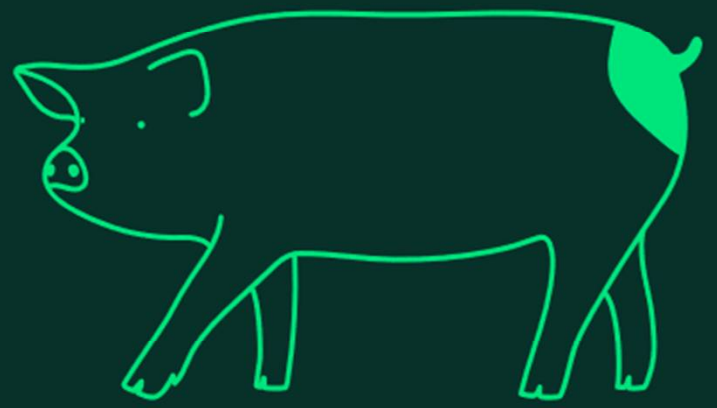
Boehringer Ingelheim

Advancing Innovation in Gut Health through Microbiome Control



Dr. Juver Membrebe – Regional Technical Manager (Swine), ASEAN, Korea, Australia, and New Zealand

Agenda

01 The Gut Health Imperative

Why gut health matters more than ever in modern swine production

1. Role of the gut in immunity and performance
2. Antibiotic reduction trends (Europe vs Asia)
3. The challenge of balancing ABU, efficiency, and disease control

02 Challenges on the Ground

Understanding the local disease landscape and practical constraints

1. Ileitis prevalence in the Philippines
2. Production performance with subclinical ileitis
3. Treatment and control

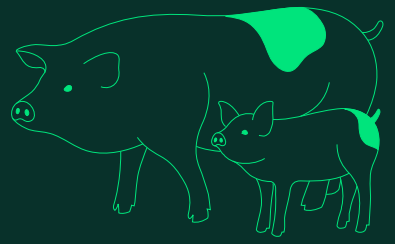
03 Innovating for Impact

How oral gel vaccination supports gut health and farm efficiency

1. Why gel vaccination?
2. Gel vaccination: how it works, benefits, and evidence

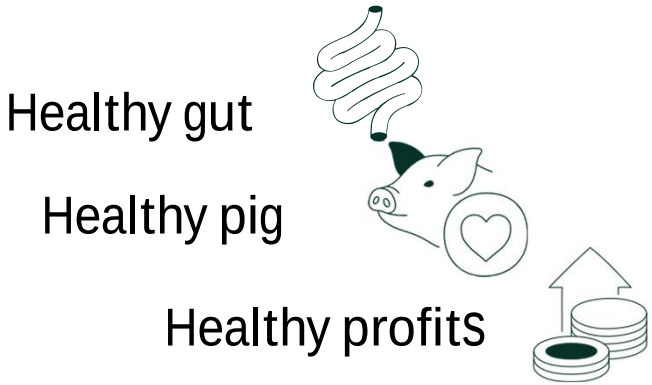
1. The Gut Health Imperative

Why gut health matters more than ever in modern swine production



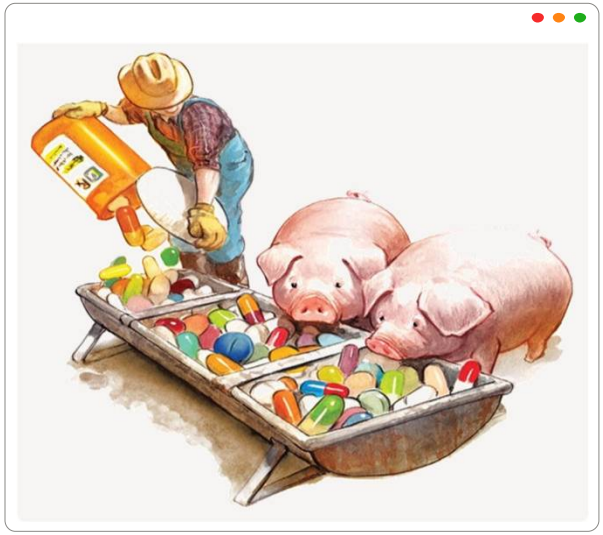
Why Gut Health Matters?

- 70% of immunity resides in the gut
- Microbiome stability = resilience against stress and diseases like ASF
- Less diarrhea and mortality – fewer treatments
- Better nutrient absorption = improved ADG and FCR
- Higher ROI through reduced losses and better uniformity



Antibiotics Overuse in Asia

- High reliance on antibiotics to enhance FCR, growth performance, and diseases prevention
- Often used prophylactically or as growth promoters especially in early life stages
- Consequence = High Antimicrobial Resistance (AMR)

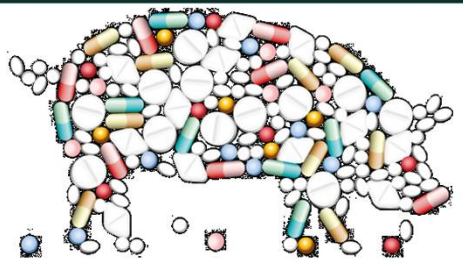


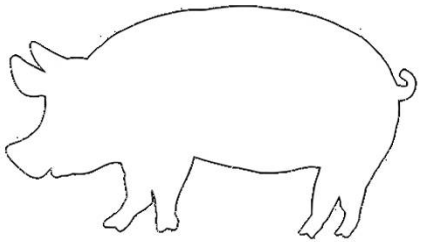
Antibiotic Use (ABU) Reduction
European Industry Context

- 1986: European Nordic countries banned antimicrobial (AM) use as growth promoter
- 2006: EU ban on AM use as growth promoter
- 2013: Agricultural European Innovation Partnership – focus group in AM reduction
- 2016: EU European One Health Action Plan against

Strong appeal for a more responsible and restrictive application of antibiotics in animal production

Antibiotic Use (ABU) Reduction
European Industry Context





NL 70% reduced

- AMR is reverted
- Lower AMR in Salmonella
- Lower AMR in E.coli isolates

Weaning age increased

21 → 30 days

Vaccination, hygiene, feed etc.

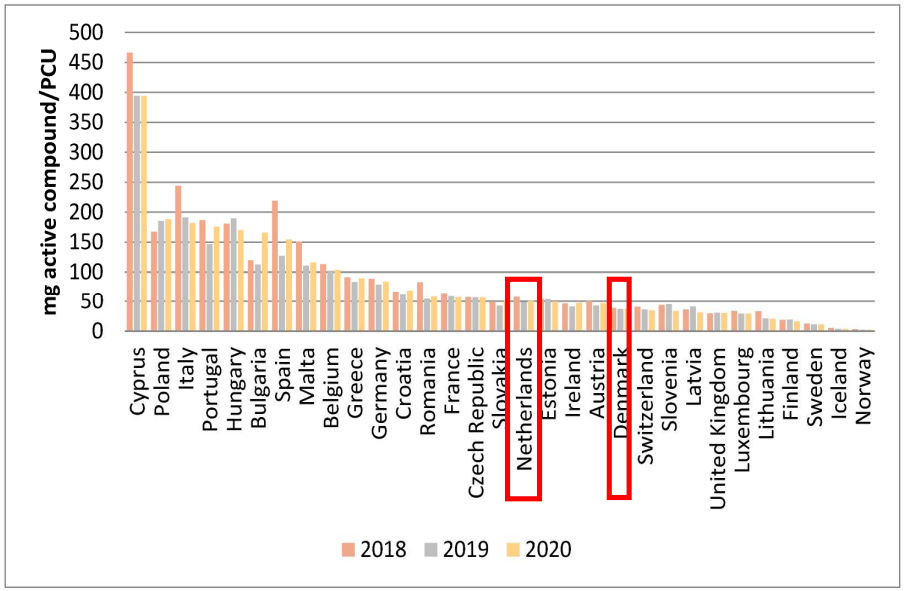
Last 30% AB reduction difficult

- Bottle necks:
  - E.coli, S.suis, APP, Lawsonia
  - Alternatives (vaccines) opportunity

South Europe: Still high AB use

Netherlands & Denmark:

Lowest AB use of the main pig producing EU countries



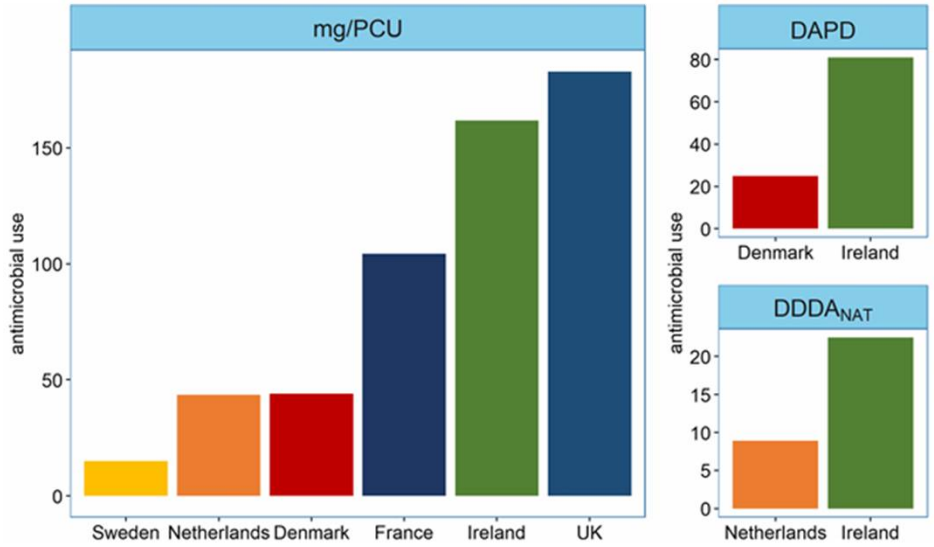


Fig. 4 Comparison of antimicrobial use between the 67 Irish pig farms and 5 European countries in 2016. The large panel shows the comparison of antimicrobial use (AMU) between the Irish sample population and five European countries expressed in mg/PCU [31]. The smaller panels show the comparison of AMU between the Irish sample population and Denmark expressed in DAPD (proportion of animal population in treatment per day) [8] and between the Irish sample population and the Netherlands expressed in DDDA$_{NAT}$ (defined daily dose animal) [9]

O'Neill et al 2020

Antibiotic reduction vs production performance

→ **Antibiotics reduced with 70%**

→ Genetic improvements

- Higher PSY ,Higher ADG, Lower FCR

→ Between 2009–2023:

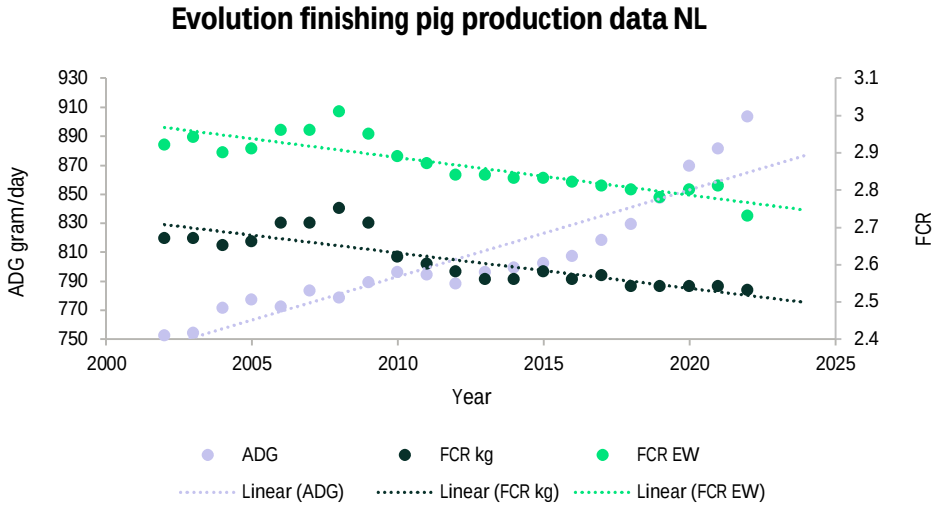
→ ADG 800 gram → 900 gram

→ FCR in kg 2.71 → 2.53

- **18 kg feed less needed**

→ FCR EW (Energy value)

- 2.95 → 2.73



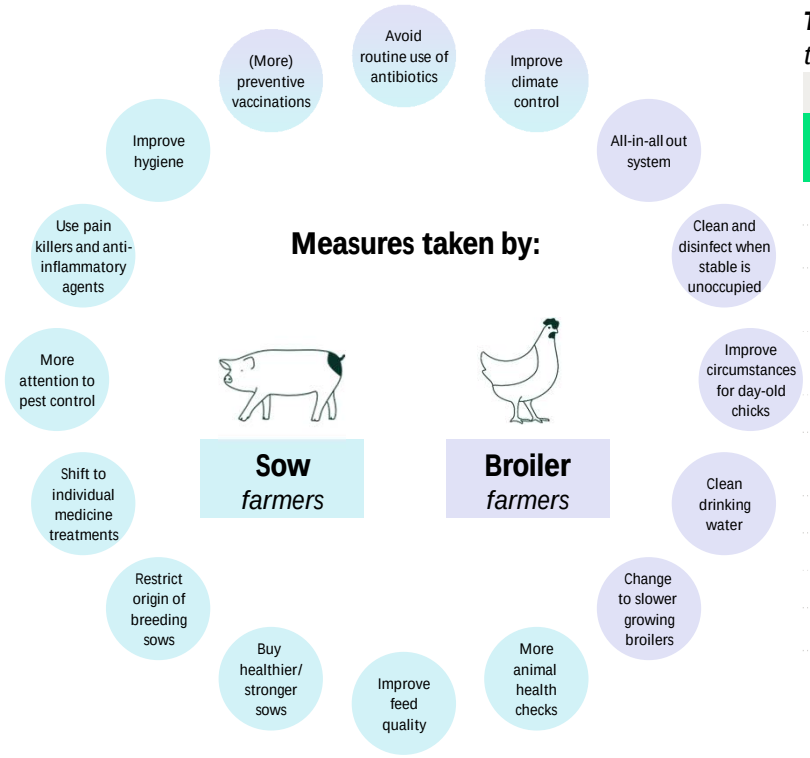


Table 2 *Measures taken by 50% or more of the interviewed sow farmers to improve the health of their animals (% of farmers)*[9]

Measures taken or not and since when						
Measure	**Number of farmers**	**Yes**	**Yes, >9 years ago**	**Yes, 6–9 years ago**	**Yes, 3–6 years ago**	**Yes, <3 years ago**
Avoid routine use of antibiotics	55	81.8	20.0	12.7	41.8	7.3
More preventive vaccinations	54	81.5	9.3	11.1	38.9	22.2
Use pain killers and anti-inflammatory agents	55	76.4	12.7	14.6	36.4	12.7
More attention to pest control (flies, rats, mice)	55	74.5	34.6	14.6	12.7	12.7
Improve hygiene	55	67.3	38.2	7.3	14.6	7.3
Shift to individual medicine treatments	55	65.4	21.8	10.9	20.0	12.7
Improve feed quality•	54	63.0	18.5	7.4	20.4	16.7
Improve climate control	55	60.0	21.8	5.5	18.2	14.6
More animal health checks	54	59.3	27.8	3.7	24.1	3.7
Restrict origin of breeding sows	55	56.4	29.1	9.1	10.9	7.3
Buy healthier/stronger sows	55	40.0	18.2	5.5	9.1	7.3

**By choosing better ingredients*

01
Vaccinations:

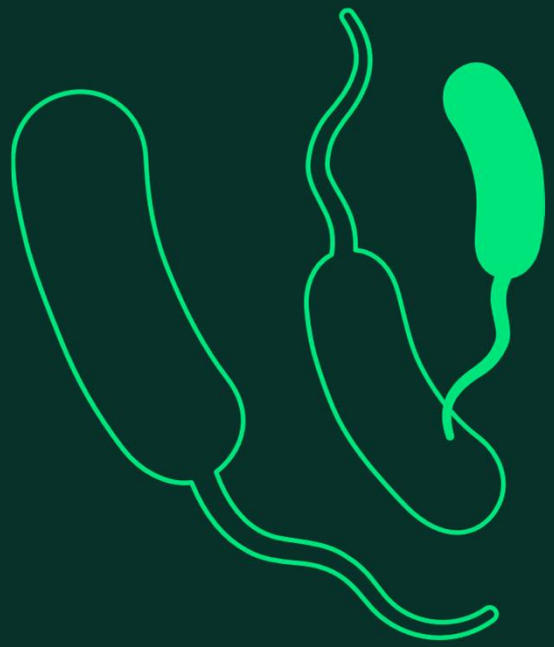
02
Very common:
PCV2, Mhyo, PRRS

03
Increasing:
Lawsonia

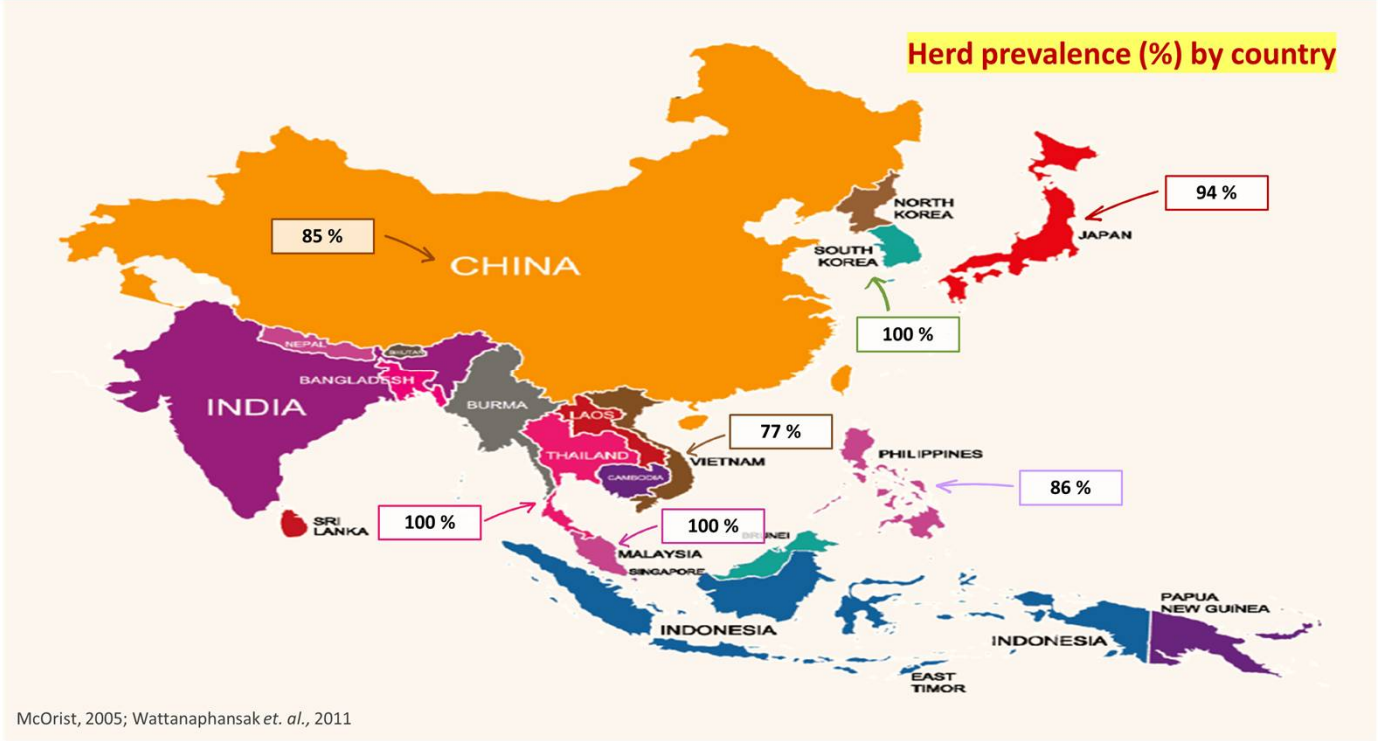
04
Specific:
E.coli, (S.suis, HPS)

1. Challenges on the Ground

Understanding the local disease landscape and practical constraints



High Level of LI Prevalence in Asia



McOrist, 2005; Wattanaphansak *et. al.*, 2011

Ileitis Prevalence in The Philippines

ILEITIS SEROLOGICAL PREVALENCE STUDY IN THIRTY PHILIPPINE SWINE FARMS II. PIG AGE SEROPREVALENCE

AC Bulay[1], CU Maala[1], RT Lising[2], H Voets[3]
[1]Boehringer Ingelheim (Phil.) Inc., MAKATI, Philippines
[2]Boehringer Ingelheim Vetmedica, SYDNEY, Australia
[3]Boehringer Ingelheim Animal Health, INGELHEIM AM RHEIN, Germany

Results and Discussion

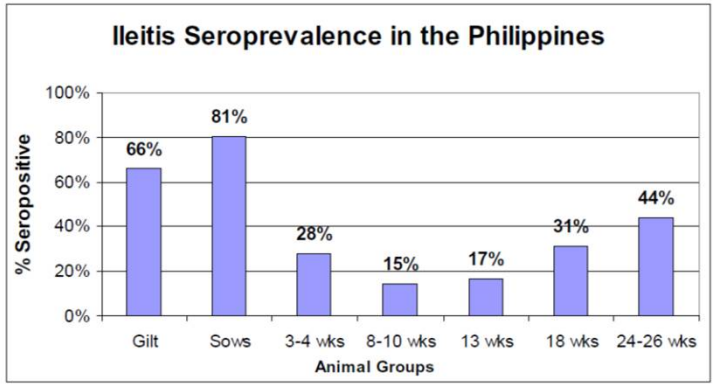


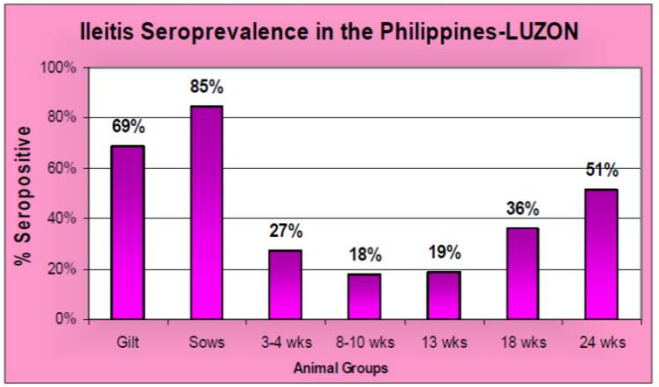
Figure 1 Age group seroprevalence (n=30 farms).

ILEITIS SEROPREVALENCE IN THE PHILIPPINES 1: LUZON

Bulay A. C.
Boehringer Ingelheim Vetmedica, Manila, Philippines

Results and Discussion

Figure 1. Age group seroprevalence (n=55 farms).



Ileitis Prevalence in The Philippines

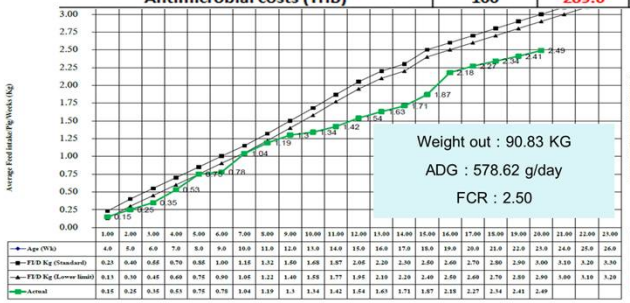
- Main source are sows
- Gilts entering the breeding herd are already exposed
- Maternal antibody effect in piglets
- Disease can be seen from end of nursery to fattening
- Cycle-like infection pattern due to inadequate quarantine procedures/replacement gilts from existing fattener population
- Masking of real LI situation due to heavy and continued use of antibiotics
    - Antibiotics do not completely prevent the persistent exposure of treated animals

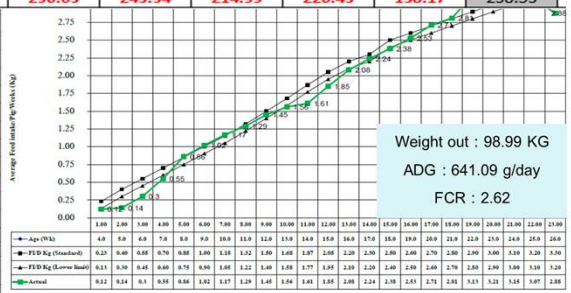
Production Performance with Subclinical Ileitis

Subclinical form now known to be of economic importance

- Commonly found in high health and high hygiene farm
- Poor growth performance issues

Wean to finisher performance (4-23 weeks)	Farm Traget	2023						
		Jan-23	Feb-23	Mar-23	Apr-23	May-23	Jun-23	Average
Initial pigs	-	1950	1477	1402	582	3377	2178	10966
Pigs out	-	1823	1306	1226	506	2785	2069	9715
Weight in (Kg)	7.5	8.26	8.25	7.61	9.12	7.89	8.52	8.28
Weight out (Kg)	105	96.29	98.33	99.33	99.73	98.99	99.14	98.64
Age (days)	164.5	178.18	162.6	150.32	154.41	158.86	159.65	160.67
Dead	1.2	1.54	2.98	2.95	4.11	5.36	2.3	3.21
Culled	2.8	4.97	8.6	9.61	8.99	12.17	2.71	7.84
%Loss (Dead+Culled)	4	6.51	11.58	12.56	13.1	17.53	5.01	11.05
Days	136.5	154.39	138.6	122.73	126.99	134	141.07	136.30
Feed Consumption (Kg)	235.2	210.71	237.63	250.71	213.28	231.09	230.68	229.02
ADG (g)	714.29	570.18	649.93	747.33	713.52	679.85	642.38	667.20
FCR (Performance)	2.41	2.39	2.64	2.73	2.35	2.54	2.55	2.53
FCR (Economic)	2.52	2.47	2.73	2.85	2.44	2.62	2.65	2.63
Antimicrobial costs (THB)	100	289.6	296.65	245.34	214.99	226.43	158.17	238.53





- ✓ Reduced ADG
- ✓ Poor FCR performance
- ✓ Low weight at market age
- ✓ Increased antimicrobial cost

Suphot Wattanaphansak

Treatment and Control of Ileitis

- Antimicrobials therapy-Clear bacteria inside pigs
  - Feed antimicrobials
  - Water antimicrobials
  - Injectable antimicrobials
- Vaccinations
  - Modified live/killed vaccine
- Pure culture inoculum + 2-3 weeks of antimicrobials
- Passive egg antibodies/ Pre, Pro, Postbiotics, immune stimulant feed supplements- gut health
- Disinfections- Clear bacteria in the environment

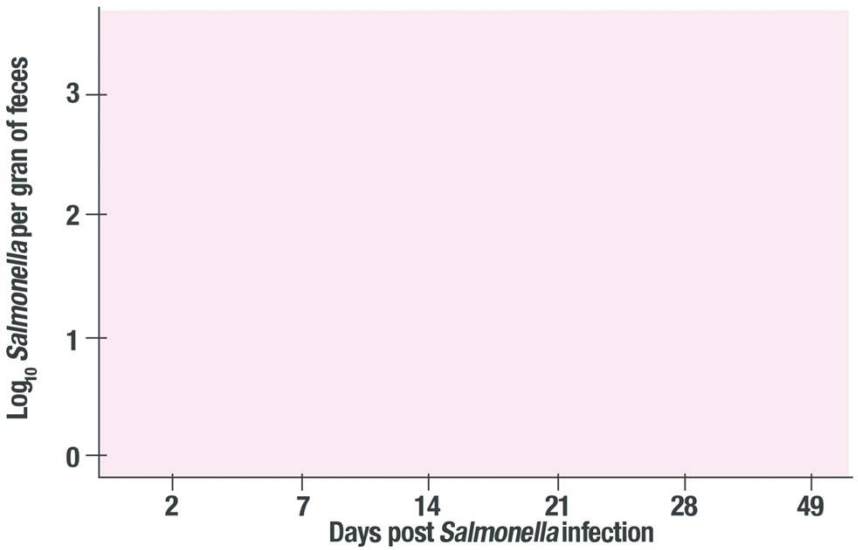
Oral Live Attenuated Vaccine

- Mimics natural infection and induce mucosal immunity
- Stimulate both HMI and CMI
- Reduced colonization of *L. intracellularis*
- Long-lasting protection
- Protection against ileitis reduce weight loss, fecal shedding, mortality, and clinical signs
- Recommended at least 3 weeks before natural infection
- Beneficial effects on the microbiome
  - Reduction of boar taint
  - Reduction of salmonella

Effect of vaccination on S. typhimurium shedding

***L. intracellularis* vaccination reduces:**

S. Typhimurium shedding in co-infected animals at the timepoints of 2, 7, 14 and 21 days post challenge.



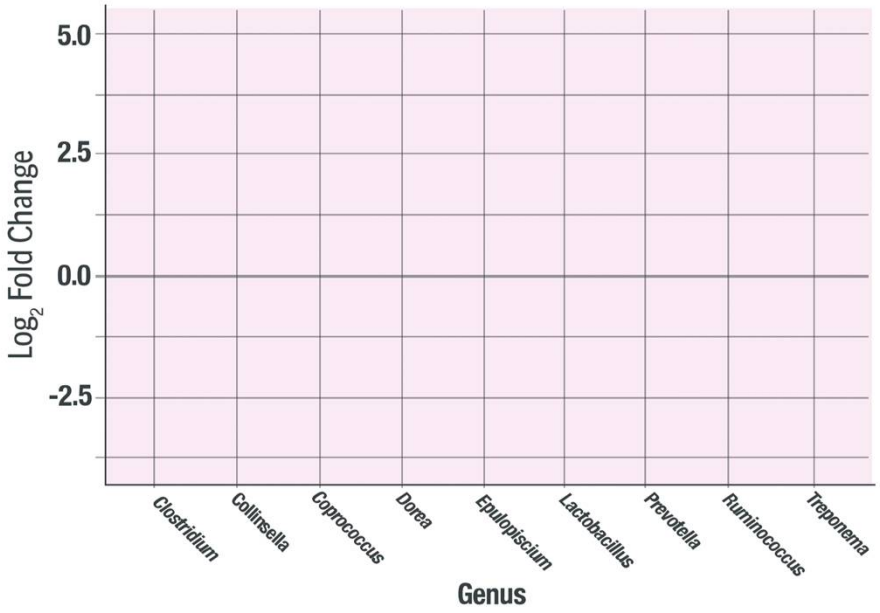
Fecal shedding of *Salmonella enterica* serovar Typhimurium over time. (Significant differences between treatment groups are designated by different letters).

Treatment

- Non-infected
- Challenge with *S.* Typhymurium
- Challenge with *S.* Typhymurium and *L. intracellularis*
- Challenge with *S.* Typhymurium and *L. intracellularis* and vaccinated against *L. intracellularis*
- Challenge with *S.* Typhymurium and vaccinated against *L. intracellularis*

Effect of vaccination on the compositional differences in the microbiome

Differences in the abundance of bacteria at the genus level at time point of seven days post challenge with *S.* Typhimurium (when *L. intracellularis* vaccination leads to the greatest reduction in shedding):



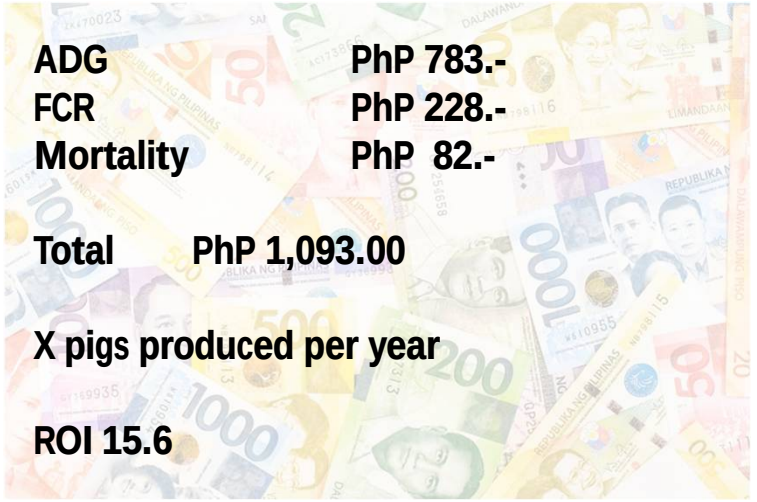
- Increase of *C. butyricum* due to Live oral vaccine
- *C. butyricum* leads to less *S.* Typhimurium shedding
- *Clostridium* species produce SCFA´s:
  - Immunosuppressive
  - Down regulate *Salmonella* pathogenicity
  - Nutrient for enterocytes

Phylum

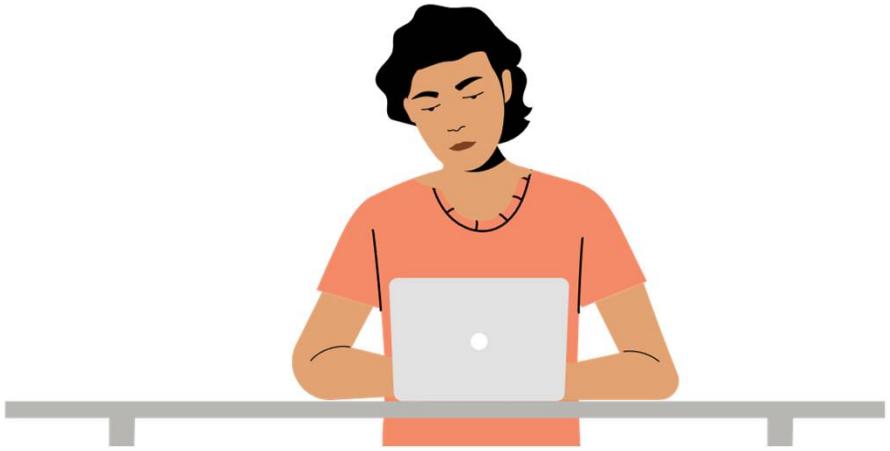
- Firmicutes
- Actinobacteria
- Bacteroidetes
- Spirochaetes

Benefits of Oral Live Attenuated Vaccine

- Significant improvement on ADG, improved mortality and cull rates (Kolb, 2003)
- Efficacious in clinical and subclinical presentations of PPE (Mcorist & Smits, 2007)
- Prevents PHE outbreaks in gilts (Waddell, 2003; Candor, 2008)
- No maternal-immunity interference (Kroll, 2004)
- 53% ABU reduction = 8.60USD higher economic benefit per pig (Voets and Hardge, 2007)
- Cost benefit ration 7:1 due to improved performance



***But Oral* application is very complicated and nobody likes it!**



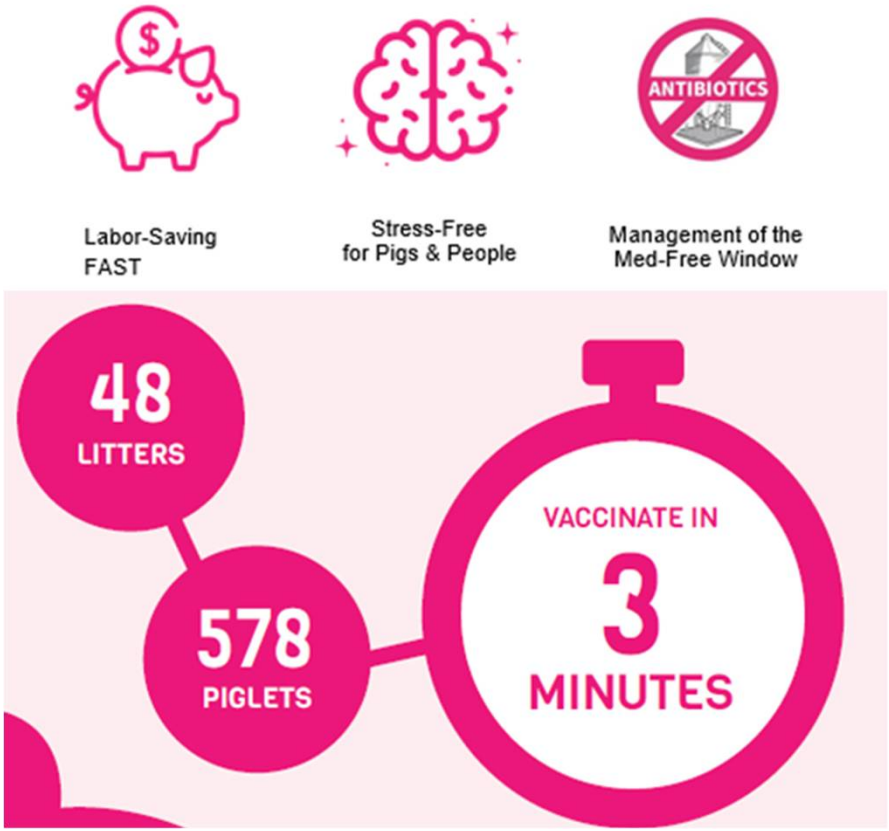
3. Innovating for Impact

How oral gel vaccination supports gut health and farm efficiency

The new way –
Gel administration

Why gel vaccination

- Gel new way
- AB free window
- Stress free
- Fast
- Convenient
- Early infections: Early vaccination and fast OOI



Conference Paper

Field experience with the oral administration of Enterisol® Ileitis by gel

February 2024
DOI:10.54846/am2024/42
Conference: AASV Annual Meeting

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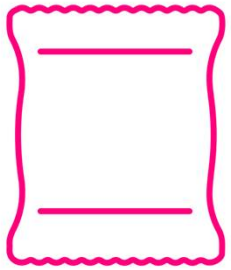
Boehringer Ingelheim Animal Health USA I...

Three Basic Steps to Oral Vaccination by Gel



1

Prepare
the gel

2

Mix
in the vaccine

3

Vaccinate
by spraying the mixture on farrowing crate mats or a surface that allows pigs to consume the gel

Trial comparing drink water vaccination with gel vaccination

Treatment	Treatment description	Pigs/Trt
1	Non-vaccinated, Challenged Controls	540
2	Oral Live Attenuated Ileitis vaccine **via gel**	540
3	Oral Live Attenuated Ileitis vaccine **via water**	540
4	Oral Live Attenuated Ileitis vaccine **+** Oral Live Attenuated Salmonella TC vaccine **via gel**	540

Gel application by applying 120mL of gel vaccine mixture per farrowing crate mat, this equals approximately 10mL/piglet assuming 12 piglets/ litter. Vaccine was used at full dose

Results

Least Square Means ± SE

	Treatment					Covariate P-value
Parameter	**Non-vaccinated, *L. intracellularis* challenged control**	**Oral Ileitis gel (14–19 DOA)**	**Oral Ileitis water (6 WOA)**	**Oral Ileitis + Oral Salmonella T/C® gel (14–19 DOA)**	**P-value**	**Commingling weight**
Allocation weight, kg	4.71 ± 0.04	4.71 ± 0.04	4.69 ± 0.04	4.69 ± 0.04	0.96	-
Commingling weight, kg	37.70 ± 0.30^{c}	**44.88 ± 0.31^{a}**	37.90 ± 0.31^{bc}	39.02 ± 0.30^{b}	**<0.0001**	-
Final weight, kg	101.34 ± 0.81^{c}	**112.57 ± 0.82^{a}**	108.74 ± 0.81^{b}	110.15 ± 0.80^{ab}	**<0.0001**	-
Final weight, kg[i]	103.40 ± 0.58^{b}	**108.90 ± 0.59^{a}**	**110.39 ± 0.59^{a}**	**109.95 ± 0.58^{a}**	**<0.0001**	**<0.0001**
ADG (allocation to commingling), g/day	471 ± 5^{c}	**517 ± 5^{a}**	476 ± 5^{c}	490 ± 5^{b}	**<0.0001**	-
ADG (allocation to final), g/day	658 ± 5^{c}	**735 ± 5^{a}**	708 ± 5^{b}	717 ± 5^{ab}	**<0.0001**	-
ADG (commingling to final), g/day	826 ± 9^{b}	**930 ± 9^{a}**	**916 ± 9^{a}**	**921 ± 9^{a}**	**<0.0001**	-
ADG (commingling to final), g/day[i]	834 ± 9^{b}	**907 ± 9^{a}**	**925 ± 9^{a}**	**921 ± 9^{a}**	**<0.0001**	**<0.0001**

Results

	Treatment				
	Non-vaccinated, Lawsonia challenge control	**Oral ileitis in gel**	**Oral ileitis in water**	**Oral ileitis + Oral salmonella in gel**	**P-value**
ADG (commingling to final), lbs/day	1.82 ± 0.02[b]	**2.05 ± 0.02[a]**	**2.02 ± 0.02[a]**	**2.03 ± 0.02[a]**	<0.0001

	Treatment				
	Non-vaccinated, Lawsonia challenge control	**Oral ileitis in gel**	**Oral ileitis in water**	**Oral ileitis + Oral salmonella in gel**	**P-value**
Removal and mortality, %	7.45 ± 0.92[b]	**4.31 ± 0.95[a]**	**4.11 ± 0.95[a]**	**3.17 ± 0.93[a]**	0.007

Gel summary

Gel is a delivery vehicle for the vaccine, similar to water, taking advantage of the oral route of administration to allow pigs to be administered vaccine passively, without the need to individually handle each pig

Evaluating 45 litters and 540 pigs per treatment group in a *Lawsonia* seeder challenge model the level of protection as measured by wean-to-finish ADG and mortality was similar among gel administration and water administration

Summary

- Antibiotic reduction possible while increasing performance
- Feed, management, biosecurity, vaccination, colostrum intake
- Gel vaccination: Easy and effective
- Oral LI vaccine boosts performance, and support reduction of antibiotic use