EUROPEAN STRATEGIES FOR REDUCING MEDICATED ZINC OXIDE AND ANTIBIOTICS IN THE WEANED PIGLET FEED

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Gilles LANGEOIRE on Banff Pork Seminar invitation

To underline the threat !

Growing concerns over antibiotic resistance and a large consumer demand for antibiotic-free meat

- That recent publication from the OXFORD university:

UNIVERSITY OF OXFORD

Antibiotic resistance has claimed at least one million lives each year since 1990

GLOBAL HEALTH | MEDICAL SCIENCES | RESEARCH

A landmark GRAM Project study of global antimicrobial resistance (AMR) burden over time forecasts a sharp rise in deaths, with 39 million lives lost between now and 2050.

To put these data into perspective:

Some main causes of death Worldwide		Nbr of Deaths/year
Cardiovascular diseases (WH0)	2019	8.9 million
Cancers (WHO)	2020	10 million
Diabetes (WHO)	2016	1.6 million
Road Traffic accidents	2020	1.3 million
Suicides	2019	703 000
Homicides	2021	458 000

In term of lost lives: The antibiotic resistance could be compared to road traffic accidents

But we know that positive signs have shown that resistance to antibiotics can be reversed by lower antibiotic usage !

In the E.U.: We faced that situation relatively early!

- E.U. started to ban AB (as growth promoter) in 2006!
  - But much more early one of the first attempt to solve the Post Weaning Diarrhoea, was the use of 3kg/t of ZnO (first in Denmark, then Worldwide)
  - But in France and the Netherland that solution was never allowed:
    - Environmental reasons mainly
  - Finaly this ban on medicated ZnO was extended to all Europe in 2022:
    - The legal dosage for ZnO: 150 mg/kg of feed
  - Currently in E.U. a stronger pressure to reduce the AB, even as a treatment!
    - i.e.: As a financial compensation: A piglet weaned without AB (and Zn0) receives an extra price!
    - At least:
      - 60% of the French, and 30-40% of the Danish piglets are weaned without medicated ZnO and AB!

What was made to face that new situation: First!

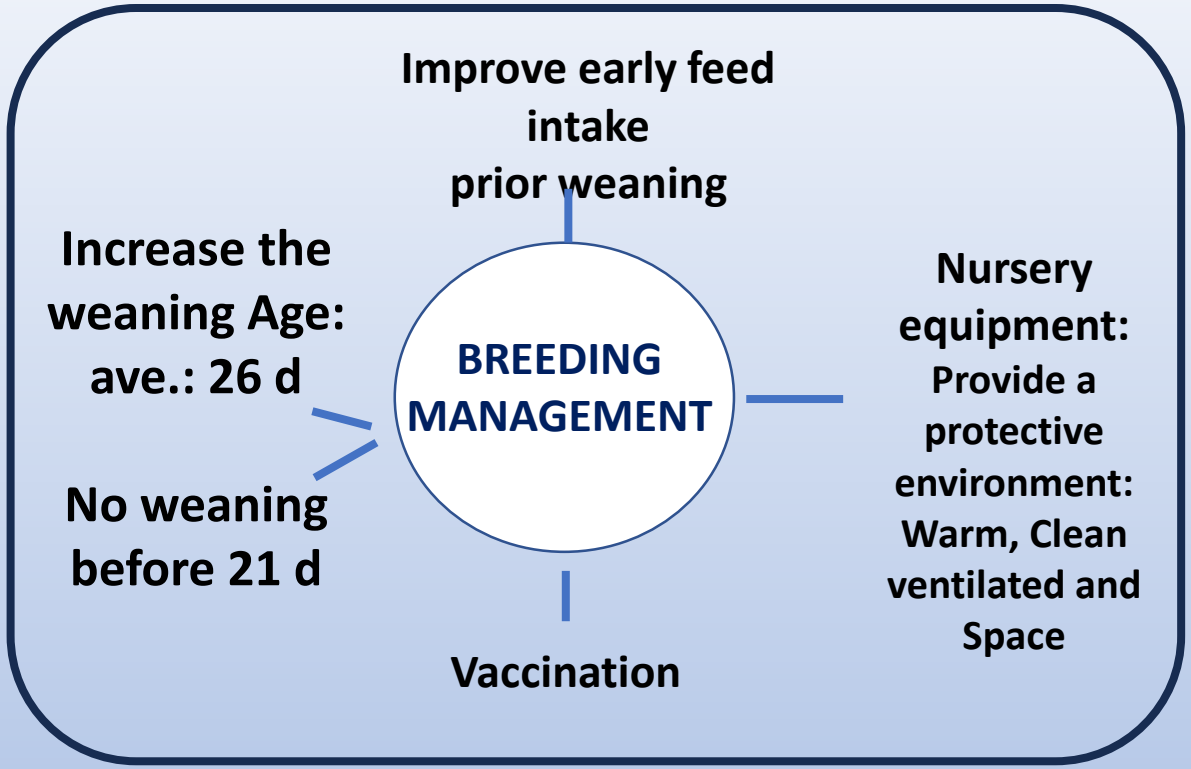
Starting point of that new approach:

- We Knew that nothing could currently be compared to the antimicrobial effectiveness of antibiotics
- No single solution to compensate for their ban

Solutions considered:

- We started to work in 2003, on a holistic approach in the piglet breeding management and the feed formulation!

BREEDING MANAGEMENT:

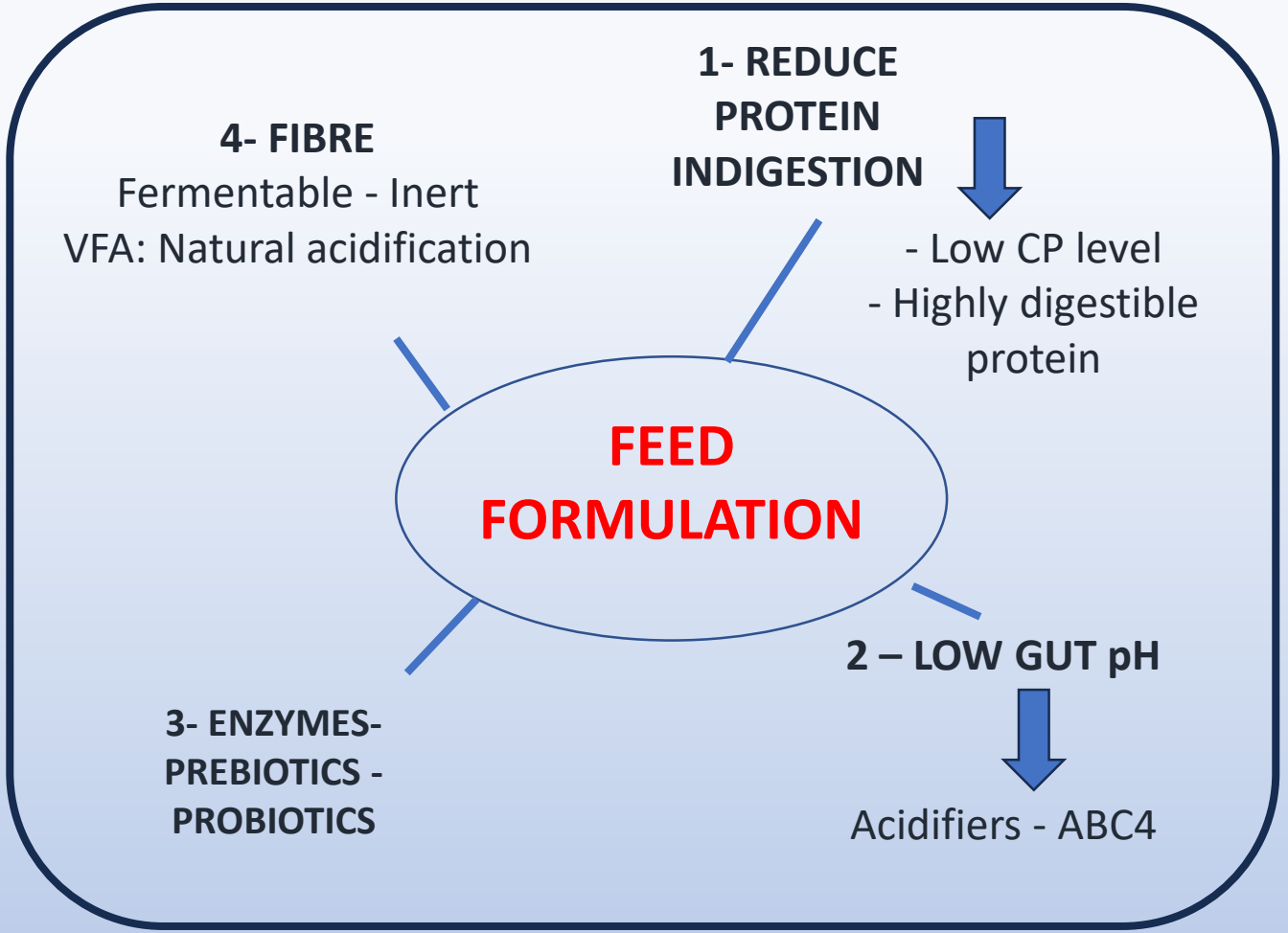


Second!

NUTRITION: 2 key points to secure the gut health:

1-Nutrients digestibility
- Mainly Protein

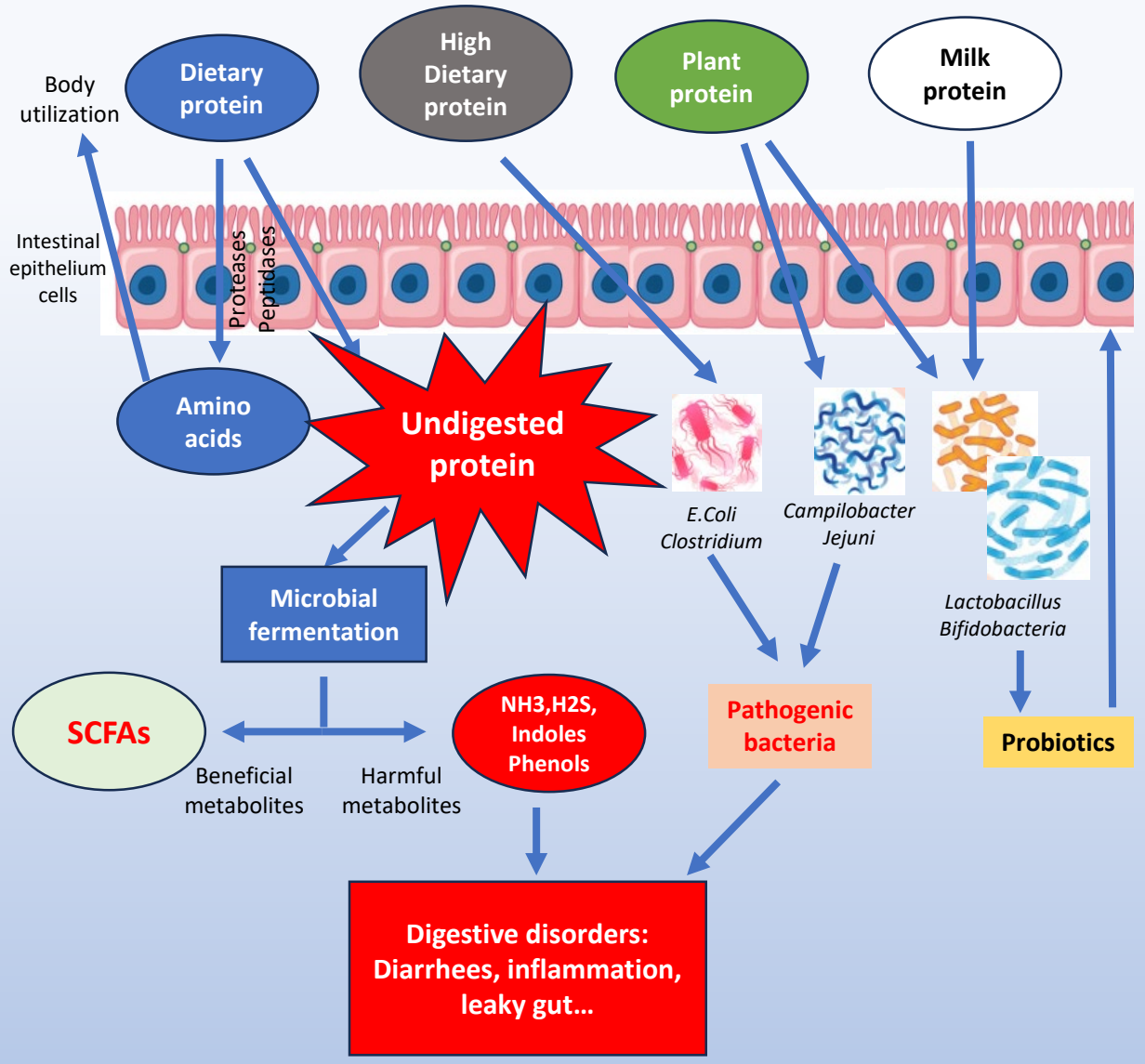
2-Gut acidification



1- Reducing the undigestible protein level in the piglet diet?

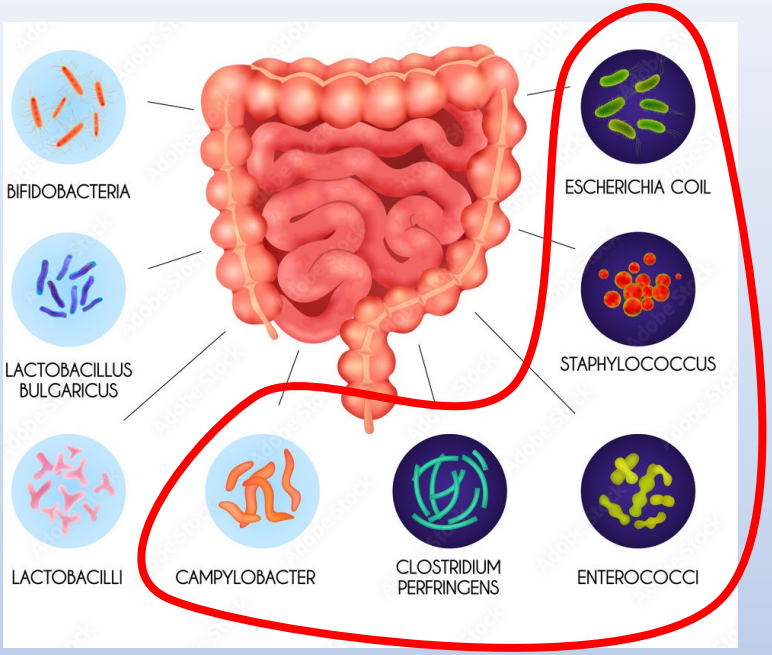
A first attempt to reduce the PW diarrhoea risk

The risk of protein indigestion!



- For a young piglet the non digestible fraction of proteins will ferment in the hind gut leading to:
  - **Toxics by products:** *mono-amines, poly-amines, ammonia, hydrogen sulfide, phenols and indoles.*
- Because the gut barrier is rapidly affected (within 24 hours after weaning)
  - These toxics threaten the intestinal integrity, leading to inflammation and gut disorders

- The protein indigestion not only reduces efficiency of feed utilization:
  - but also **increase the intestinal microflora populations that thrive on protein**:
    - *Escherichia coli*, *Klebsiella* spp., *Campylobacter* spp., *Streptococcus* spp., *Clostridium perfringens*, *Clostridium difficile* et *Bacteroides fragilis*…



Many of them are pathogens!!!

- It was therefore important to limit the Protein undigestible fraction entering the hind gut :
  - Low protein diets
  - Highly digestible protein

But: Feeding nursery pigs with very low protein diets resulted generally in decreased feed intake, growth performance

Different recent studies

Results: comparison High vs Low CP

The effect of CP level on piglet growth performance between day 0-35 PW

Treatment	High CP + SBM/SPC	Normal CP + SBM/SPC	LSD	P-Value
Body Weight, kg	7,64	7,64	0,167	0,99
ADG, g/d/piglet: d 0-14	203	190	17,3	0,16
ADFI, g/d/piglet: d 14 -35	690	719	37,8	0,13
Faecal Score:				
d 0 -14	5,17	5,63	0,523	
d 0- 35	5,80	6,00	0,412	

- With Low CP diet:
  - ADG:
    - No statistical difference but a tendency to lower growth during the first period
  - ADFI:
    - Tendency to increase feed intake during the second period
    - Compensatory consumption due to uncover needs during the first period (?)
  - Faecal score:
    - Tendency to improve the faeces

other trial reducing the CP level in Pre starter feed, improve the faeces consistency, but reduces the growth performance

Nursery Phase

According to **NRC (2012)** and **Brazilian Tables (Rostagno et al., 2017)**, a **corn and soybean meal-based diet** for 7 kg body weight pigs typically contains approximately **20.5% CP**.

According to the current meta-analysis, the estimated breakpoint for **CP** was **18.4%**, below which **average daily gain (ADG)** would be reduced. Taking into account **feed efficiency, the estimated level was 18.3% CP**.

The suggested **minimum CP level** for **nursery pig diets** is **lower than the levels recommended by NRC (2012)** and **Brazilian Tables** (*Rostagno et al., 2017*), suggesting that **CP levels** lower than those provided in the Tables can be used for **diet formulation in this phase**.

Moreover, the study also estimated the highest levels of industrial lysine that could be supplemented without compromising ADG and feed efficiency, which were 0.42% and 0.43% L-lysine, respectively.

This is equivalent to 0.54% L-lysine HCl (78.8% purity) or 0.71% L-lysine sulfate (60.0% purity).

ELSEVIER

Animal

Volume 15, Issue 1, January 2021, 100075

Low protein diets without medicinal zinc oxide for weaned pigs reduced diarrhea treatments and average daily gain

J.C. Lynegaard, C. Amdi, N.L. Kjeldsen, I.K. Boche, N.B. Weber, C.F. Hansen, J.P. Nielsen

Conclusion

Reduced dietary protein decreases diarrhea post-weaning but is still not as rewarding as medicinal ZnO. The PC pigs supplemented with 2 500 ppm medicinal ZnO had 42% fewer diarrhea treated pens compared to NC pigs without medicinal ZnO during the overall trial period from 6 to 30 kg. The LLH pigs had a significant reduction of 26% in the number of treatment days per pig compared to NC pigs. However, a low protein supply also resulted in a 16 g lower ADG in the LLH and VMH pigs.

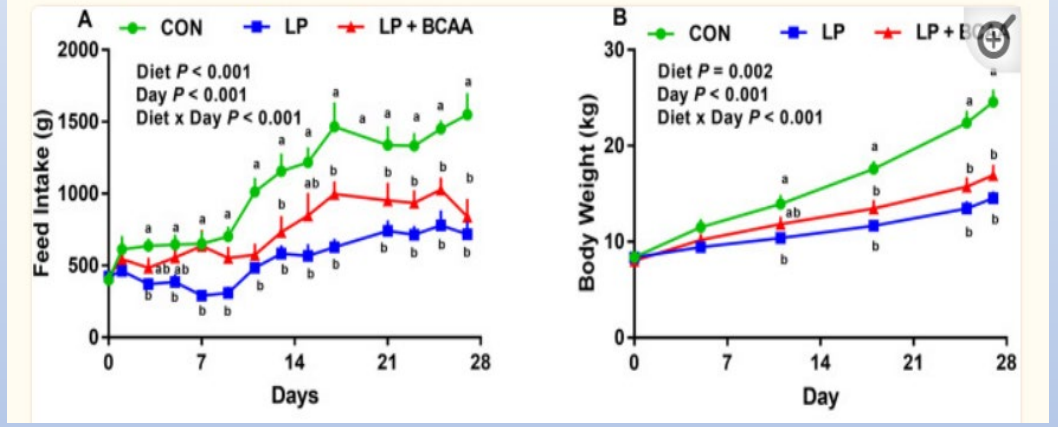
Effect of feeding low protein diets supplemented with selected essential amino acids on growth performance and gut health in early weaned Large White Yorkshire piglets

Dr.Jith John Mathew

Journal of Veterinary and Animal Sciences

Effect of very low-protein diets supplemented with branched-chain amino acids on energy balance, plasma metabolomics and fecal microbiome of pigs

Shelby Spring, Hasitha Premathilake, Chloe Bradway, Cedrick Shili, Udaya DeSilva, Scott Carter, and Adel Pezeshki



But resulting also in A BETTER FAECES CONSISTENCY: The risk of diarrhoeas is limited !

During the second period: (10-25kgBW)?

No medicated ZnO
No AB

- The low level of protein can be balanced with a correct AA supplementation
- For similar performance!

Crude protein,%	22,4	20,4	18,4	16,9
Ingredients, kg/t				
Wheat	203	220	240	266
Corn	193	216	235	238
Barley	203	220	240	266
SBM	365	302	240	177
L-Lysine HCl		2	4	6
DL-Methionine	0,2	0,8	1,4	2
L-Threonine		0,9	1,8	2,7
L-Tryptophan			0,3	0,7
L-Isoleucine			0,1	1,2
L-Valine			0,9	1,9
Performance				
Feed intake, g/d	959a	1039b	1061b	1048b
Weight gain, g/d	642	661	690	663
Feed efficiency, kg/kg	1,5	1,58	1,54	1,58

The low feed intake is probably due to the high SBM level and its ANF

Same performance with a good AA ratio

Effect of the crude protein level and free amino acid s supplementation, on performance of piglets from 12 to 27 kg BW (Le Bellego and Noblet, 2002)

Many studies have shown that feeding low protein level is one of the major solution to reduce scouring problem on farm

Eggum and al.,				
Crude protein,%	25,4	16	11	7
Diarrhoea cases,%	17	16	11	7
Eggum and al.,				
Crude protein,%	26,6	23,1	19,5	
Diarrhoea cases,%	14	3	4	
Bolduan and al.,				
Crude protein,%	20,2	18,4	16,3	
Diarrhoea cases,%	3,2	2,4	0,8	
Le Bellego and Noblet				
Crude protein,%	22,4	20,4	18,4	16,9
Diarrhoea cases,%	18,1	18	4,6	11
1 % of days with soft or liquid faeces				

From Ajinomoto 2002

Questions:

- Low CP feed formulation costly ?
  - Especially with ME formulation
  - High variation of the synthetic AA costs
- Risk of secondary AA deficiencies
  - Low Feed intake, low Growth
  - Mainly during the pre starter period
- So Low CP% is a major solution to reduce scouring problem on farm

Yes, but not only !

The main question is the protein digestibility!

Using Highly digestible protein source will improve the gut health of the young piglets

A first digestibility trial from SFR (ND), measured on young piglets, had shown large differences on the CP digestibility of diverse components

Feedstuff level: Ileum of young piglets at weaning (26d).

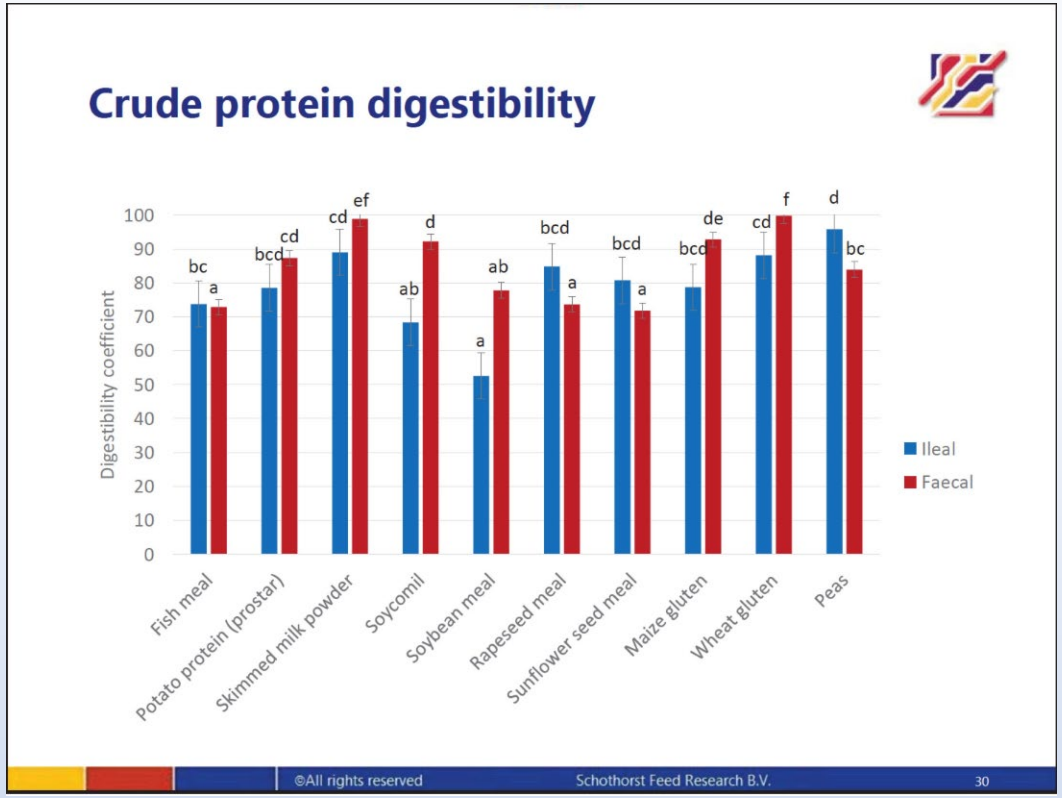
Trt	Diet	Description	CP, %
2	B	Soybean meal	72.5[a]
3	C	**Highly Digest. SPC**	84.9[b]
4	D	FF LT Supreme	70.6[a]
		LSD	8.05
		P-value	**0.005**

In case of low protein diet: The inclusion of highly digestible protein sources, became major !

Components	CP %	Protein Dig %	Dig Lysine	NE g MJ	NE s MJ
Acid Whey powder	9,7	96	0,65	11,38	11,28
Milk powder (LACTA 285)	29	97	2,7	11,35	11,30
Milk Protein concentrate	65	85	4,2	10,2	10,3
Fish meal	65 - 72	70	4,3	9,94	9,89
Soy Protein Concentrate AX3	68	85	4,1	12	12,2
Potato protein concentrate	77	90	5,24	10,23	10,30
Wheat Gluten protein	75	85	15,2	10,9	11,3
Corn Gluten (Roquette)	61,6	88	10,9	11,4	12
Pea protein (Lysamine)	80,1	75	4,8	11,2	11,4
Extruded SBM Danex	34,8	73	1,88	10,71	11,52
Plasma protein (ADM)	73	88	8,7	10,2	10,3
Soy Bean Meal 46%	43,5	72	5,2	8,3	8,9

The new piglet feed formulation was calculated including the protein digestibility of the components

- Recommendation for the feed formulation:
  - Maximum of CP %
  - Minimum of Digestible Protein %



Personal experience

FEED	PRESTARTER		STARTER	
BW, kg	5,5 – 10 Kg		10 – 25 Kg	
	mini	maxi	mini	maxi
Crude Protein, %	17,5	20	17	18,5
Digest. Protein, %	16,5		15,5	

2- A low gut pH for a better health and a better digestibility

Gastric acidification

Low ABC4

- A low pH in the feed and in the upper intestinal tract:
  - Reduces the proliferation of the feed endogenous microflora (Yeast, mold, bacteria …)
  - Limits the pathogens in the stomach and in the small intestine:
    - Most pathogens will not multiply below a pH of about 4

Optimum gut pH levels for pathogen growth:

E. coli 6-8
Streptococci 6-7.5
Salmonella 6-7.5
Staphylococci 6.8-7.5
Pseudomonas 6.6-7.0

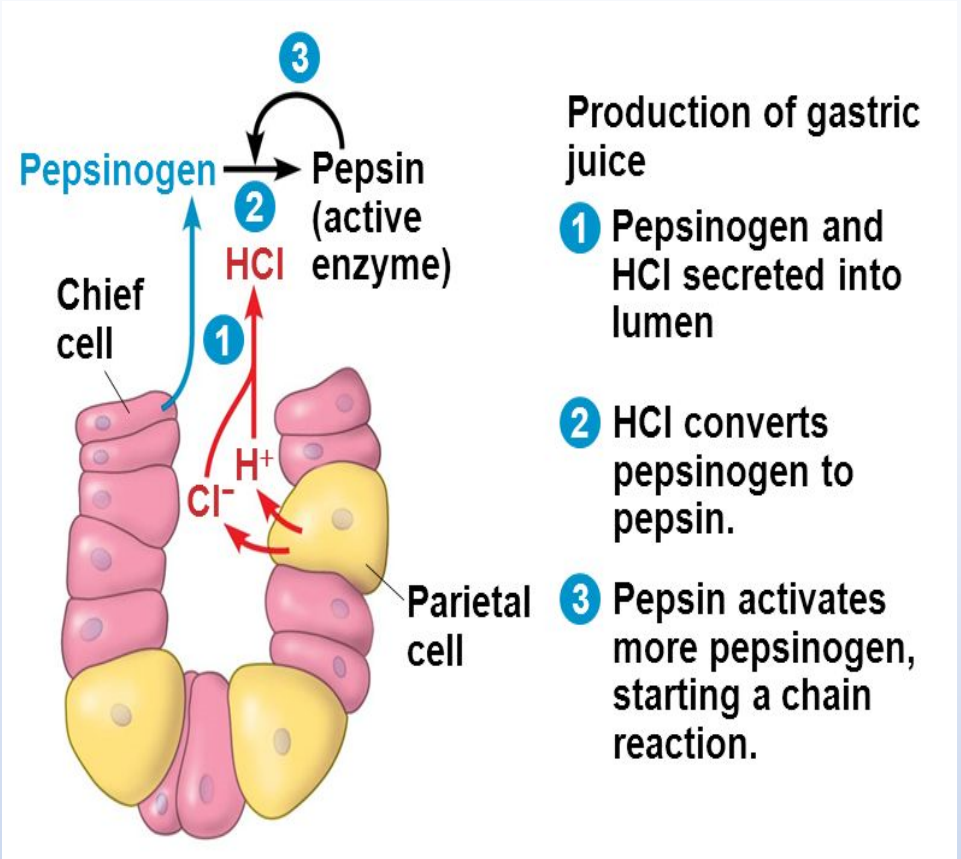
- A low gut pH and a Low buffering capacity: IMPROVE THE DIGESTIBILITY OF THE DIET, especially protein

	Low ABC4		*High ABC4*	
Acid	-	+	-	+
pH	5,2	4,3	7,4	5,8
Digestibility: %				
CP	73,6a	80,9b	71,0	76,2
GE	71,8a	74,5b	64,4	70,7
LYSINE	83,4a	89,0	74,2	80,1
METHIONINE	86,2	88,7	79,6	82,0
THREONINE	68,8a	77,1b	64,1	72,3

Blank et al., 1999

Process of acidification in the stomach

- For a young pig the acidification in the stomach is mediated by both hydrochloric and lactic acids:
-
  - Hydrochloric acid is secreted by the gut parietal cells
  - Lactic acid is produced by dietary lactose fermentation and lactobacillus



Diet acidification + low buffer capacity will improve the HCl and Lactic acid efficiency

Gastric physiological acidification

The Gastric acid production depend of how old is the animal

- Very poor for the suckling piglet
  - Acidification comes from the milk lactose fermentation.
- Still poor for the weaned piglet :
  - Poor ability to produce gastric enzyme
  - Few dietary lactose
- Optimum for the growing and adult pigs :
  - Full enzymatic system

Other factors

- Level of feed intake :
  - *Ad Libitum* / restricted
- Particle size :
  - Fine / Coarse
- And : **A LOW ACID BINDING CAPACITY OF THE DIET**

Different solutions to improve the gut acidification

Point 1: Acidification of the upper part of DT

Use of organic acids

Since the ban of AB as growth promoter we started to use Organic acids:

- **SCFA first** **(formic, lactic, propionic, fumaric…)**
- **MCFA** **(C6-C8-C10-C12)**

Because of their efficient anti microbial properties

		Stomach pH value	
		Control	Treatment
BOLDUAN et al.	Formic acid	4,0	3,7
ROTH et al.	HCl Fumaric acid	4,73 4,73	4,45 4,01
RISLEY et al.	Fumaric acid Citric acid	4,07 4,07	3,87 3,82
RADCLIFFE et al.	Citric acid	3,6	3,33
DECUYPERE	Citric acid	4,5	3,8

Point 2: Acidification of the Lowest part of DT

Use of fibre

Then we started to use Fibre because of their fermentable properties leading to the VFA production and a natural gut acidification

Point 3: Improvement of OA and gastric acidification efficiency

Formulation with a low ABC diet

Importance of the diet Acid Binding Capacity (ABC)

- Definition: A solution's resistance to any pH variation due to acid or base addition

- ABC can be measured in the laboratory :
  - Lund Jensen Method : Maximum amount of either strong acid (HCl) or strong base (NaOH) that can be added to 1kg of feed to reach pH 3 (ABC3) or pH4 (ABC4) at a T° of 37°C.
  - ABC (milliequivalent of HCl/kg)=((Molar concentration of HCl (mole/ml) x Volume of acid (ml))/ (weight of sample (g)) x 1000

Different effect of nutrients on the ABC

- **Energy** from Starch and lipids : little impact on acid binding capacity
  - Their catabolism produce CO_2 and Volatile Fatty Acids
- **Protein** : Increase the acid binding capacity
  - The protein catabolism produces ammonia, ketones bodies … which increase the gut pH
- **Minerals :** Large impact on ABC

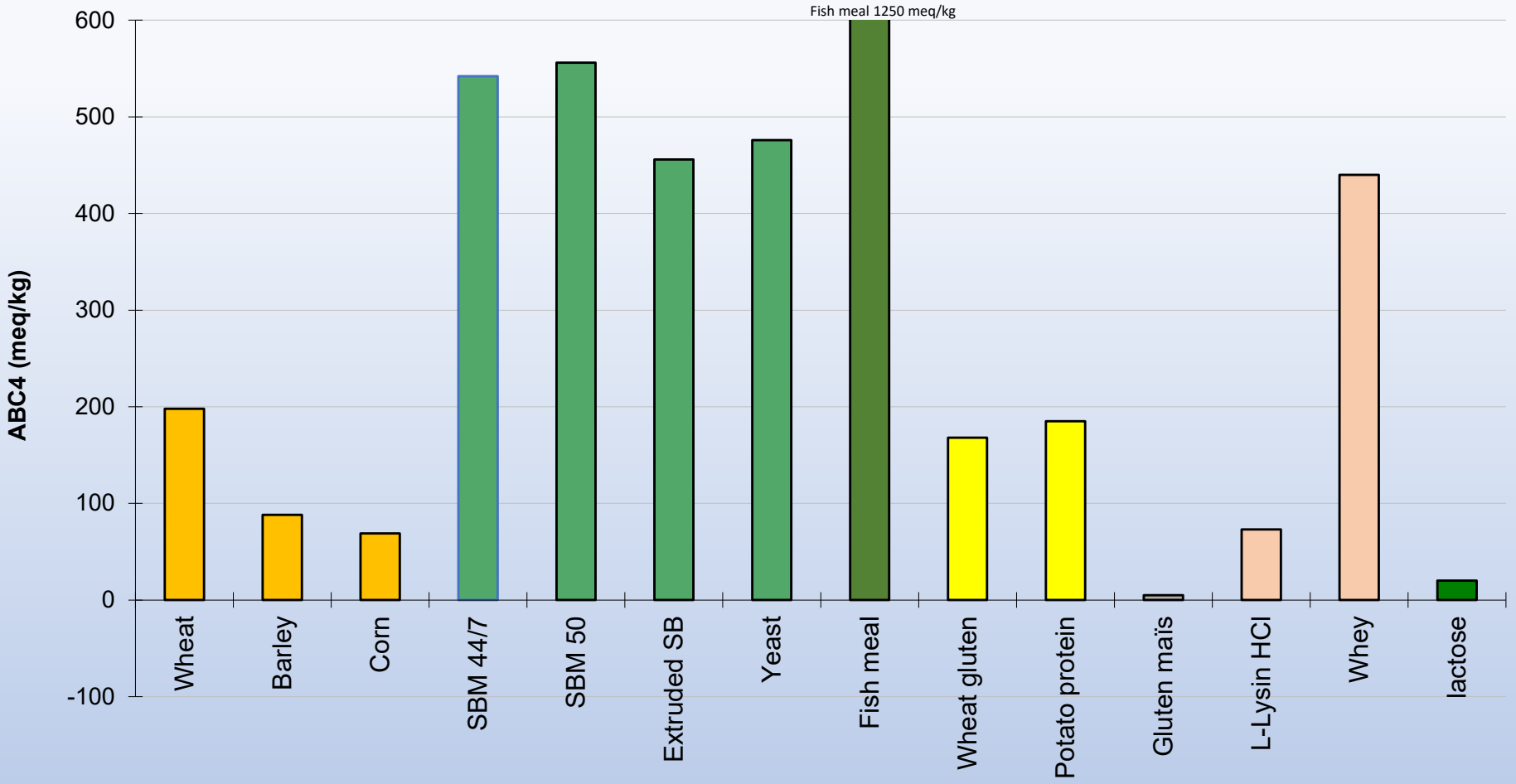
For the weaned piglet feed formulation:

ABC4 should be considered

(Acid Biding capacity to a titration of pH4)

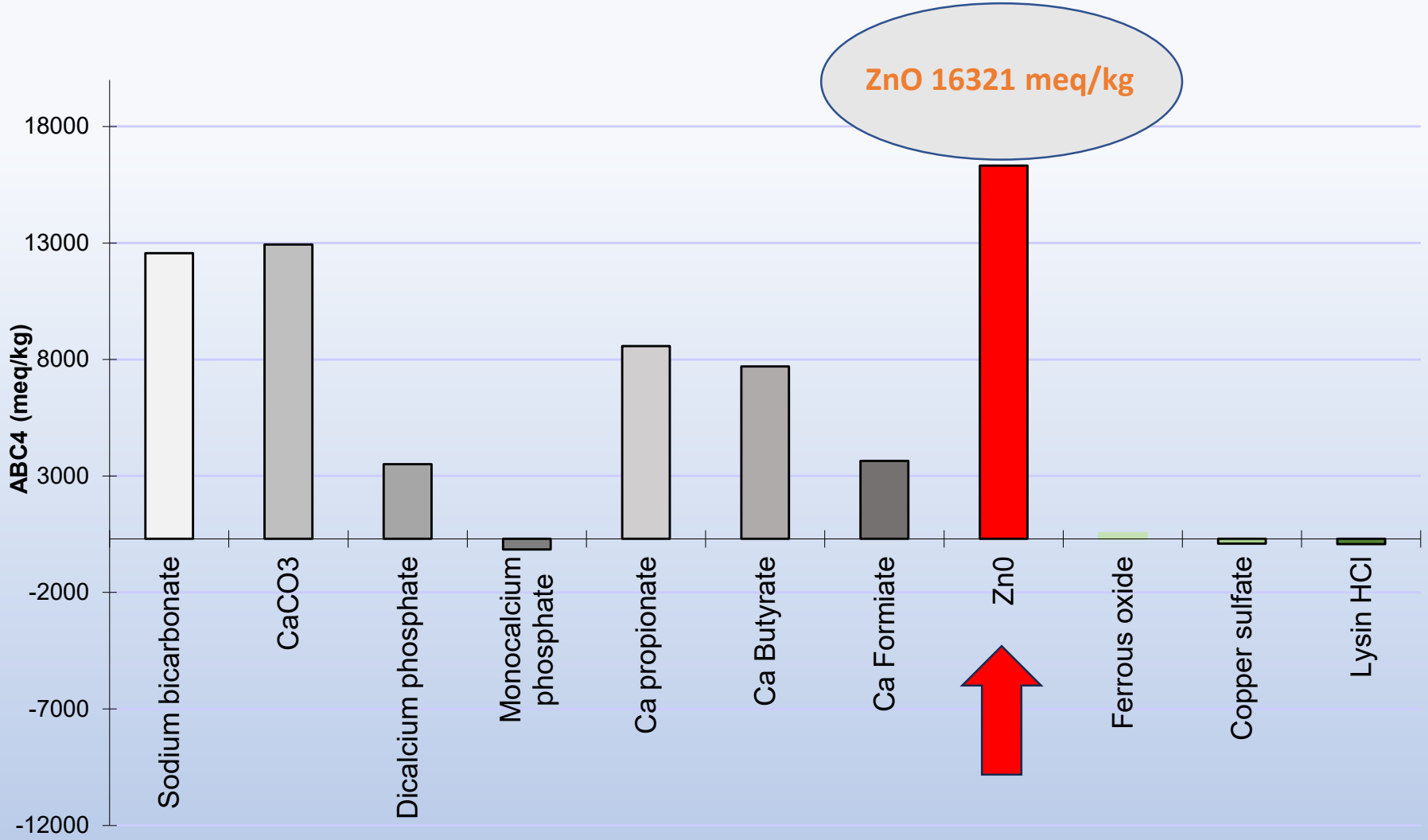
- Physiologically enough for weaned piglet feed because :
  - At weaning the optimum gastric pH is about 4
  - A low gastric pH 2-3 is reach about 50 days after weaning
- ABC3 would be considered for growing and adult pigs, which are rarely affected by gastric acidification.

Acid binding Capacity values of the main piglet feed commodities From P. Lawlor



Minerals' acid binding capacity is very High

- Between : 5 000 to 15 000 meq/kg



How to reduce the ABC4 value of the piglet feed?

- Choose organic acids with high ABC4 negative values (formic, fumaric …)
    - Choose a low ABC4 calcium source

- Reduced mineral requirement :
    - Reduced Calcium carbonate level:
    - Use MCP instead of DCP and phytase to improve the P digestibility and improve the ABC4

- Reduce the ZnO which will buffer the beneficial impact of the OA !
- Use potentiated ZnO to improve the antimicrobial efficiency with a low inclusion rate

Organic acid	pH	ABC4 meq/kg	Anti microbial effect
Orthophosphoric a.	1.6	-8858	+++
Fumaric a.	2.3	-10862	+++
Formic a.	2.3	-13550	+++
Citric a.	2.2	-5605	
Ascorbic a.	2.8	-217	-
Malic a.	2.2	-7214	++
Lactic a.	2.4	-5079	++
Acetic a.	2.9	-2283	+
Propionic a.	3.0	-1358	+
Benzoïc a.	2.5-4	- 8650	+++
Sorbic a.	3.5	-220	-

ABC4 requirements for the piglet feed

- ABC4 requirements : Low Zn0 and no antibiotics
  - **1st period 6-12 kg: 140 and 200 meq/kg feed**
  - **2nd period 12-27 kg: 200 – 250 meq/kg**

With a lower level: (100meq/kg)

- Short term: Low feed intake
- Long term: Bone demineralization, lameness and fractures

With a higher level: (350-400 meq/kg)

- Low protein digestibility:
- Loss of OA efficiencies
- Low growth performances,

Improve the protein digestibility:

- reduce the risk of a high dietary CP level
- Limit the proteolytic fermentation

A better efficiency of the in-feed OA inclusion

Using Fibre in the piglet diet: A new nutrient
Some definitions

- Dietary fibre is the sum of Non Starch Polysaccharides (NSP) + Lignin
  - Different polymers for different fibre composition: Cellulose, Hemicelluloses: (β-glucan, arabinoxylans, xylan…), Pectins, gum, mucilage's…

- Definition from KE Bach Knudsen: NSP are resistant to digestion by endogenous enzymes in the small intestine thereby becoming the main substrate for bacterial fermentation, particularly in the large intestine

- So: The digestible NSP will ferment, lignin and the non digestible NSPs are not fermentable and inert

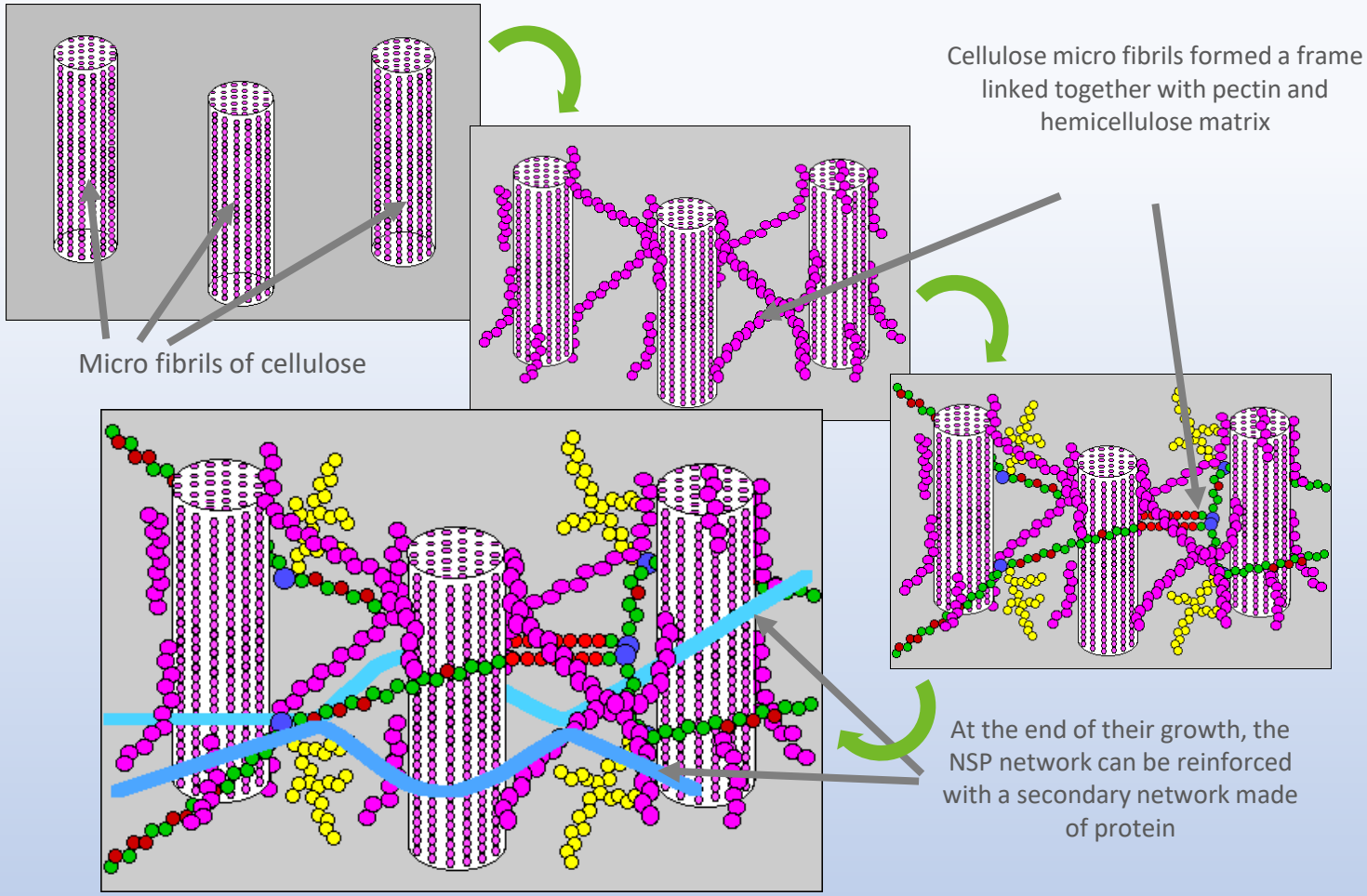
Why these difference in digestibility-fermentability?

The plant cell wall

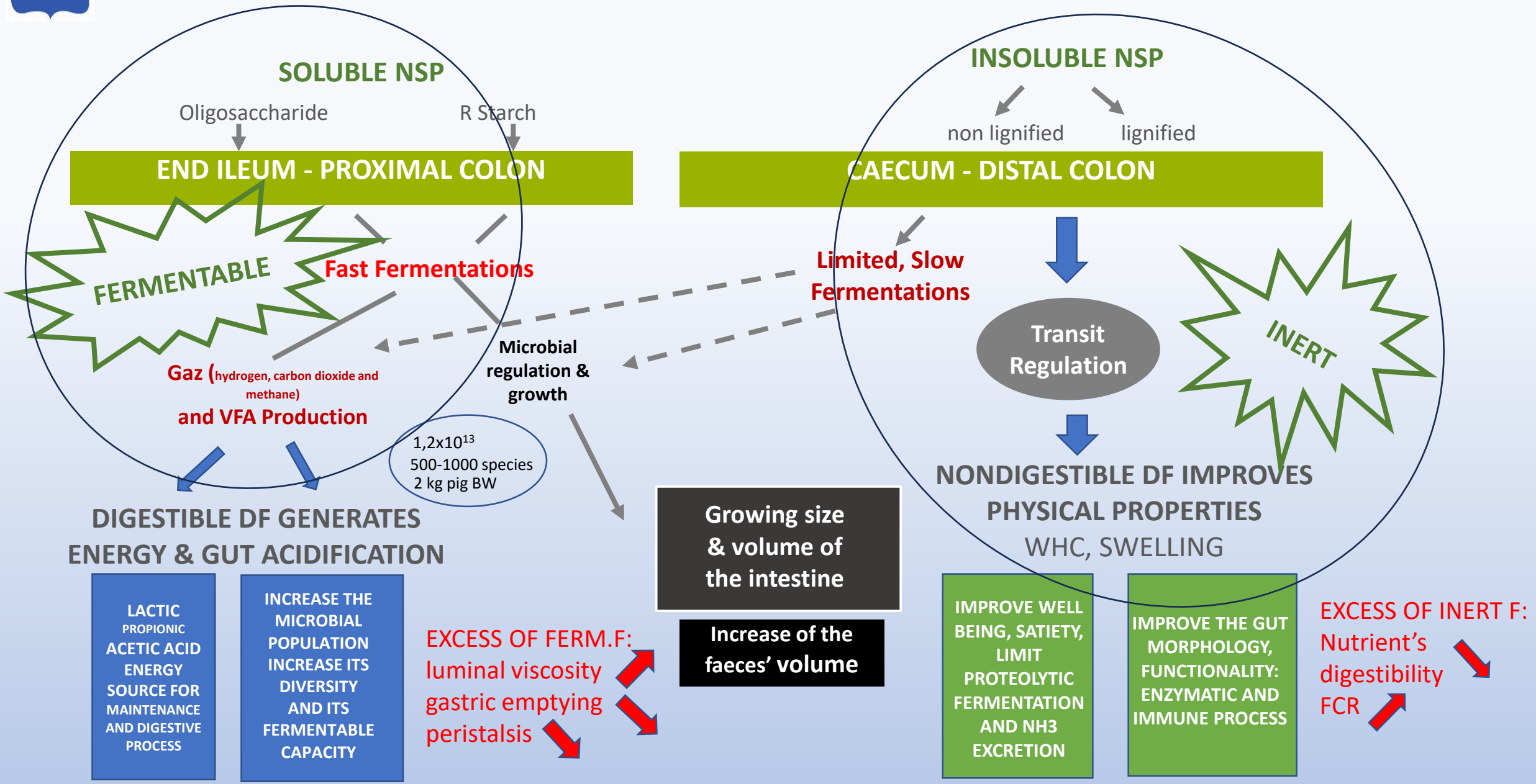
<u>The fermentability will depend of the NSP digestibility:</u>

- depending on:
  - Chain length
  - Degree of ramification

- Mainly related to solubility



Effects of fermentable and Inert fibre in the **LARGE INTESTINE**



Adapted from K.E.Bach Knudsen

How to use Dietary Fibre in the piglet feed:

- Two situations must be distinguished:

  - **For the Creep-weaner feed:**
    - Positive effect of Inert fibre:
      - Gut development: Volume, size and functionalities
      - Preparing to weaning: for a higher feed intake
    - Needs SMALL AMOUNT OF INERT FIBRE (= non digestible NSP + Lignin)

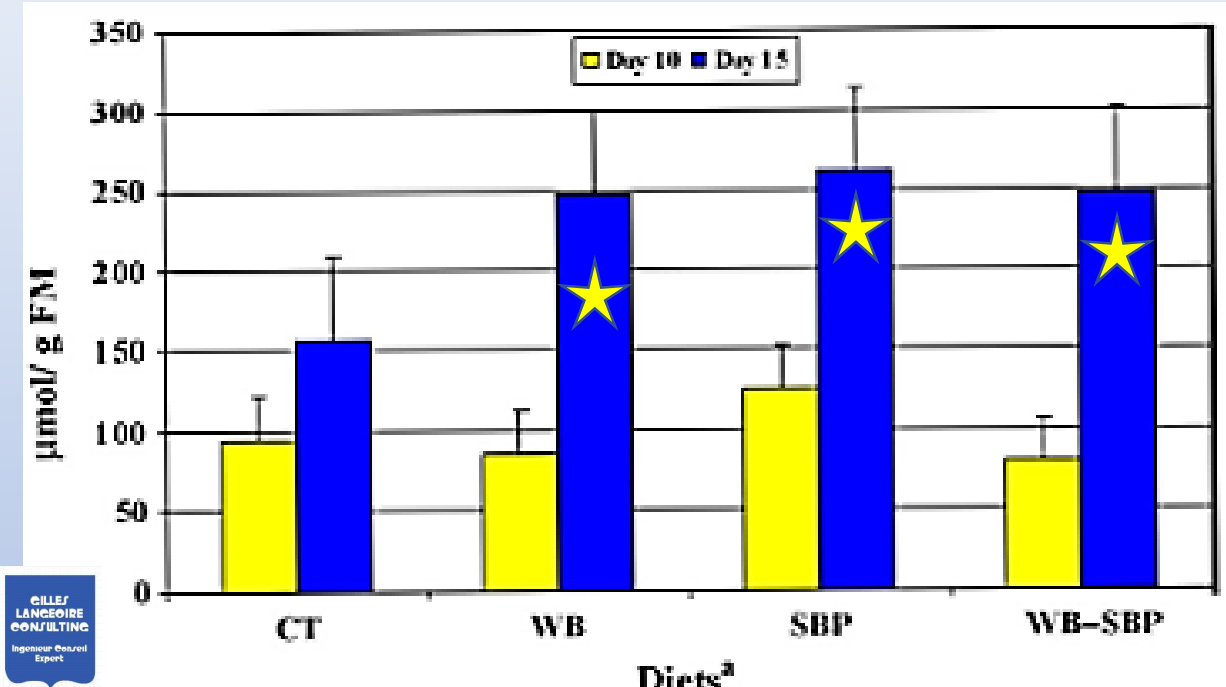
  - **For the Starter feed:**
    - Positive effect of fibre fermentation:
      - For a low gut pH
      - Limiting the pathogens development
      - Improving the gut immune function
    - NEEDS A GOOD PROFILE FERMENTABLE / INERT FIBRE
      - Depending of the health status and the diarrhea risk

More Dietary Fibre: More fermentation, less enterobacteria

From Molist & al. 2009 Schothorst Feed Research BV

- 32 weaned piglets : 24 days,
  2 period: w-10 days, 11 - 15 days
- 4 diets:
  - Control :
  - CT+Wheat bran: WB: 8%
  - CT+Sugar Beet Pulp: SBP: 6%
  - CT+Wheat Bran + Sugar Beet Pulp:4%+3%

Total SCFA concentration in digesta



	CT	WB	SBP	WB +SBP
ADG 0-10d,g/kg	199	306	295	218
ADG 10-15d,g/kg	222	361	317	323
Formic	0,9	1,2	1,1	1,1
Butyric acid	11,7	**35,9**	12,2	**31,3**
Lactic acid	20,8	34,6	**54,7**	6,7
Enterobacteria	11,1	**10,0**	10,8	**8,3**
Lactobacilli	11,7	12,0	11,9	11,5

Based on the results of the present study, it can be concluded that an increase in the amount of NSP in the diet may enhance the fermentation activity in the large intestine of piglets after weaning. Diets with a higher amount of insoluble NSP or a combination of insoluble and soluble NSP promoted a beneficial shift in the microbial colonization, with a higher production of butyric acid in the large intestine and lower enterobacteria counts in the digesta.

One recent trial from Denmark

A new feed formulation for young piglets

Weaning piglets without medical zinc

- 1072 piglets weaned at 25 days, trial duration 42 days
- A study without medical zinc oxide, for **weak piglets: Average BW: 4,2kg**

Control diet:
Wheat heat treated: 20%
Wheat: 24,3%
Corn flakes: 3%
Milk powder: 18%
Lactose: 9,1%
Soy protein concentrate: 10%
Potato protein: 7%
Fat: 2,7%
Benzoic acid: 0,5%
Calcium formate: 0,5%
Zinc Oxide Px: 0,3%
Px MTE: 4,6%

ABC4: 388 meq/kg
F.Ferment: 3,8%
F.Inert: 3,1%

FU/kg Feed: 1,3
Protein SID: g/FUp: 131
Lysine SID: 15%

Test diet: SR Elite
Wheat heat treated: 52,8%
Barley: 13,5%
Milk powder: 16%
Soy protein conc. : 5%
Plasma: 5%
Fat: 1%
Benzoic acid: 0,5%
Calcium formate: 0,5%
Lignocellulose: 1,5%
Bacillus subtilis: 0,8%
Potentiated ZnO: 150ppm
Px MTE:3,8%

ABC4: 220 meq/kg
F.Ferment: 5,1%
F.Inert: 5,5%

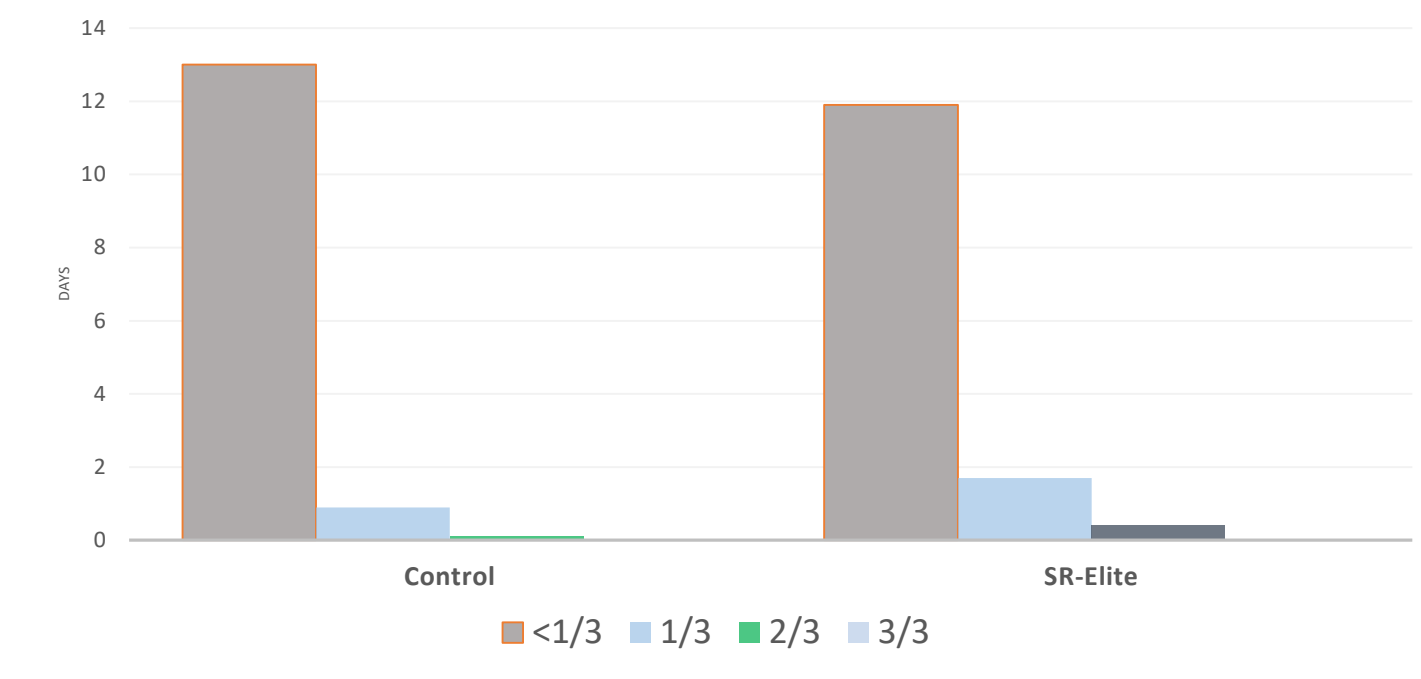
FU/kg Feed: 1,27
Protein SID: g/FUp: 127
Lysine SID: 15%

To substitute the medicinal ZnO level, SR-Elite, applies different safety solution:

Low ABC4
Low but highly digestible protein
Use of probiotics
Higher fibre content
Potentiated ZnO

Similar faecal score

- Faeces scoring:<1/3, 1/3, 2/3 or 3/3 as part of the faeces on the pen's floor during 2 weeks after weaning



- No liquid faeces in any pens
- Only 1 piglet (of 534) was treated with antibiotics

Technical & Economical approach of the diets

- Similar overall technical results!
- Even better during the weaning phase

PHASE 1 (1-14d)	Control	SR-Elite
Weight gain, kg	2.4	2.8
ADG, g/d	265	275
FCR, kg/kg	1.51	1.4
Feeding Cost, USD/piglet	2.50	2.90
PHASE (14-43d)		
ADG, g/d	549	533
FCR, kg/kg	1.43	1.38
Feed Cost, USD	700.0	740.0
Feeding cost total, USD/piglet	18.7	18.9

- Economically, the SR-Elite feed is slightly more costly, but the good growing results during the first weaning phase, will be valuable during the rest of the piglet career.
- At the end of PW: **The feeding cost is similar for both diets**

Qualitative evaluations on 3 commercial farms

- At day 14: FI and ADG were similar or better for the pigs fed the SR-Elite diet compared to pigs fed a Pre starter diet with medicinal doses of zinc oxide.

- Treatments for diarrhea were slightly higher for pigs fed the SR-Elite diet. The general prevalence of diarrhea was low.

Conclusion from 3 recent publications from KSU (Swine Day 2024)

Effects of Increasing Dietary Zinc in Low ABC-4 Diets on Nursery Performance, Fecal Dry Matter, Serum Zinc, and Zinc Excretion

Julian Arroyave, Mike D. Tokach, Jason C. Woodworth, Joel M. DeRouchey, Robert D. Goodband, Katelyn N. Gaffield, and Jordan T. Gebhardt

Effects of Dietary Acidifiers and Low Acid-Binding Capacity-4 (ABC-4) Formulation Strategies on Nursery Pig Performance and Fecal Dry Matter

Ethan B. Stas, Mike D. Tokach, Joel M. DeRouchey, Jason C. Woodworth, Robert D. Goodband, and Jordan T. Gebhardt

Evaluation of Dietary Acidifiers in Low Acid-Binding Capacity-4 (ABC-4) Diets on Nursery Pig Performance and Fecal Dry Matter

Ethan B. Stas, Mike D. Tokach, Joel M. DeRouchey, Jason C. Woodworth, Robert D. Goodband, and Jordan T. Gebhardt

- These studies illustrate the complexity of low ABC-4 diet formulation, and while dietary acidifiers are an important part of a low ABC-4 diet formulation strategy, there are other dietary aspects such as protein digestibility or lactose sources, Ca levels, P source, and other methods that must be considered to achieve an optimal ABC-4 level and improve nursery pig performance without therapeutic ZnO.
- I should add: don't forget adequate fibre supply

Using Antibiotics and medical zinc oxide is not any more a fatality

- Thank you very much for your kind attention!

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- Thank you very much for your kind attention!

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