Making the transition from research trials to field application

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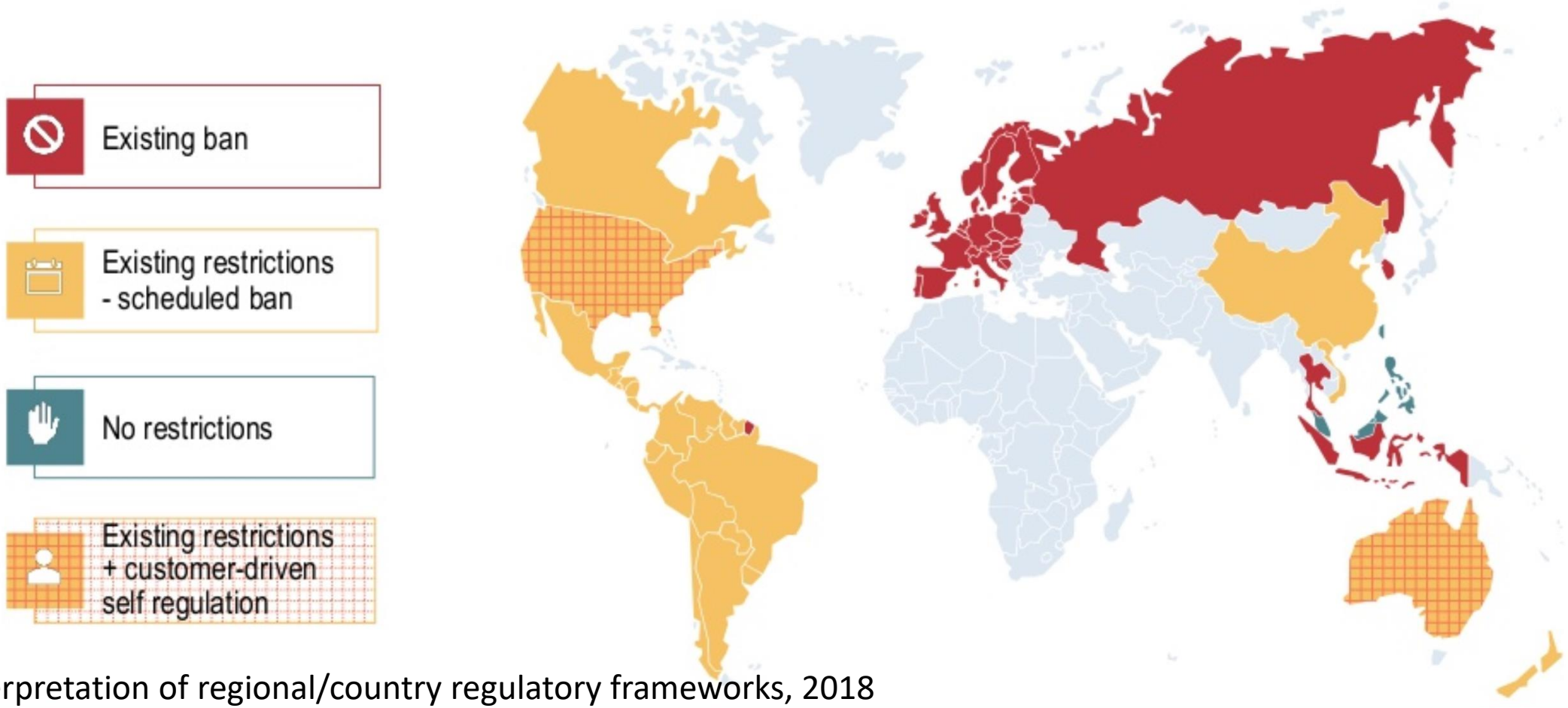
REGULATION OF ANTIBIOTIC GROWTH PROMOTERS (AGP) WILL ACCELERATE

AGP regulatory status in leading markets



DuPont interpretation of regional/country regulatory frameworks, 2018

Alternatives to antibiotics

- Niche markets vs industry-wide adoption
  - Product differentiation (US, Canada, etc.)
    - May command a premium
  - Legislation (EU, exporters to EU, etc.)
    - AGP-free is the standard to be able to sell chicken
    - No premium

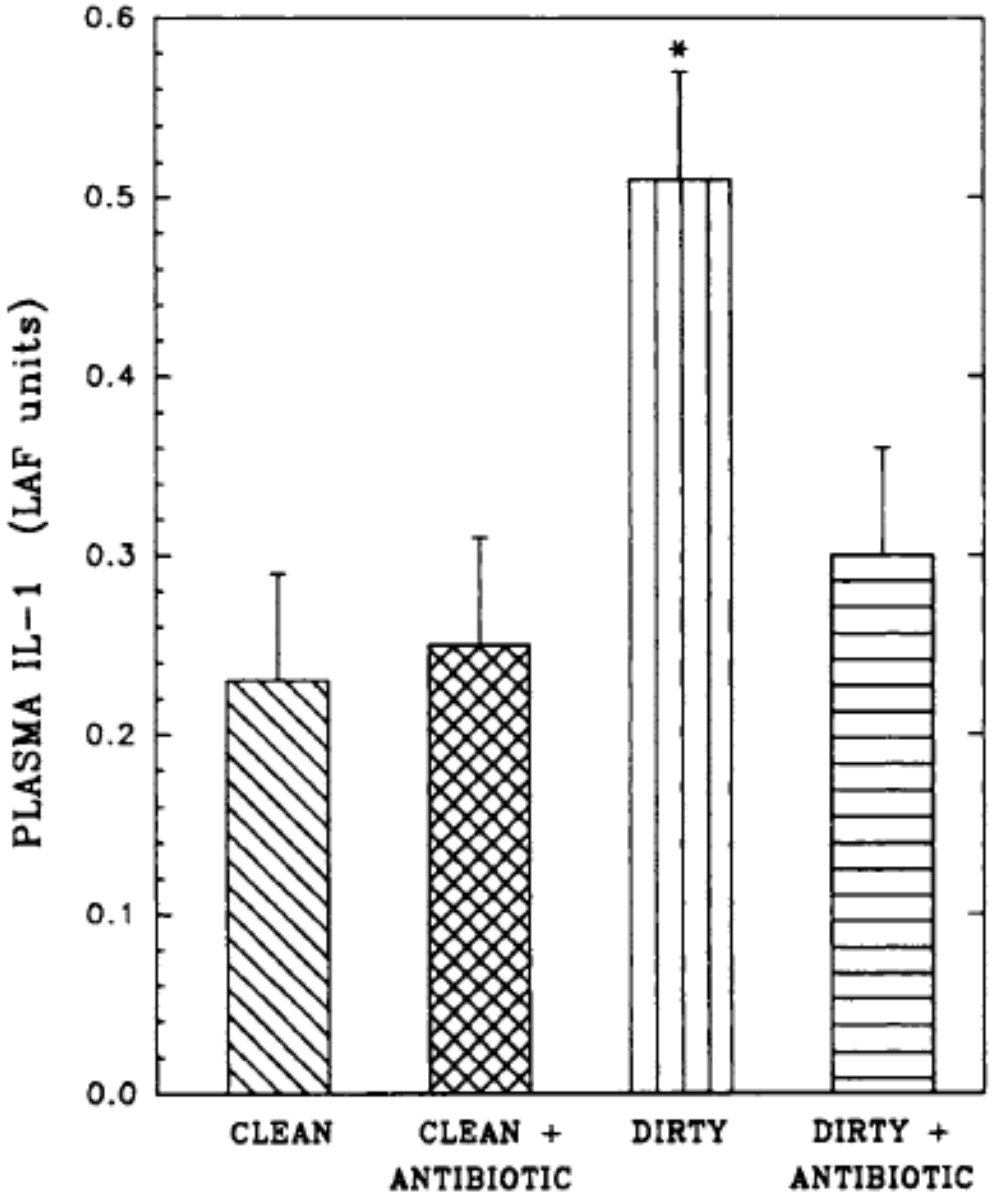
- In either case, the objective is to maintain
  - Production efficiency
  - Animal health
  - Food safety
  - Profitability

Influence of environment and antibiotics (AB) on weight gain and feed efficiency in chicks (Experiment 1)[1]

Treatment[2]	Weight gain	Feed efficiency
	g/(chick·d)	*g gain/g feed*
Clean	12.65[a]	0.66[a]
Unsanitary	12.10[b]	0.54[b]
Clean + AB	12.72[a]	0.67[a]
Unsanitary + AB	12.57[a]	0.63[a]
Pooled SEM	0.14	0.02

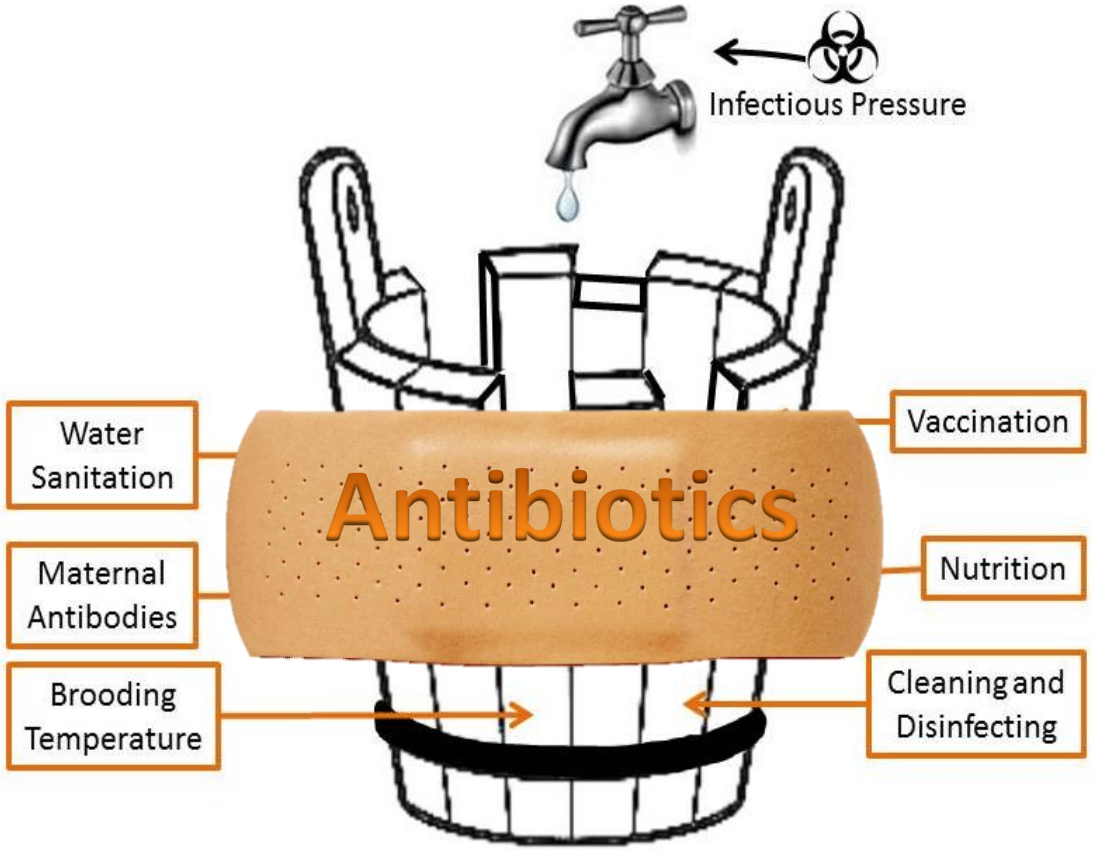
[1]Means in a column with different superscript letters are significantly different ($P < 0.05$).

[2]Sixty-four chicks were raised for 14 d (from 3 to 17 d of age) in each of the two different environments (clean or dirty) and fed diets either without antibiotic or with streptomycin (100 mg/kg) and penicillin (100 mg/kg).



Roura et al., J. Nutr. 1992 122:2383-2390

Alternatives to antibiotics



- Antibiotics covered a wide range of problem organisms
  - Multiple predisposing factors
    - Incubation
    - Stress
    - Feed quality
    - Biosecurity
    - Environment
- Greater response with increased infectious pressure

Alternatives to antibiotics

- Removal of AGP presents opportunities for a wide range of potential pathogens
- Reduce negative interactions between the host and gut microbes
  - Local and systemic effects
    - Disease
    - Reduced performance
- Protect humans from food-borne illness
  - Immunological tolerance by the bird

Alternatives to antibiotics – an effective “fence”?

Evaluating an antibiotic alternative strategy

- AGP increased growth and efficiency by 3-5%

Dahiya et al., 2006

- Positive response 72% of the time

Rosen, 1995

- Compared to what?
  - …not using AGP
- Shouldn't we evaluate alternatives to AGP in the same context?

Evaluating an antibiotic alternative strategy

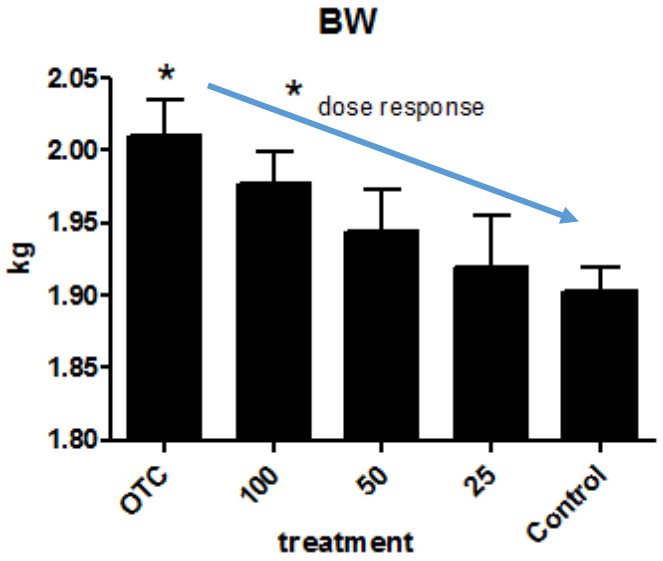
- Characteristics of a viable alternative
  - be efficacious
  - economically feasible
  - simple to apply consistently under field conditions
  - be accepted by consumers
  - not promote microbial resistance

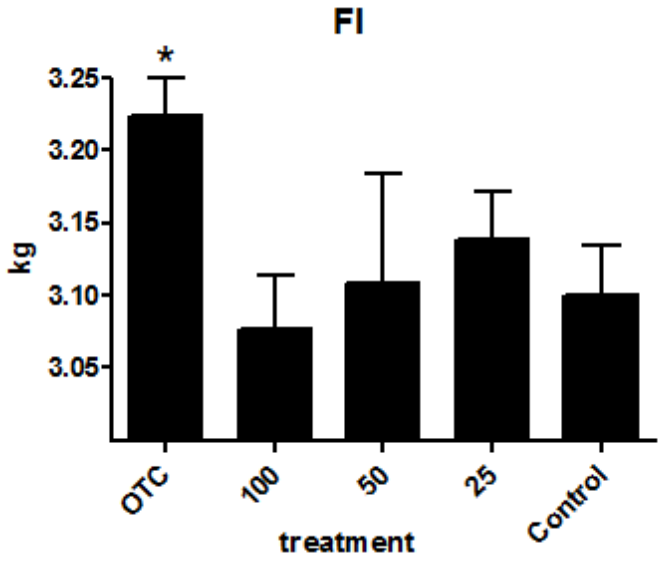
Evaluating an antibiotic alternative strategy

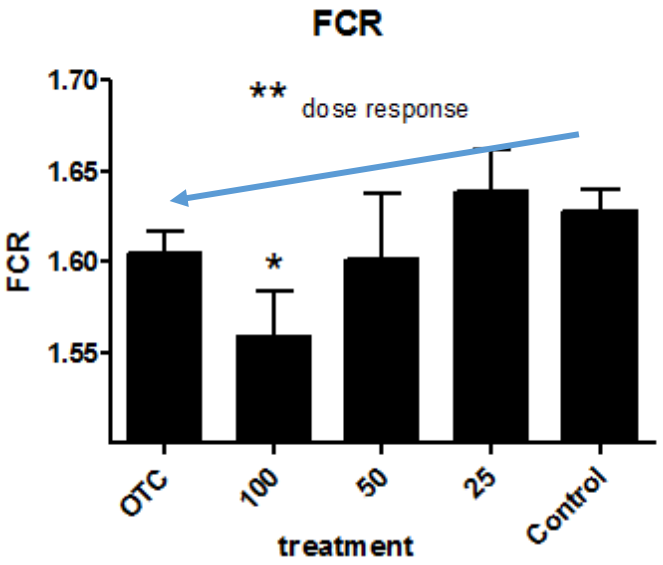
- Many products have evidence of some direct or indirect influence on inflammation or antimicrobial activity
  - Cell culture/in vitro antimicrobial activity
  - Tissue gene expression
  - Plasma/tissue mediators of inflammation
- Are there links to effects on performance?
  - Efficacy

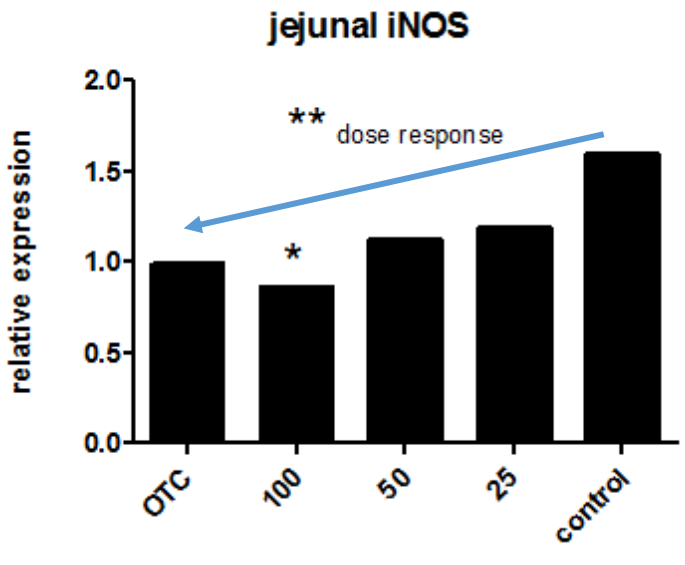
Evaluating an antibiotic alternative strategy

- Sound experimental design
  - Positive control (with AGP) negative control, (no AGP)
    - Loss of performance in NC
  - NC plus experimental treatments
    - Full or partial recovery of performance







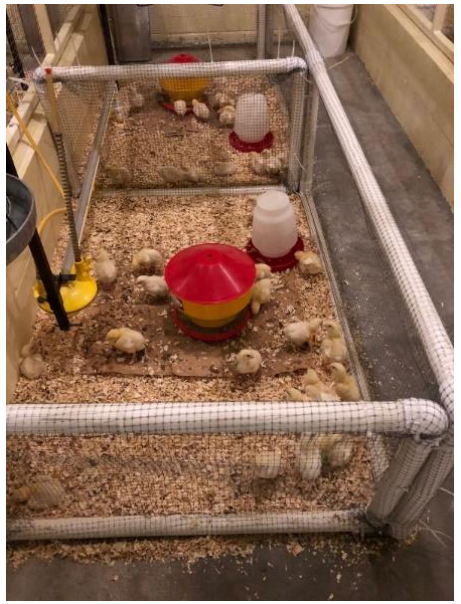


Growth promotion in broilers by both oxytetracycline and *Macleaya cordata* extract is based on their anti-inflammatory properties.
Khadem et al. 2014. Br. J. Nutr. 112, 1110–1118

Evaluating an antibiotic alternative strategy

- University – small scale, intensive, highly controlled research facilities





- Are research results applicable to the real world?
  - Do the experimental ideas work?
  - Are they feasible?

Evaluating an antibiotic alternative strategy

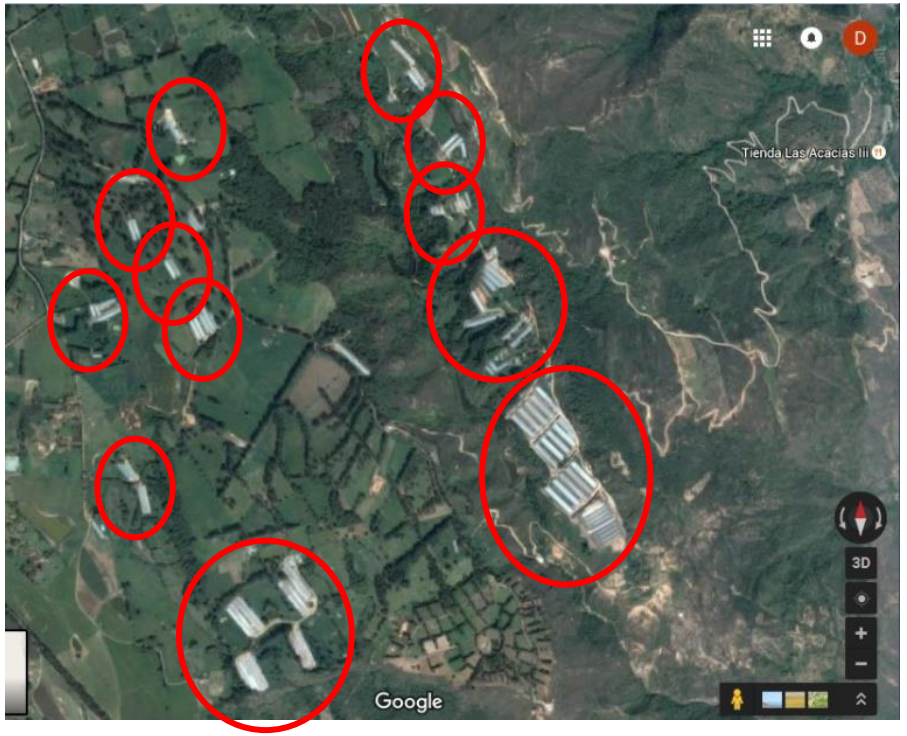
- Experimental challenge models
  - Do the experimental studies reflect what happens in the field?
    - Single vs multiple challenges
      - Which pathogens?
    - Clinical vs sub-clinical challenges
    - Natural vs artificial challenges
      - Effect of challenge model on response
    - Prophylactic vs therapeutic uses
    - What about the environment/location?

Evaluating an antibiotic alternative strategy – field trials

- Clear research question (hypothesis)
  - Change a limited number of factors
- Experimental design
  - Controls
  - **Replication of treatments**
  - Blocking
  - Sampling
- Conducting the study
  - Appropriate measurements
  - Quality control
  - Response to errors
- Objective evaluation
  - Statistics
- Interpretation
  - Is the product effective in the face of a challenge?
  - Is the performance of the PC birds relevant to commercial production?

Evaluating an antibiotic alternative strategy – field trials

- Advantages
  - Large numbers of barns
  - Replication on a farm/over time/across a large number of facilities



Evaluating an antibiotic alternative strategy – field trials

- Limitations
  - Lack of negative controls
  - Variation
    - Barn to barn
    - Farm to farm
    - Geographical location
    - Statistical differences vs trends




Dietary Treatments

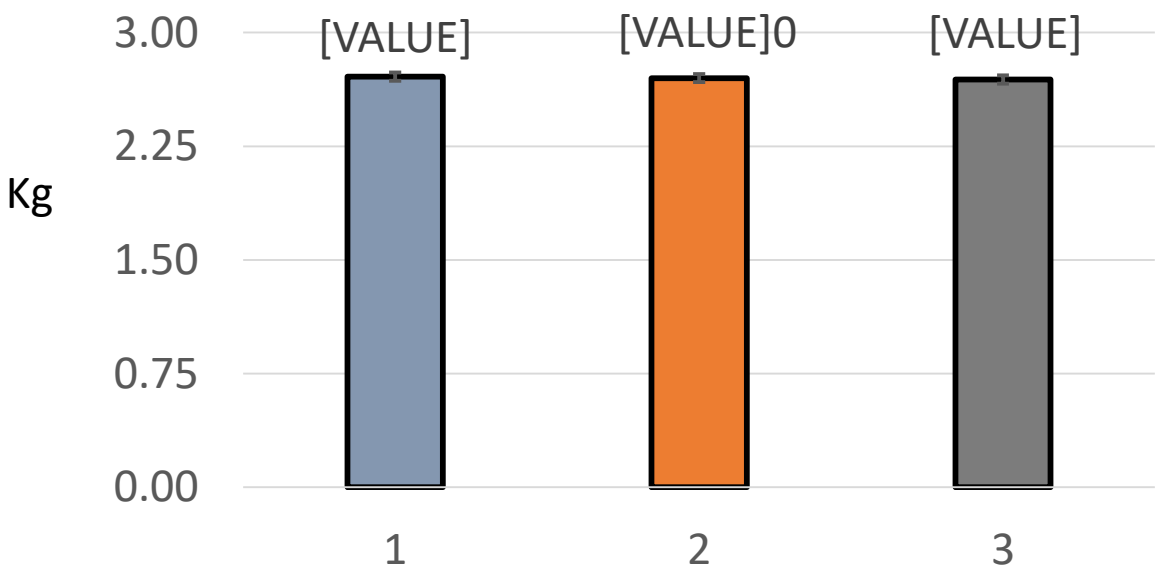
	T1	T2	T3
Basal Diet**	AVISID	AVISID	AVISID
AGP	✓	✗	✗
Butyrate	✓	✓	✗
MOS (Mannan-oligosaccharides)	✓	✓	✗
Essential Oil + Benzoic Acid	✓	✓	✓
Enterococcus faecium	✓	✓	✓
Bacillus subtilis – Bacillus licheniformis	✗	✓	✓
Protease + Xylanase + Amylase	✓	✓	✓
Phytase (1000 FYT/g)	✓	✗	✗
Phytase (2500 FYT/g)	✗	✓	✓

** Pre-starter, starter, grower and finisher (mash form)

Sanabria et al., International Poultry Scientific Forum
February 11, 2019, Atlanta, GA, USA

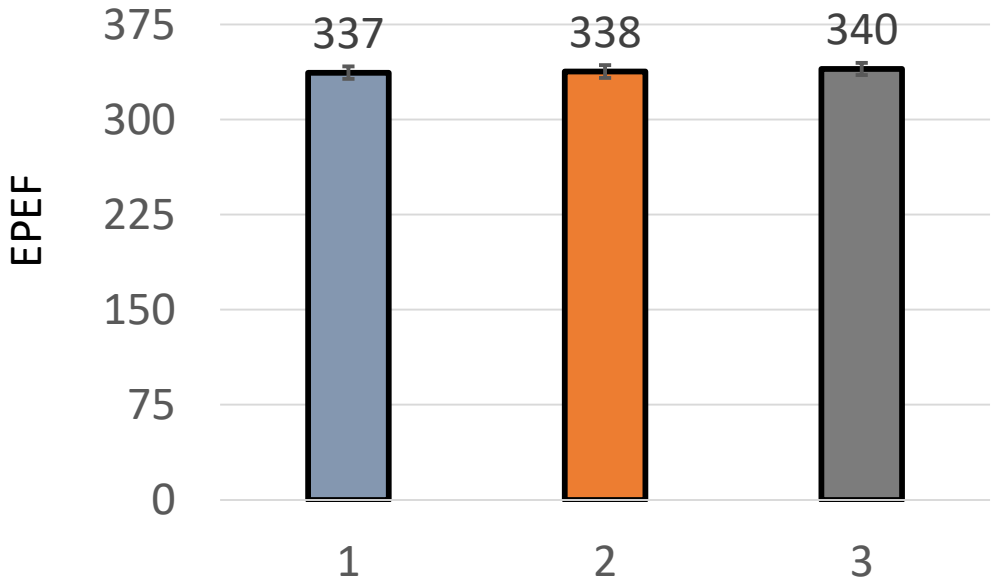
Alternatives to antibiotics – commercial trial

Body weight D44*



P = 0.8613

European Performance Efficiency Factor D44*



* Kg/m^2 and age at slaughter as a covariate

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Evaluating an antibiotic alternative strategy – field trials

- Production realities
  - Disease outbreaks
  - Staff time/attention to detail
    - Production takes priority over research
  - Large number of steps/people involved
    - E.g. getting feed into the right bin/barn
      - Coloured feed bags/tags/bin labels
  - Responsibility for maintaining experimental protocol
    - What happens when a mistake is made?
    - What happens when someone changes things?

Evaluating an antibiotic alternative strategy – economics

- Cost of implementation
  - Removing a single product (AGP)
  - Replacing with a group of different products, each with its own cost

- Additional costs
  - Vaccinations
  - Reduced performance
  - Lower stocking density
  - Longer down times between flocks
  - Increased biosecurity/improved facilities
  - Feed supplements
  - Immune modulation
  - Feed quality
    - Nutrients, contaminants and mycotoxins

Evaluating an antibiotic alternative strategy – economics

Traditional supplements

- E.g. phytase vs inorganic phosphate
  - What alternatives will achieve the same performance at the same or lower cost?

Antimicrobial alternatives

- Multiple products/approaches to replace a single product
  - Higher costs
  - Will I be able to sell my product or not?”
    - Legislation, export markets
    - Consumer preferences

Alternatives to antibiotics

- Likely need multiple products with multiple mechanisms
- Different pathogens require different strategies
  - Likely multiple pathogens of concern
- Specific challenges will change over time
- Complementary strategies
  - If one approach is not effective, others will be

Alternatives to antibiotics – take home message

- Replace the outcome, if not the exact mechanisms of antibiotics
  - Animal health
  - Animal performance
  - Animal welfare
  - Food safety
  - Profitability
- Use with strategies unrelated to antibiotics
  - Vaccination
  - Immunomodulators
  - Etc.

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