PROHEALTH

PROHEALTH Industry Workshops and Scientific Symposium, 27-28 November 2018

Venue: Het Pand, Onderbergen 1 Ghent (www.ugent.be/het-pand/en)

Tuesday 27 November 2018

Industry workshops Poultry and Pigs

12.30-13.25 Registration + coffee
13.25-17.30 Two parallel sessions: 30 min timeslots (25 min presentation + 5 min discussion) Presentation: part I: own findings; part II: relevance to wider stakeholders.

Time	Poultry		Pigs	
	Chair: Ilias Kyriazakis		Chair: Sandra Edwards	
	Speaker	Title	Speaker	Title
13.25-13.30	Ilias Kyriazakis	Welcome and introduction PRO-HEALTH	Sandra Edwards	Welcome and introduction PRO-HEALTH
13.30-14.00	Tommy Van Limbergen	Biosecurity and risk factors for production diseases in Poultry	Ilias Chantziaras	Biosecurity and risk factors for Production diseases in pigs
14.00-14.30	Jens Peter Christensen	*Escherichia coli* infections in broiler production	Fanny Pandolfi	Risk factors for pig neonatal mortality
14.30-15.00	Panagiotis Sakkas	Reassessment of the vitamin D requirements of broilers	Vivi Aarestrup	Improving pig neonatal mortality
15.00-15.30	Sotiris Papasolomontos	Egg disinfection protocols in poultry	Nathalie LeFloch	The role of hygiene in the expression of production diseases in pigs
15.30-16.00	*Coffee break - posters*			
	Chair: Paul McMullin		Chair: Carlos Pineiro	
16.00-16.30	Sara Perez	Development of new biosecurity protocols in poultry farms	Carlos Pineiro	Risk factors and disease prediction using (big) data in swine
16.30-17.00	Tim Giles	Novel markers for production diseases in poultry	Fabrice Robert	Nutritional strategies to preserve health and performance and reduce antibiotics
17.00-17.30	Philip Jones	The economic costs of production diseases in poultry	Jarkko Niemi	The economic costs of production diseases in pigs

This project has received funding from the European Union's Seventh Framework Programme under grant agreement No. 613574.

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Wednesday 28 November 2018

Scientific symposium

Chair: Ilias Kyriazakis		
Time	**Speaker**	**Title**
8.50-9.00	Ilias Kyriazakis	Welcome and introduction PROHEALTH
9.00-9.30	Tommy Van Limbergen	Biosecurity and risk factors for pigs and poultry
9.30-10.00	Hélène Quesnel	Advances in enhancing neonatal piglet survival through housing and nutrition
10.00-10.30	Jens Peter Christensen	Improving leg health in poultry?
10.30-11.00	*Coffee break - posters*	

Chair: Nathalie LeFloch		
Time	**Speaker**	**Title**
11.00-11.30	Anne Boudon	Leg disorders in growing pigs : risk factors and perspective for early detection
11.30-12.00	Carlos Pineiro	Predicting the effects of the environment in pig and poultry farms
12.00-12.30	Neil Foster	Novel markers for production diseases in pigs and poultry
12.30-14.00	*Lunch - posters*	

Chair: Jens Peter Christensen		
Time	**Speaker**	**Title**
14.00-14.30	Ivan Rychlik	The use of probiotics to avoid the abuse of antibiotics in chickens
14.30-15.00	Beth Clark	What do stakeholders want in relation to the control of production diseases
15.00-15.30	Jarkko Niemi	Economic consequences of novel solutions to control production diseases in Pigs and poultry
15.30-16.00	*Coffee break - posters*	

Chair: Dominiek Maes		
Time	**Speaker**	**Title**
16.00-16.30	Filip Van Immerseel, UGent	Production diseases in poultry: challenges for the next five years
16.30-17.00	Peter Davies, U of Minnesota	Production diseases in pigs: challenges for the next five years
17.00-17.30	*Round table discussion with keynote speakers*	

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Production diseases in broiler chickens: challenges for the next five years

Filip Van Immerseel

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Changes in broiler production

One of the most sustainable types of production of animal protein is chicken meat production. Chicken production uses less feed consumed for each kilogram of meat produced and uses less land and water for both farming and feed production. The major cause is the continuously improved animal performance, reflected by an ever decreasing feed conversion (kg feed consumed per kg body weight) and reduced time to achieve market weight. Continuous improvements in performance parameters include genetic selection for high-performing chicken lines, technological developments in hatching and housing conditions, feed optimization and management practices that support (intestinal) health. Among the latter, the use of antimicrobial growth promoters is a practice that has been stopped in the EU since 2006 (other countries have and are following this practice) but the use of therapeutic antimicrobials in the animal production industries is still high, though decreasing (especially prophylactically). This has caused a situation in which the animal and its microbiota is experiencing a big change, as the animal breeds have been used for more than 50 years almost exclusively in a production system where antimicrobial were common practice. Reducing or stopping this practice has caused different diseases and syndromes to emerge, most of which are of intestinal origin. Indeed, about 60% of therapeutic antibiotic usage in broilers is to control intestinal diseases. The move away from antimicrobials has led to increasing concerns about gut health that is affected by bacterial diseases, enteritis, dysbiosis, and poor digestibility, and result in poor growth performance of birds. In fact all these entities have common denominators and these are microbial shifts that go hand in hand with epithelial permeability increases, inflammation and thus performance losses, and are often related to nutrient excesses in the intestine, or feed-derived issues (poorly digestible nutrients, excess of energy or protein levels). In the current paper, coccidiosis is not discussed. This is a disease that has been the most important problem in broiler production for many years, and is controlled using anticoccidials. While legislation can change so that also these compounds are banned, potentially leading to changes in control strategies, for now this is only the case in specific countries and thus the challenges remain identical as before. Below, challenges for the recent future are discussed.

Intestinal diseases and syndromes in broilers, associated with performance

The most severe example of a disease that has emerged in broiler chickens after the ban on growth-promoting antibiotics in animal feed is necrotic enteritis, imposing a significant economic burden on the poultry industry worldwide. This disease is typically caused by nutritional excesses in the gut and predisposing epithelial defects (caused by mycotoxins, coccidia), and is occurring in the animals with the highest body weight gain, so clearly related with production parameters. The causative agent of necrotic enteritis are netB-toxin containing Clostridium perfringens (type G) strains. Necrotic enteritis can occur as an acute clinical form which is characterized by a sudden increase in mortality, and as a subclinical form which results in a lower weight at slaughter age. In both cases, macroscopic necrotic lesions are found at the mucosa of the small intestine upon necropsy, and thus the intestinal barrier is compromised and severe mucosal inflammation occurs.

A disease syndrome that has clearly emerged in the EU broiler industry simultaneously with the ban of growth promoting antibiotics is the so-called ‘dysbacteriosis’. This is a poorly described condition of the gut and is either or not a synonym for conditions such as ‘wet litter’, ‘non-specific bacterial enteritis’, ‘small intestinal bacterial overgrowth’, ‘malabsorption’, and many more. The common clinical denominator is thinning and ballooning of the small intestine, increased water content of faeces and reduced digestibility of feed with indigested residues visible in the faeces. In many cases, but not all, this is linked to increased feed conversion, decreased body weight and poor performance. Moreover, wet litter leads to various complicating disease conditions such as pododermatitis, breast blisters and ‘hock burn’, and these are criteria used to evaluate animal welfare. It is generally believed that the so-called 'dysbacteriosis' is a condition in which the interaction between the gut microbiota and the host is impaired, such that the gut health is not optimal. It is suggested that the altered composition of the gut microbiota induces changes in the gut wall, including morphological changes (villus length decreases, crypt depth increases, epithelial cell damage, …) and inflammatory reactions (infiltration of immune cells in the wall). This is influenced by nutrition. The combination of a suboptimal microbiota combined with effects on the gut wall would then most likely interfere with digestive processes, eventually leading to poor performance, and induce enteritis.

As broilers are often having gut barrier integrity issues (increased permeability), toxins, feed antigens, but also bacterial products and bacteria can cross this barrier and spread systemically. This also aids locomotory diseases that are a consequence of both the high body weight and the pressure this puts on the skeleton of the animal, but also of bacteria that attach to bones at different sites in the body. Indeed, lameness in broiler chickens is a significant animal welfare problem, which is increasingly occurring (up to 1% of all animals). Bacterial chondronecrosis with osteomyelitis is a disease characterized by bacterial infection in rapidly growing bones under repeated mechanical stress and typically occurs in tibiae, femora and the thoracic vertebrae. The terminology is often confusing and names such as 'kinky back', spondylitis, spondylolisthesis, femoral head necrosis and others are given to describe similar or equal syndromes. It is assumed that bacteria cross the intestinal barrier, enter the bloodstream and hematogenous spread to osteochondrotic clefts or to microfractures at the growth plates. When colonizing the growth plates, the bacteria are rather inaccessible to antibiotics and the host immune system, making them able to induce necrosis. Bacteria that are found in BCO lesions are commensal intestinal bacteria that have translocated through the intestinal epithelium and have spread systemically. Bacterial genera and species that are isolated from BCO cases are, amongst others, opportunistic bacteria including staphylococci, *Escherichia coli*, and enterococci. These kind of disease entities are thus again originating from high performance and partly have an intestinal origin.

Challenges for the future

It is clear that future animal production needs to be sustainable. Sustainable poultry production means that poultry is produced while preserving the natural environment, fulfilling the need of society and still being profitable in economic terms. When one of these three is missing, poultry production is not sustainable. There is a clear interaction between these three pillars, and one is affecting the other. For example, consumers are more and more aware of the effects of animal production on environmental pollution and thus one seeks ways to reuse waste for other purposes (eg. biodegradation and energy production). More and more consumers demand for food that is produced under high animal welfare standards and also in this regard, changes have been introduced the last decade (eg prohibition to use battery cages for layers in EU) to comply with these requests. Also protection against foodborne pathogens, minimizing levels of residues and reducing antimicrobial usage are key aspects of a sustainable animal production. Using feed sources that are less in competition with human food (by-products of industries, such as DGGS) is also a practice that can be important for sustainability. The poultry industry has adopted practices to comply with many of these societal and environmental needs, without compromising profitability, but a lot of the above mentioned items have effects on intestinal health (less antimicrobials, changing feeding practices). One key issue in a sustainable poultry production is thus related to intestinal health, as animals with poor intestinal health perform less (more usage of feed per kg produced meat), are more vulnerable to disease and colonization by zoonotic pathogens, and will inevitably need to be treated more with antibiotics, resulting in a higher chance of residues and spread of antimicrobial resistance. In this regard there are some future challenges that deserve attention. One is the smart development of non-antibiotic solutions for gut health problems. Nowadays there are numerous feed additives on the market to prevent or control gut disorders and diseases and improve performance, but for many of these, the mechanism of action is unclear and often companies tend to copy compound and products from competitors. This makes it difficult for veterinarians and farm managers to decide on the choice of interventions that are meant to replace antimicrobials. This is immediately linked with a second major future challenge, being the development of good biomarkers for gut health, that can be applied in the field to evaluate whether interventions are needed, and can also be used to design products that have good efficacy in maintaining intestinal health. As intestinal health depends on the relation between feed – microbiota – host it is also of utmost importance to understand better this complex interaction, in which the microbiota is playing a crucial role. Indeed, it has been shown already in many studies that the microbiota composition is playing a pivotal role in the risk of developing necrotic enteritis, dysbacteriosis, gut inflammation and even systemic diseases that originate in the gut, and that modulating the gut microbiota can prevent disease.

Some specific future research challenges related to intestinal health are thus to generate:

1) Knowledge on the microbiota composition and its relation to animal performance and health

To understand how microbiota-host interactions drive intestinal health and function and how this can affect animal performance and disease resistance, we need to gain more insight in microbial community organization and characterization of the functional activities of these communities. While quite some work has been done on describing microbiota composition in the different segments of the intestinal tract of chickens, there is a clear need to further investigate microbial taxa that are over- or underrepresented in the gut of chickens in specific experimentally-induced or field cases of intestinal health problems. There is a need to evaluate the significance and relevance of these changes for animal performance and disease control, as the mere observation of a change does not necessarily implicate relevance. Thus, future studies should target functional pathways present in the microbiota using metagenomic or other approaches, to correlate the functionality of a microbiota with intestinal health parameters and performance.

2) Knowledge on the relation between feed-microbiome-host to be able to nutritionally steer towards beneficial microbial profiles

Microbial composition and functionality, and thus the metabolites produced by the bacteria, are driven by feed sources, their composition and the substrates present in these feed sources. It is evident that, using feed additives or nutritional interventions, shifts in microbial functionality should be targeted. When health-promoting microbial profiles are induced, this will lead to better animal performance, and less animal disease and antimicrobial use, so improved sustainability. Thus development of new feed additives can contribute to sustainability of the poultry industry. Prebiotics, probiotics and molecules of any nature could thus be designed to generate a set of microbial signals that reduce inflammation, inhibit pathogen outgrowth and favor digestion when delivered in-feed. In addition, novel molecules that not only target bacteria but aim to directly modulate intestinal barrier function and regeneration of the epithelial layer in the continuously challenged gut is a new domain for the future.

3) Data on good intestinal biomarkers for performance and intestinal health to be able to rationally measure the effect of interventions to promote intestinal health, and as diagnostic tool

Biomarkers for intestinal health are critical for different reasons. First, they are an essential tool to evaluate animal health and are important to support (or not) treatment of animals with intestinal syndromes (eg. wet litter) that do not have a clear diagnosis (based on pathogen identification). Secondly, easy-to-measure criteria are an essential tool when one wants to develop pharmaceuticals and/or feed additives with either or not a claim to improve intestinal health. Research efforts to identify markers for human intestinal inflammation and disease has focussed on quantification of proteins involved in various pathological processes, including intestinal epithelial cell damage, leakage of serum proteins, inflammatory cell influx, among others. Because of a lack of protein homology between human and avian proteins these tests cannot be used in birds. There are thus several important aspects related to the identification and quantification of gut health biomarkers. One is the identification part, and animal models and field samples need to be used for discovery (the latter sample type will yield high variability). The second one is test development, as a field test should be easy, rapid and cheap. Identifying protein (or other) markers is one aspect, but likely a lot of these protein markers are not stable in faecal material, so that test development can be troublesome. Also microbial biomarkers can have value, and thus identifying microbial taxa and pathways as discussed above can be useful. Clearly DNA markers are the target here, and the development is easier as compared to protein biomarkers for gut health, that are likely derived from the host cells.

Clearly, there are many more challenges for the broiler and poultry production in general, including seeking ways to cope with the complex regulations on product development, controlling zoonotic agents, preventing diseases that are emerging because of globalization and climate changes, controlling mortality due to *E. coli* infection in newly hatched chickens, increasing consumer confidence in the animal production industry, amongst many others.

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Production diseases in swine: future challenges

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Defining production diseases

All livestock (and crop) farming systems are artificial and provide settings that depart greatly from the natural environments of domesticated species. The facilities and operations of livestock farms have evolved enormously, and continue to do so in most countries, notably with increasing herd sizes, species specialization, and replacement of labour with capital. In part due to the economic demands underpinning much of this evolution, overall we have seen improvement in health and productivity of major livestock species in developed countries over time, and in the safety of food. However, consistent with the principles of epidemiology, the profiles and relative importance of 'diseases' has also shifted consequent to changing farming practices. Salient factors include animal genetics, the macro- and micro-environments in which animals are reared (climate, housing, ventilation), nutritional practices, reproductive management, population turnover and animal density and flow, specific herd health preventive strategies (e.g., biosecurity, vaccination), and stockmanship. It is a truism to state that we have selected for the problems that we are now confronting.

Veterinary involvement in managing the health and productive efficiency of livestock co-evolved with farming systems to successively confront the most pressing problems of the time. Through the first half of the 20th century, veterinary services focused on infectious diseases causing high mortality at a regional or national level, or having significant human health concerns. As these problems were solved, attention shifted to the most significant clinical diseases in individual herds or flocks, and later to prevalent endemic problems that can impair production efficiency in the absence of significant clinical disease, such as poor reproduction performance, or subclinical mastitis in dairy cattle (Blood et al., 1978). A logical consequence of this evolution was the introduction of increasingly sophisticated tools for measuring the biological and financial performance of farmed animal populations, which in turn opened the door to defining 'disease' more broadly in the context of suboptimal productivity and/or profitability at the herd/flock level. At the individual animal level, Bergmann (1992) defined "performance-related health disorders" as 'catabolic phenomena and pathological processes that are related to or caused by high productivity levels'.

A generally accepted definition of what constitutes a "production disease" has yet to be developed, and some variability is expected amongst species. Metabolic diseases, such as ketosis in dairy cattle and negative energy balance in lactating sows, are recognized examples of 'production diseases', while specific nutritional deficiencies usually tend to be excluded. However, iron deficiency in piglets is a direct consequence of indoor rearing and therefore should arguably be considered a production disease. Similarly, endemic parasitic diseases are a major challenge in intensive pastoral production of small ruminants, but of minor concern in intensively housed swine. A general and pragmatic definition may be health or production problems that have increased in importance with intensification of production within a given species and enterprise type (e.g., dairy vs. beef; broilers vs. layers). The ProHealth project has defined production diseases as 'Diseases which tend to persist in animal production systems and, typically, become more prevalent or severe, in proportion to the potential productivity of the system'.

Looking at future challenges in swine production, a case can be made to consider all endemic health and performance problems of swine to be production diseases. At a societal level, one could consider ethical issues surrounding intensive animal production to be viewed as 'production diseases', and these are likely to increase as more sophisticated metrics become available for assessing metabolic and immunologic indicators of stress in pigs and other species (Marco-Ramell et al., 2016; Giles et al., 2017)). Although it is usual to focus on the animal or herd/flock as the level of concern for production diseases, one could also consider geographical scale, particularly in relation to transmission of pathogens among farms. Viral pathogens such as PRRS and influenza

A virus, have proven difficult to control or eliminate in regions of high swine density in the United States, and particularly where movement of infected animals among farms is common (e.g., transport between phases in multiple site production systems). The difficulty of managing these diseases is in part attributable to the industry demographics and operations at an area level – that is, intensification and greater productivity at a regional scale.

Optimization vs. Maximization

Striving for the most efficient and sustainable systems for animal production is a complex optimization problem. Traditional optimization tools, such as linear programming, have been widely adopted in livestock production, particularly for genetic selection of breeding stock and nutrition (least cost rations, optimizing nutrition to minimize environmental impact). Similarly, optimization models have been used to analyse endemic disease control decisions (Stott 2009) and more complex farming systems, particularly involving sustainability and environmental impacts (Groot et al, 2012). Inherent in optimization is formal recognition of trade-offs and constraints, and the basic approach is to define an 'objective function' to be minimized or maximized subject to a set of prevailing constraints (Jalvingh et al., 1997). In conventional commodity markets, minimization of cost of production or return on investment has been, and largely remains, a core driver of production practices. Simplistically, optimization at a herd level (e.g., maximizing kg of pork sold per year from a farm) may involve suboptimal production at an animal level (e.g., less space allocation per pig leading to reduced mean daily gain, but greater total production per unit of space). A feature of livestock production in developed countries in the current era is the growing impact of societal constraints, relative to biologic or economic constraints, upon animal production systems. That is, we confront the challenge of optimizing multiple, and changing, objectives.

All decisions in livestock farming have inherent trade-offs. The seemingly rational goal of increasing litter sizes brings trade-offs in relation to in utero growth retardation, piglet birth weights and survivability, and likely metabolic demands on sows, particularly when coupled requirements for with longer lactation lengths. Choice of the fineness of grind of feed involves trade-offs between economic and environmental factors (feed conversion efficiency) and pig health (risk of gastric ulceration). Choice of weaning age involves trade-offs between reproductive herd output and growing pig performance, and the economic optimization of weaning age will be influenced by factors such as the cost of feed and energy, and the quality of facilities and stockmanship. Increasingly, this decision is being further constrained by limitations on tools for mitigating health challenges in weaned pigs, notably use of antibiotics and zinc. As we introduce further constraints based on consumer or customer perceptions of the acceptability of specific practices (e.g., stall housing, tail docking, castration, etc.), determinants of farming practices shift from biological and data-driven criteria to more value based criteria. As values are, in part, culturally based we can expect diversity in how systems evolve in different parts of the world. A fundamental question is the extent to which regulatory measures will constrain livestock farming (e.g., banning of tail docking or castration), relative to marketed oriented approaches that provide consumer choices regarding the sourcing and cost of animal products (simplistically commodity vs. value added systems).

What might the future hold?

Infectious diseases

Controlling respiratory and enteric diseases has been the overriding challenge of raising animals in confinement, and is to some extent a function of herd size and animal density counterbalanced by interventions to reduce the risk of pathogen transmission and promote host resistance. The profile of predominant diseases has changed over time in line with the industry demographics (Davies, 2012).

Over the last four decades, the US swine industry has experienced three major disease epidemics – PRRS, PCV2, and PED (excluding the 2009 HINI influenza epidemic which had minimal clinical impact). All are highly host specific viruses, with relatively rapid rates of mutation, and were associated with swine for years to decades before highly pathogenic disease syndromes were manifest (Davies, 2015). It is naïve to assume that similar events will not continue to occur. Although PCV2 has been managed effectively with vaccination, the structure and operations of the modern industry likely played a central role in the introduction (PED) and maintenance (PRRS) of these diseases in the USA. In particular, sow farms continue to increase in size with the goal of providing uniform batches of weaned pigs to off-site facilities to maximize health. The likelihood that larger herds are more at risk for introduction of agents transmitted by air may have contributed to the ongoing challenges faced by the US swine industry with respect to PRRS and influenza viruses. Furthermore, larger herd sizes may favour the persistence of IAV as an endemic problem in herds and regions, rather than occurring in sporadic and transient outbreaks.

The use of antimicrobials and its implications for human health from antimicrobial resistant organisms are the most contentious issues in livestock production, and ongoing pressures to reduce antimicrobial use in all food animal industries must be anticipated. The consequent impacts on swine health and production will depend on the nature of future restrictions, but the principal effects are likely to be seen with opportunistic bacterial pathogens that are normal flora or common commensals of swine (e.g., *S. suis*, *H. parasuis*, *E. coli*, *L. intracellularis*). Re-emergence of some important swine pathogens, particularly *Brachyspira hyodysenteriae* may also be expected in some industries. *S. suis, H. parasuis*, and *L. intracellularis* are essentially ubiquitous organisms that might be considered normal flora of pigs (certainly at the population level). Although in most herds these agents continue to cause predominantly sporadic problems, the risk of significant outbreaks appears to be much higher in modern systems. While it is not uncommon to see 'stress' being attributed as the trigger for such diseases, outbreaks of these diseases often occurred on well-managed farms and in pigs with relatively high health status. Altered patterns of population immunity associated with changes in pig flow are an equally plausible explanation.

Advances in vaccinology will mitigate some of these endemic bacterial problems, but will not be a silver bullet. For enteric disease, much unrealized potential may lie in some combination of advanced nutrition and feed preparation, development of alternative products to antimicrobials, and advancing the basic science related to gut health through microbiome related research, biomarkers and metagenomics.

What might the future hold – non-infectious diseases?

Emerging non-infectious production diseases may occur due to increasing prevalence or severity, but also through a reduction in acceptability of endemic levels of 'disease', particularly those perceived to be welfare realted (for example, shoulder ulceration in sows in Denmark). A vexing problem relates to hunger in gestating sows, in which feed restriction is desirable with respect to reproductive and lactation performance, as well as associated environmental benefits. The importance of proper staffing, training, and incentives to support appropriate stockmanship skills will advance with concern and scrutiny of injuries, lameness and related problems that are endemic, and often have been tolerated, in animal production (Grandin 2018). Furthermore, the interaction of facilities and stockmanship should be emphasized, particularly when farmers face mandatory conversion of facilities, most obviously in sow housing. The existence of trade-offs with sow housing is well documented, and the difficulty in assessing animal welfare comprehensively (versus multiple measures of unknown relative importance) remains problematic (Verdun et al., 2013). Although measurement of all problems is a necessary step to addressing them, in complex systems there is a danger that 'problems' will be identified and benchmarked using specific tools or markers of animal health, wealth, immune function etc., without comprehension of their holistic significance for the animal population. For example, comparison of lesions in slaughtered pigs from different production systems have identified pigs from free-range systems to have a higher prevalence of several lesions compared with conventional systems, but lower prevalence of some others (Alban et al., 2015; Kongsted and Sørensen, 2017). Again, this illustrates the inherent trade-offs between farming practices, but also the likelihood of unintended consequences if recommendations are based on piecemeal rather than comprehensive understanding of the implications for animal health and welfare.