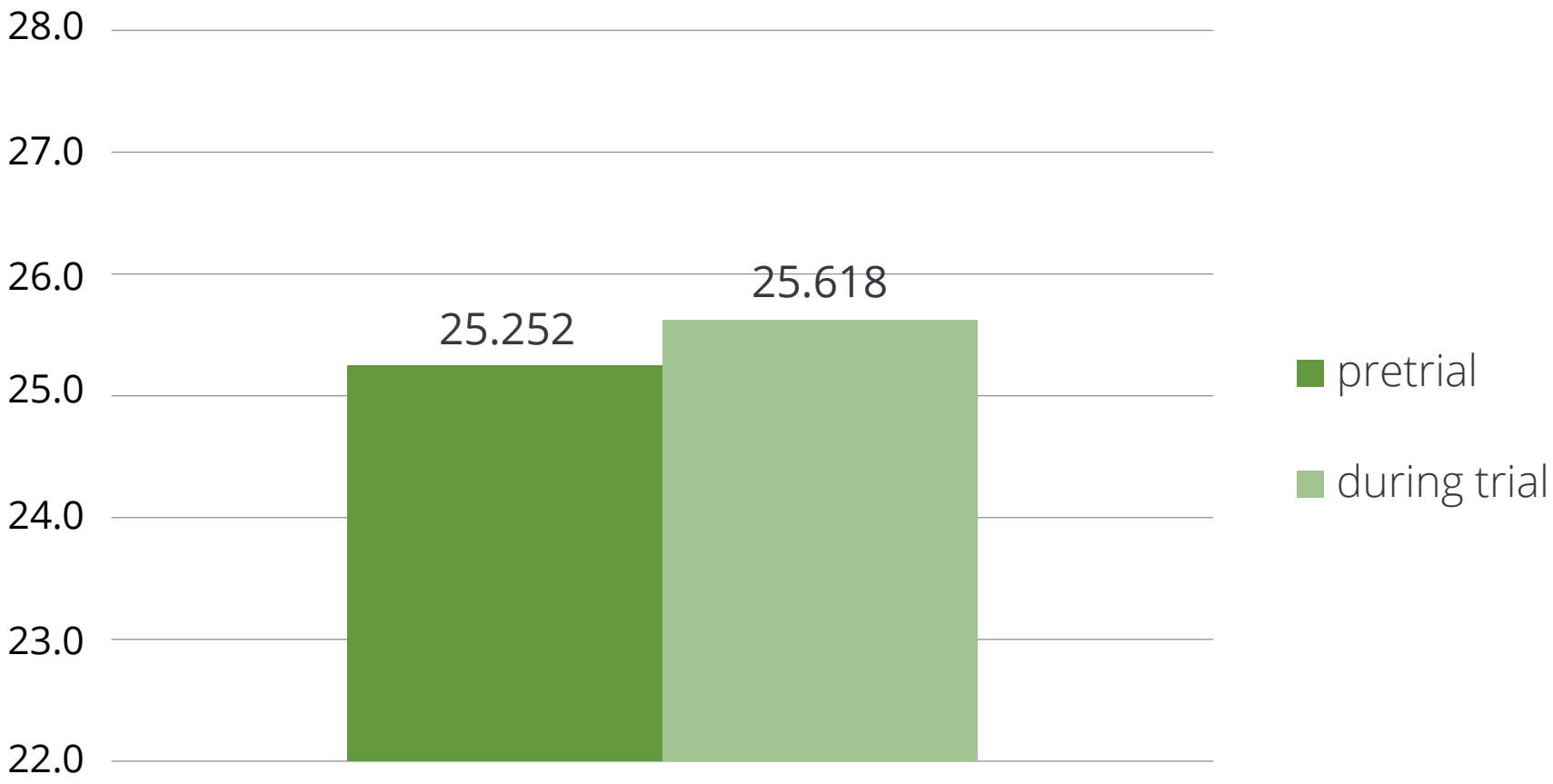
12.6

Year 2013



2.6

Fricke et al.: body weight at sale (KG)



Potential increase of performance - I

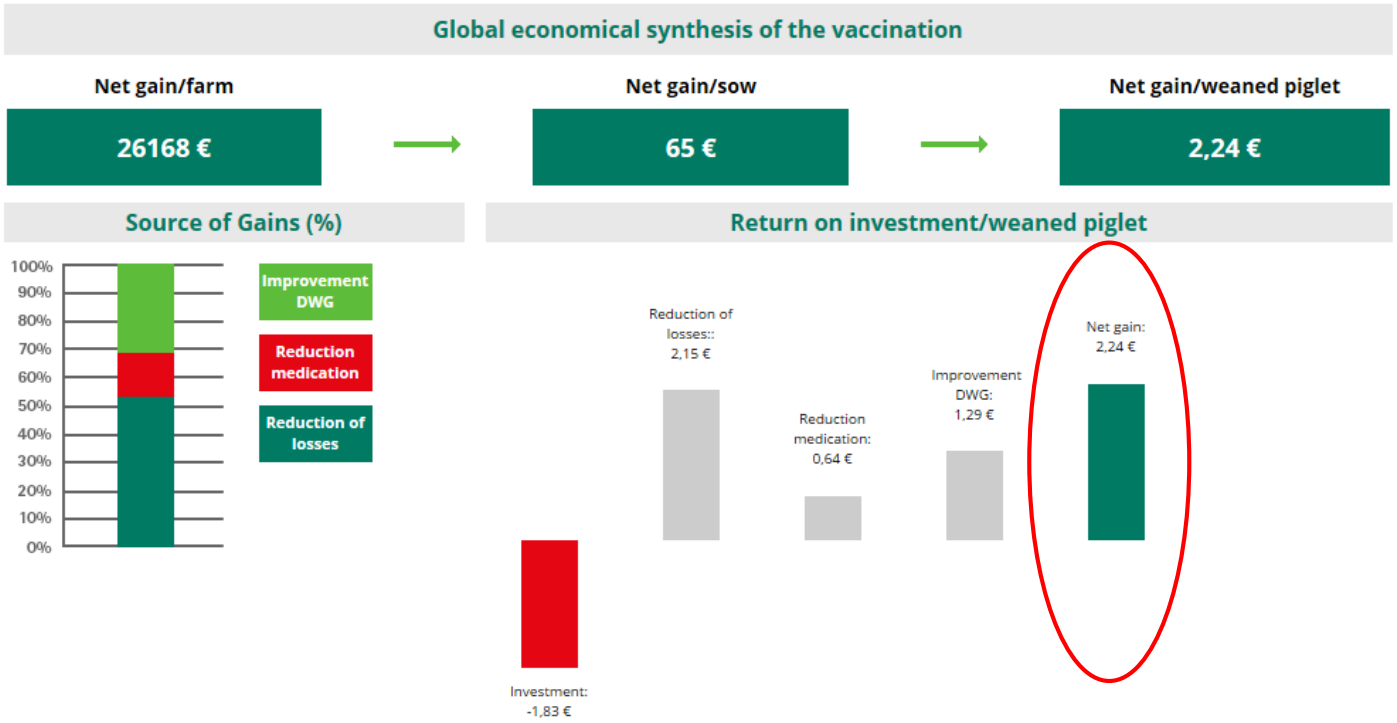
Results from French field trials (UET, 6 months before and after vacc.)
32 farms
184 935 piglets

	Non vaccinés	Vaccinés	Ecart	
Piglets (un)	99259	85676	en Valeur	en %
% Mortality PW	6,96	1,69	**-5,26**	**-76%**
Wheight end PW (kg)	28,83	31,05	**2,21**	**8%**
Atb Reduction (€)			**0,46**	
Other costs			**0,18**	
DWG PW	442	475	**33,06**	**7%**

Diff: 5.27 % mortality due to ED

Potential increase of performance - I

Positive Return On Investment - ROI
Example for 400 sow herd



https://www.shigatoxin.com Category: „Economy“

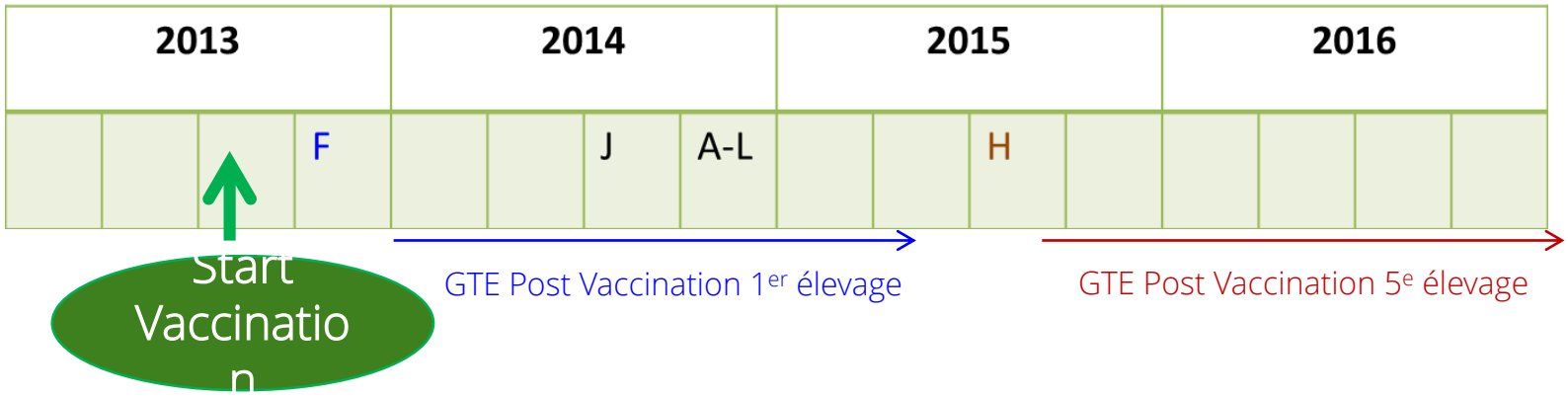
Potential increase of performance - II

Longitudinal study in France (before and after vacc.)

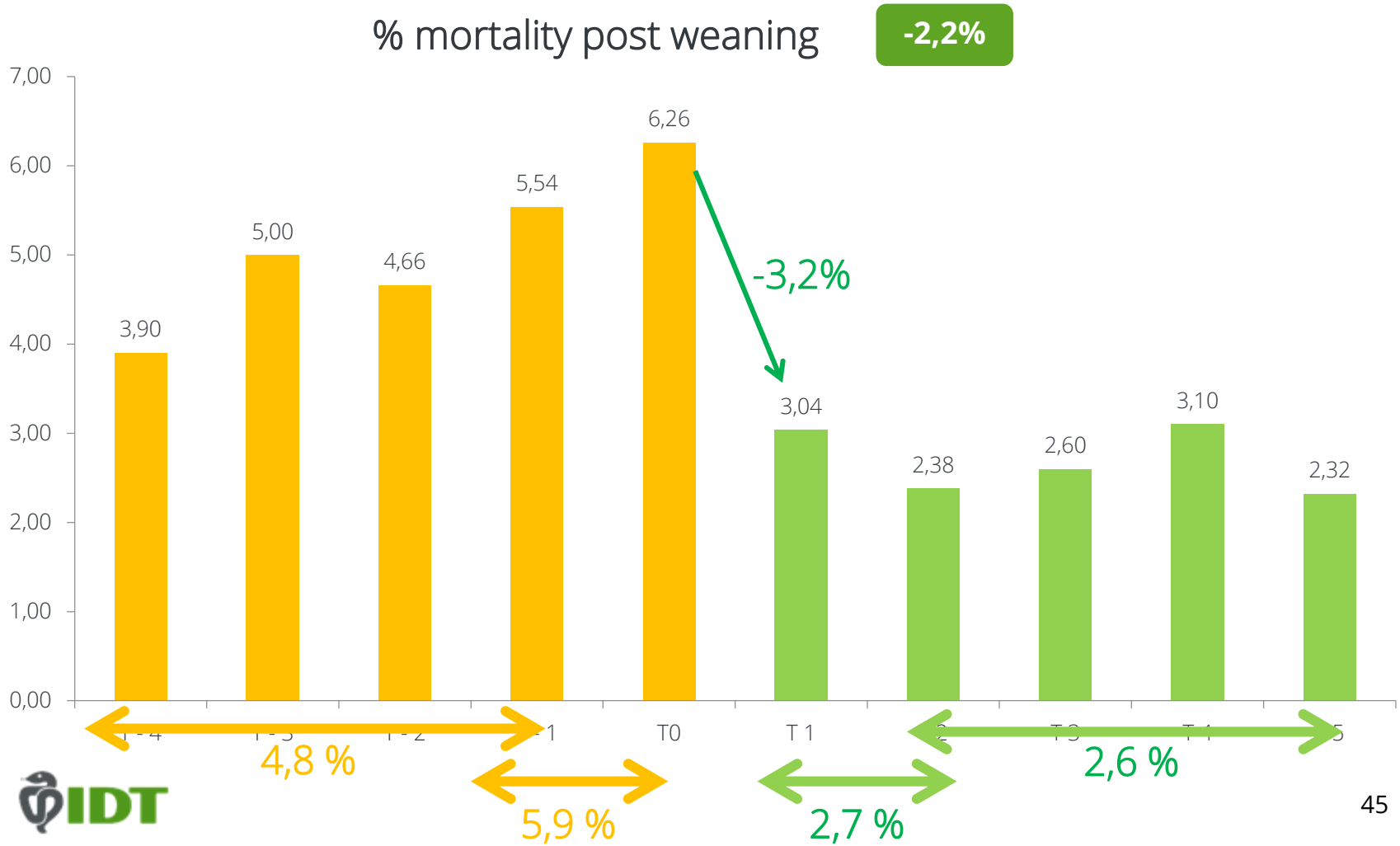
Farm Selection:

- 5 farms selected
- Criteria: History OD, quarterly report&software, any relevant change

Calendar:

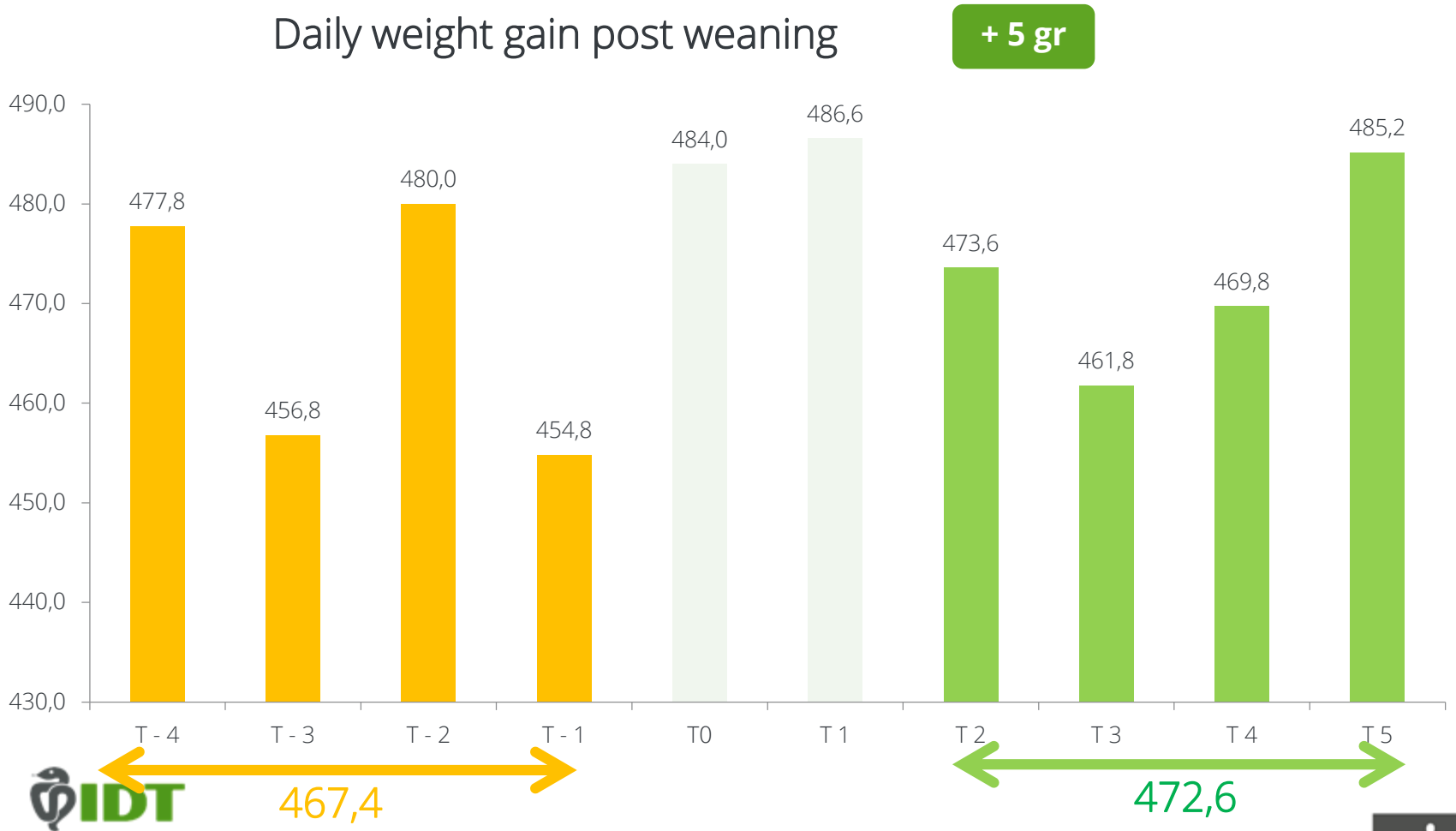


Potential increase of performance - II



T4 : Eleveur A exclu car arrêt momentané de vaccination. 8% pertes PS

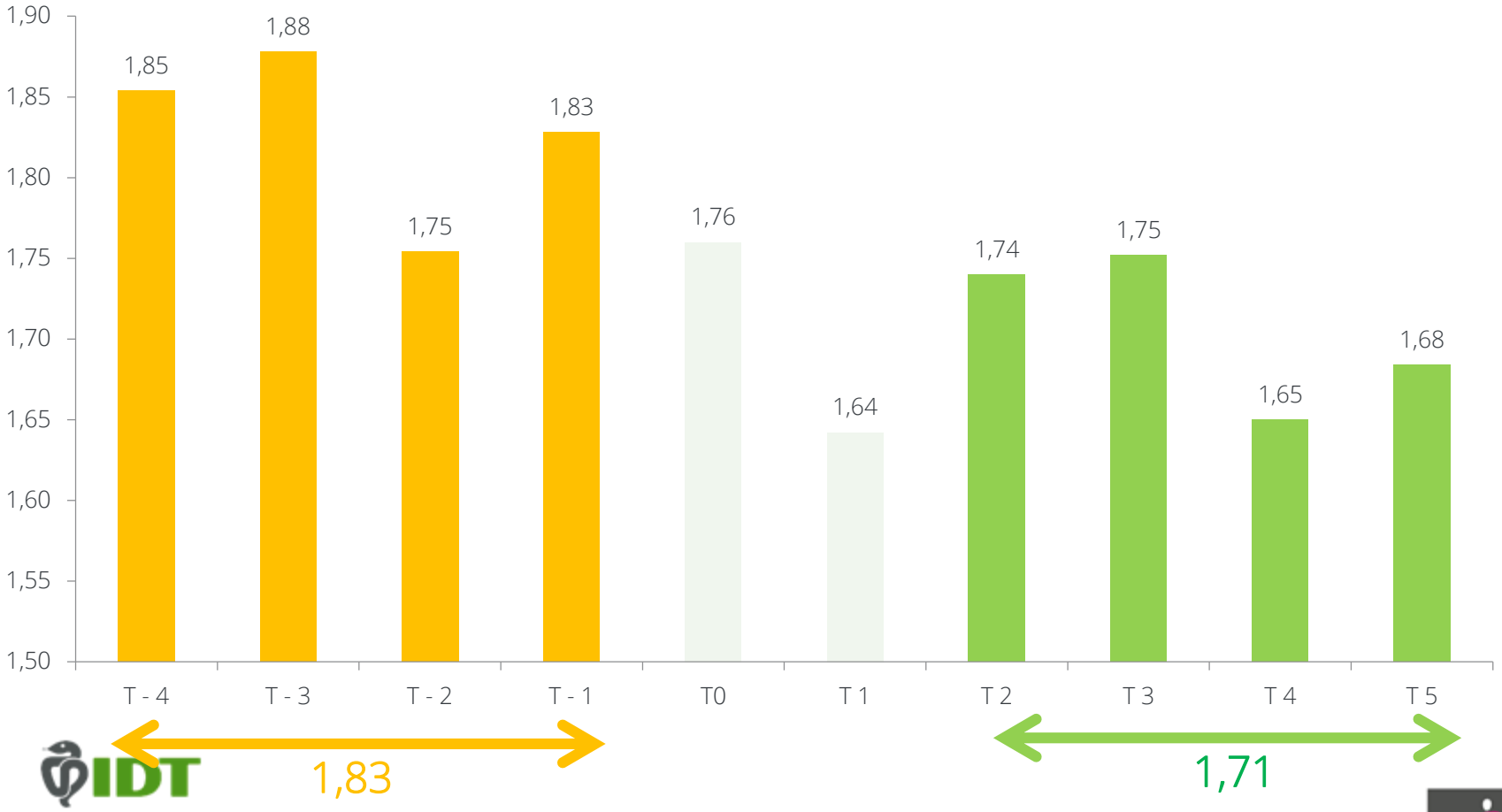
Potential increase of performance - II



Potential increase of performance - II

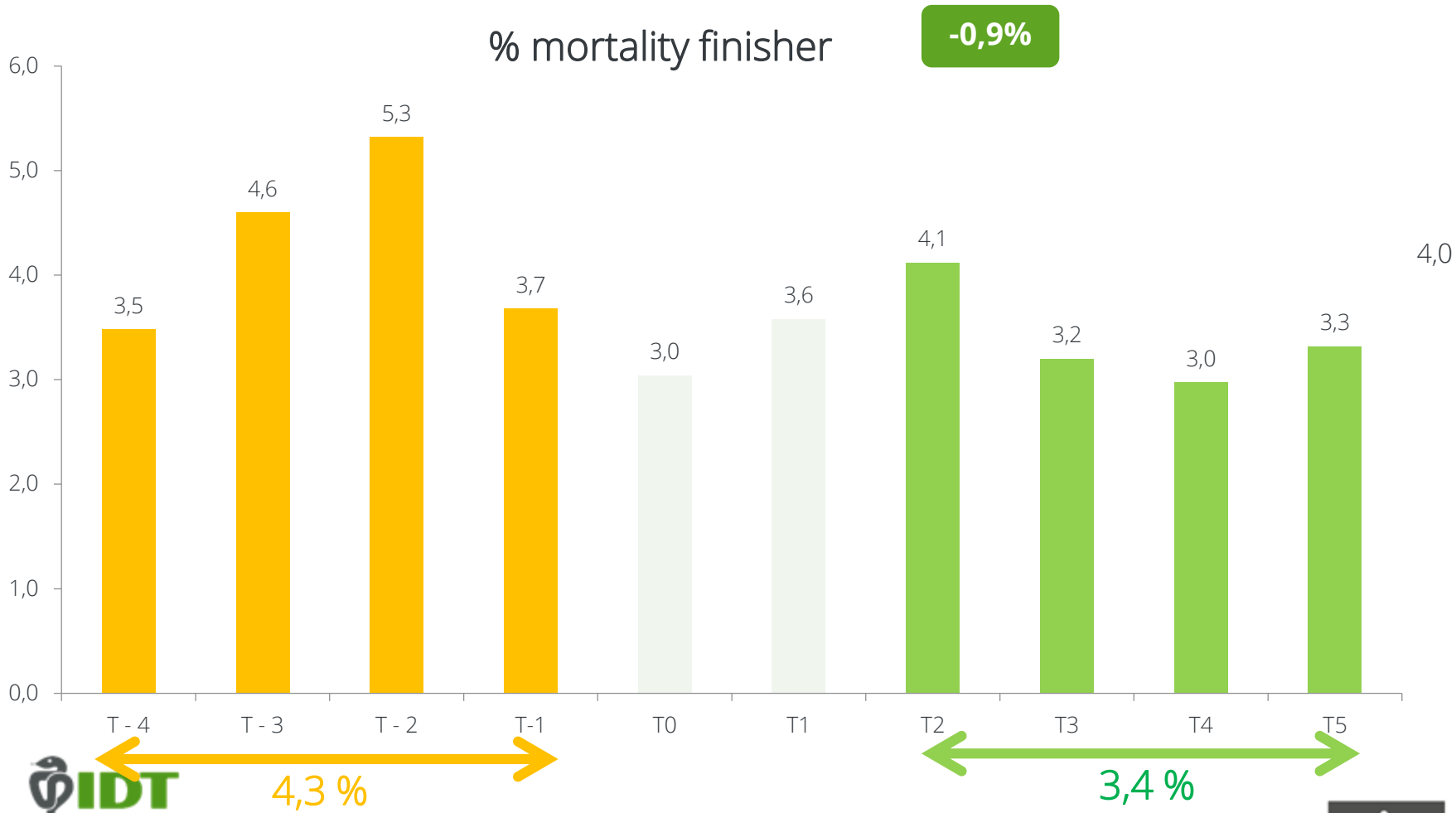
Feed conversion rate post weaning

- 0,11

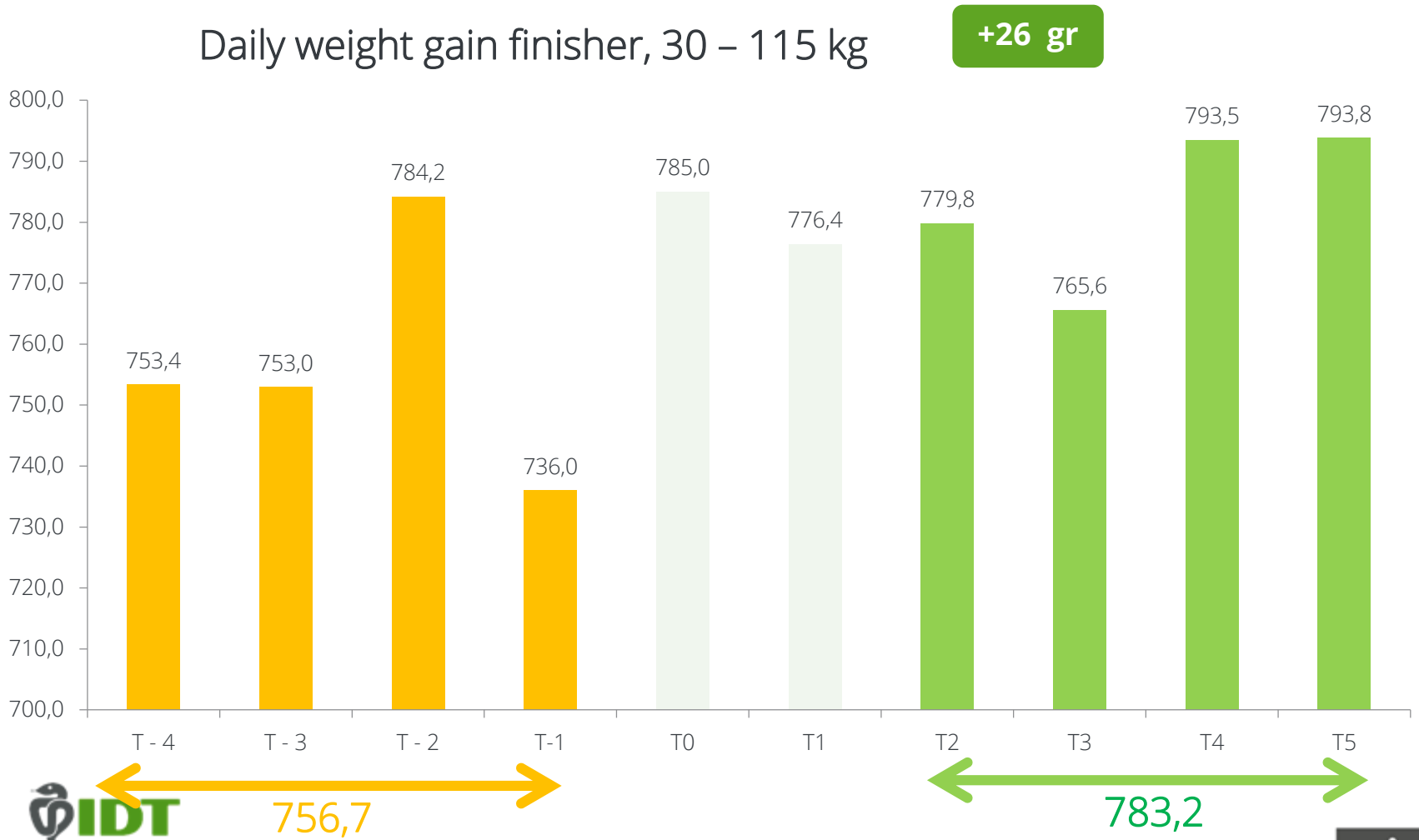


(*)Indice économique 8-30 pris en compte

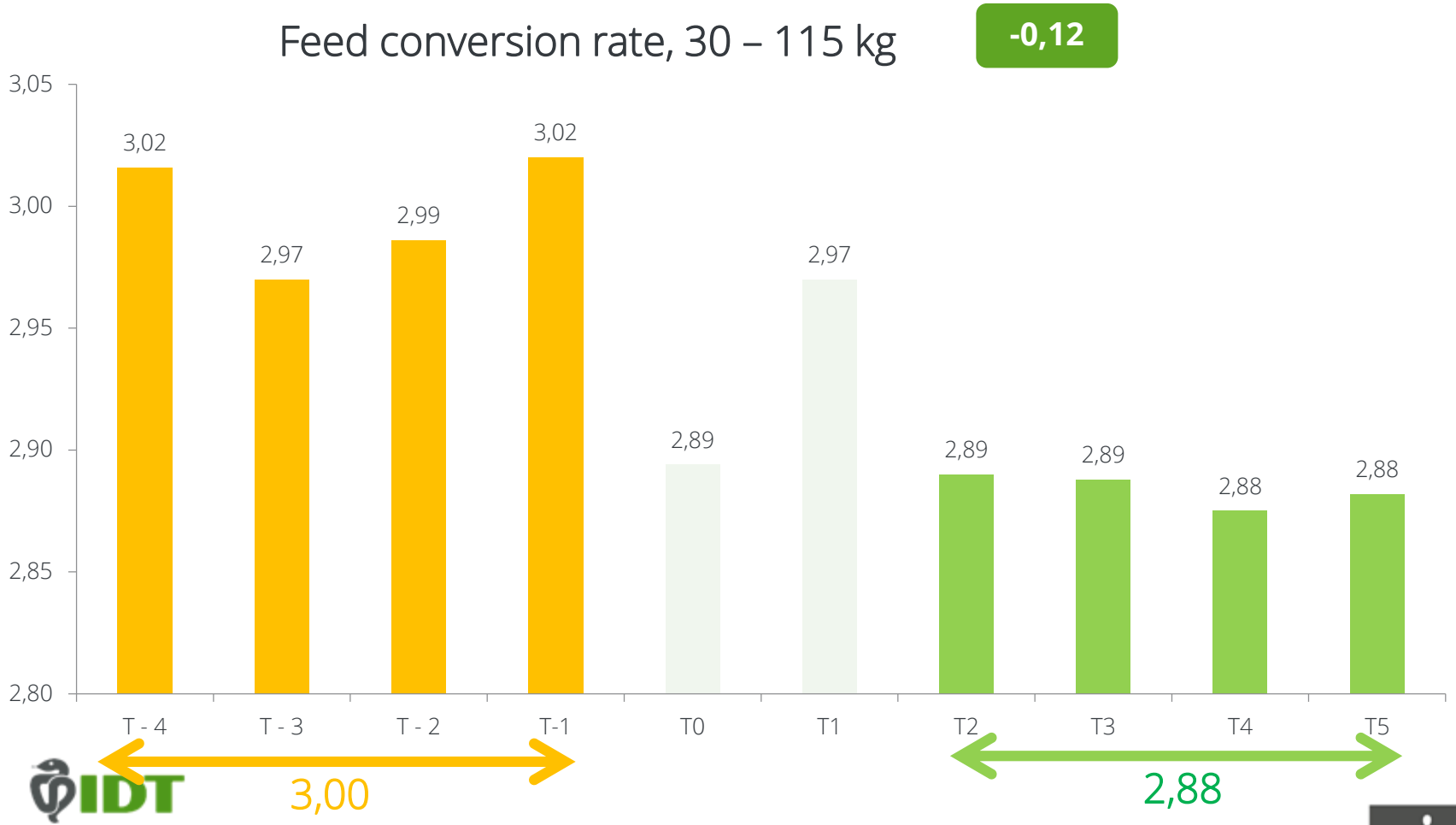
Potential increase of performance - II



Potential increase of performance - II

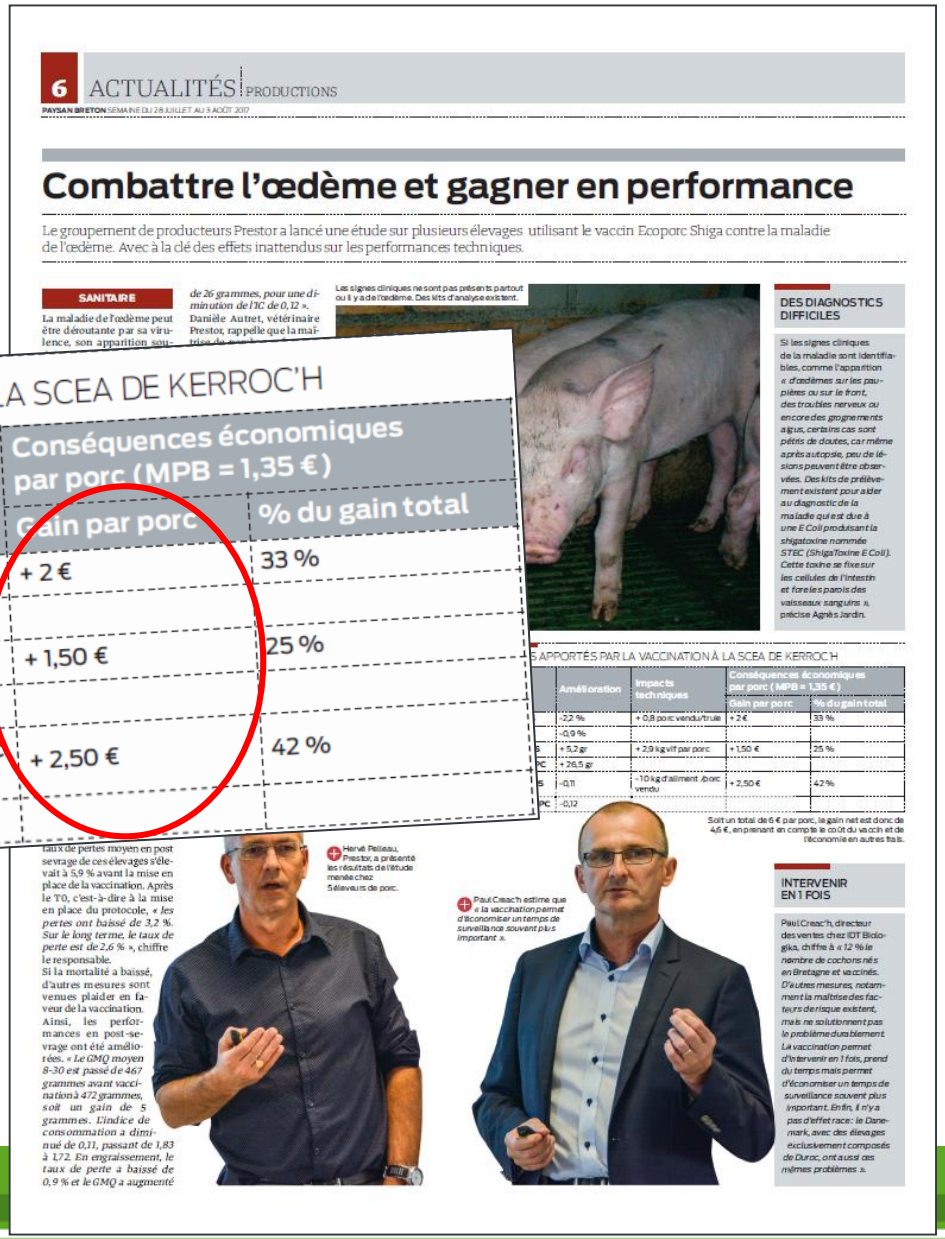


Potential increase of performance - II



(*)Indice économique 30-115 pris en compte

Potential increase of performance - II



6 ACTUALITÉS | PRODUCTIONS

PAYS AN BRETON SEMAINE DU 28 JUILLET AU 3 AOÛT 2017

Combattre l'œdème et gagner en performance

Le groupement de producteurs Prestor a lancé une étude sur plusieurs élevages utilisant le vaccin Ecoporc Shiga contre la maladie de l'œdème. Avec à la clé des effets inattendus sur les performances techniques.

SANITAIRE

La maladie de l'œdème peut être déroutante par sa virulence, son apparition sou-

de 26 grammes, pour une diminution de l'IC de 0,12 ».

Danièle Autret, vétérinaire Prestor, rappelle que la maî-

Les signes cliniques ne sont pas présents partout où il y a de l'œdème. Des kits d'analyse existent.

DES DIAGNOSTICS DIFFICILES

Si les signes cliniques de la maladie sont identifiables, comme l'apparition *« d'œdèmes sur les paupières ou sur le front, des troubles nerveux ou encore des grognements aigus, certains cas sont pétits de doutes, car même après autopsie, peu de lésions peuvent être observées. Des kits de prélèvement existent pour aider au diagnostic de la maladie qui est due à une E Coli produisant la shigatoxine nommée STEC (ShigaToxine E Coli). Cette toxine se fixe sur les cellules de l'intestin et fore les parois des vaisseaux sanguins »,* précise Agnès Jardin.

S APPORTÉS PAR LA VACCINATION À LA SCEA DE KERROC'H

	Amélioration	Impacts techniques	Conséquences économiques par porc (MPB = 1,35 €)	
			Gain par porc	% du gain total
	-2,2 %	+ 0,8 porc vendu/truie	+ 2 €	33 %
	-0,9 %			
S	+ 5,2 gr	+ 2,9 kg vif par porc	+ 1,50 €	25 %
PC	+ 26,5 gr			
S	-0,11	- 10 kg d'aliment /porc vendu	+ 2,50 €	42 %
PC	-0,12			

Soit un total de 6 € par porc, le gain net est donc de 4,6 €, en prenant en compte le coût du vaccin et de l'économie en autres frais.

taux de pertes moyen en post sevrage de ces élevages s'élevait à 5,9 % avant la mise en place de la vaccination. Après le T0, c'est-à-dire à la mise en place du protocole, *« les pertes ont baissé de 3,2 %. Sur le long terme, le taux de perte est de 2,6 % »,* chiffre le responsable.

Si la mortalité a baissé, d'autres mesures sont venues plaider en faveur de la vaccination. Ainsi, les performances en post-sevrage ont été améliorées. *« Le GMQ moyen 8-30 est passé de 467 grammes avant vaccination à 472 grammes, soit un gain de 5 grammes. L'indice de consommation a diminué de 0,11, passant de 1,83 à 1,72. En engraissement, le taux de perte a baissé de 0,9 % et le GMQ a augmenté*

Hervé Pelleau, Prestor, a présenté les résultats de l'étude menée chez 5 éleveurs de porc.

Paul Creach estime que *« la vacchation permet d'économiser un temps de surveillance souvent plus important ».*

INTERVENIR EN 1 FOIS

Paul Creach, directeur des ventes chez IDT Biologika, chiffre à *« 12 % le nombre de cochons nés en Bretagne et vaccinés. D'autres mesures, notamment la maîtrise des facteurs de risque existent, mais ne solutionnent pas le problème durablement. La vaccination permet d'intervenir en 1 fois, prend du temps mais permet d'économiser un temps de surveillance souvent plus important. Enfin, il n'y a pas d'effet race: le Danemark, avec des élevages exclusivement composés de Durac, ont aussi des mêmes problèmes ».*

LES GAINS APPORTÉS PAR LA VACCINATION À LA SCEA DE KERROC'H

Critères	Amélioration	Impacts techniques	Conséquences économiques par porc (MPB = 1,35 €)	
			Gain par porc	% du gain total
% Pertes PS	-2,2 %	+ 0,8 porc vendu/truie	+ 2 €	33 %
% Pertes PC	-0,9 %			
GMQ 8-30 PS	+ 5,2 gr	+ 2,9 kg vif par porc	+ 1,50 €	25 %
GMQ 30-115 PC	+ 26,5 gr			
IC éco 8-30 PS	-0,11	- 10 kg d'aliment /porc vendu	+ 2,50 €	42 %
IC éco 30-115 PC	-0,12			

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PRESTOR Eleveurs de Porcs en France

Potential increase of performance - II

Ecoporc SHIGA® vaccination and performance improvement

D. Autret (1), Ph. Leneveu (3), A. Jardin (3), H. Pelleau (2), T. Goues (2), O. Perrot (2), P. Créac'h (3), V. Gotter (4)
(1) Selas de l'Iroise, (2) Prestor, (3) IDT Biologika France, (4) IDT Biologika GmbH

Introduction and Objectives

Edema disease (ED) is a disease due to an enteric bacteria, ***E. coli* producing Shiga toxin 2e (Stx2e).** Since October 2013, **Ecoporc SHIGA®**, a **vaccine against Stx2e** is available in France. The vaccine reduces mortality and clinical signs due to ED, but **users observed that vaccinated pigs showed a better global health and better performance**. This **study** was conducted **to scientifically verify** these observations.

Materials and Methods

Inclusion criteria of the farms (n = 5; 35 000 weaned piglets per year) were:

- ✓ Clinical ED post weaning (PW) and implementation of Ecoporc SHIGA® for over 1.5 year

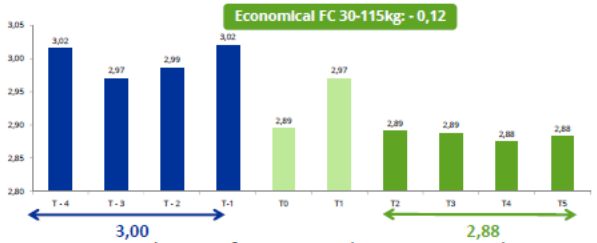
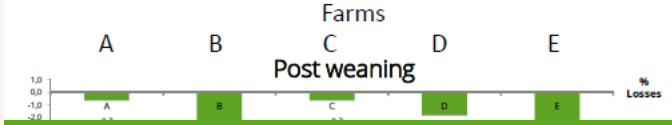


Figure 1 : evolution of economical FC 30-115 in the group

Criteria (weaning to slaughter house)	Gain	Technical Impacts	Benefit/pig (Carcass market price=1,50€)	% of total benefit
% losses	3%	+0,8 pig/sow	2,0 €	33%
ADG	+20 gr	+3 kg /pig	1,5 €	25%
FC	-0,12 pt	- 10 Kg feed/pig	2,5 €	42%
Total			6 €	100%

Table 1: evolution of performances of the group, 1 year before / 1 year after vaccination and technical and economical impact (see separated PW and fattening data in proceedings)



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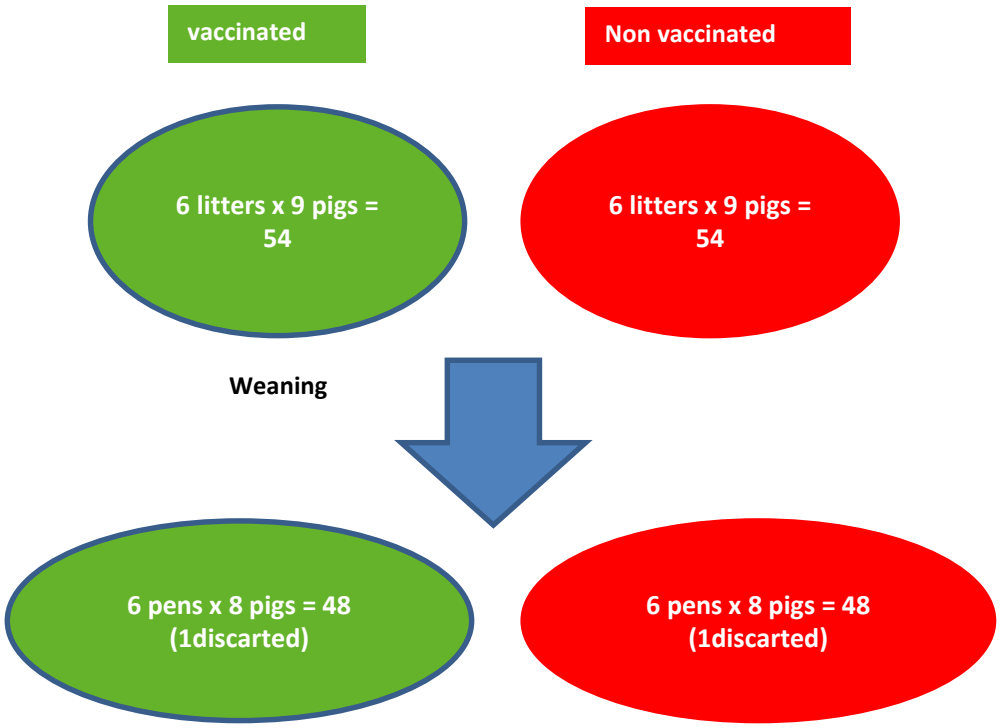
Potential increase of performance - III



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- 15 batches tested without antibiotics in feed
- Removing 1 batch with unusual consumption + removing outliers (Cox test).

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Potential increase of performance - III

Longitudinal trial, vaccinated and non vaccinated batches in parallel

	BODY WEIGHT (kg)			AVERAGE DAILY GAIN (g/d)			AVERAGE DAILY FEED INTAKE (g/d)			FEED CONVERSION RATIO (g/g)		
	DAY 0	DAY 14	DAY 56	PRESTARTER	STARTER	TOTAL	PRESTARTER	STARTER	TOTAL	PRESTARTER	STARTER	TOTAL
CONTROL	7,72	10,22	17,18	183,1	369,9	291,4	232,7	543,0	410,5	1,365	1,482	1,416
VACCINE	7,88	10,13	17,31	175,3	386,4	298,0	223,9	578,1	428,1	1,331	1,502	1,439
SEM	*0,088*	*0,066*	*0,131*	*5,060*	*5,209*	*4,266*	*4,708*	*8,823*	*6,112*	*0,035*	*0,018*	*0,013*
P TREAT	*0,1895*	*0,3413*	*0,5078*	*0,2766*	***0,0270***	*0,2828*	*0,1894*	***0,0056***	***0,0440***	*0,5001*	*0,4282*	*0,2114*
P BW0	-	*<.0001*	*<.0001*	*0,6213*	*<.0001*	*<.0001*	*0,5609*	*<.0001*	*<.0001*	*0,6438*	*0,4292*	*0,4008*

n=6 per batch

total n=90 per treatment group

	DEATHS (%) chi-cuadrado		
	PRESTARTER	STARTER	TOTAL
CONTROL	0,29	3,24	3,53
VACCINE	0,45	0,30	0,75
P TREAT	*0,6422*	***<.0001***	***0,0004***

Diff: 2.78 % mortality due to ED

Potential increase of performance - III

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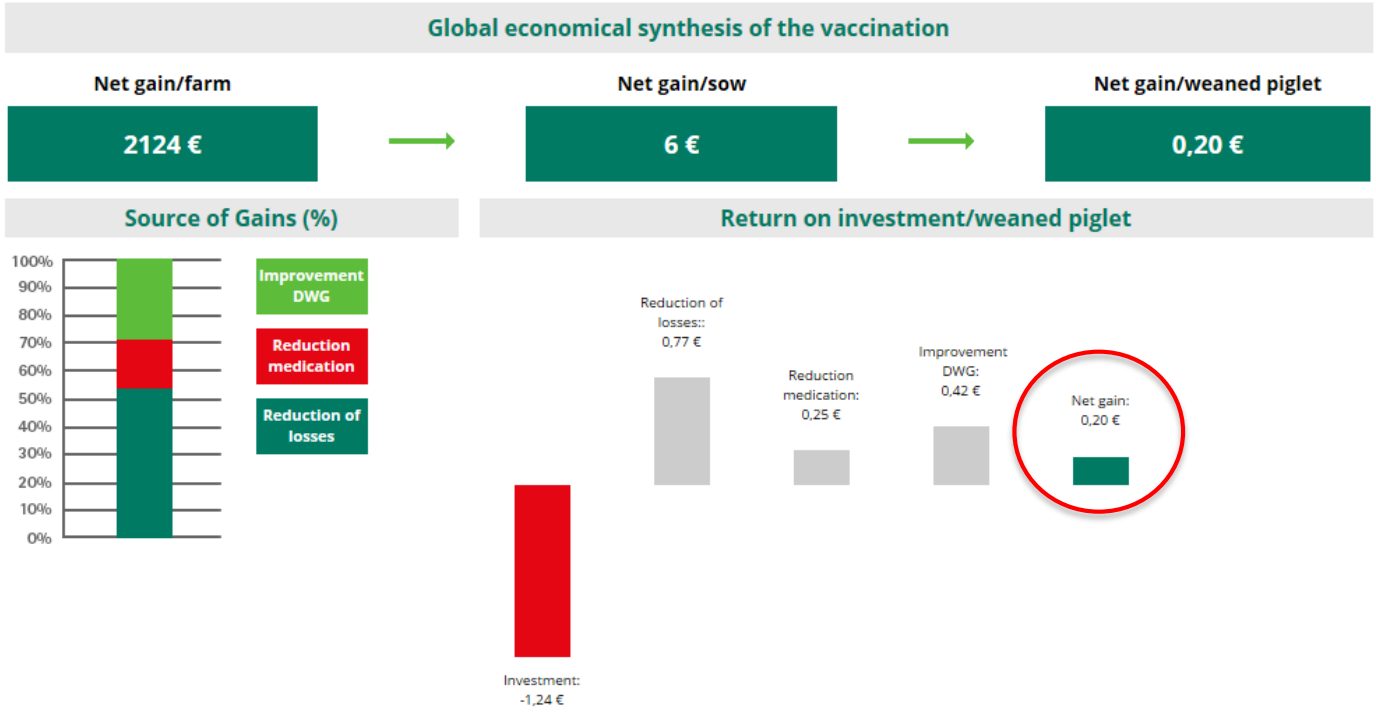

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https://www.shigatoxin.com Category: „Economy“

Summary and Conclusions

Summary: Information on ED & STEC

1) Edema Disease is a problem everywhere in the world

2) Shigatoxin 2e (Stx2e) producing *E. coli* (STEC) are the cause of Edema Disease

3) Edema Disease can present itself clinically in numerous ways – which is why **differential diagnostics** are crucial

Conclusion

Diagnostics

are the basis of success

with

Ecoporc SHIGA

Thank you for your attention!