UNIVERSITY OF BIRMINGHAM
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Considerations for Developing Bacterial Vaccines for Veterinary Infections

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Workshop organised by the BactiVac, the Bacterial Vaccines Network, as part of the International Veterinary Immunology Symposium 2025

The workshop "Considerations in Developing Bacterial Vaccines for Veterinary Infections" was held on 11 August 2025 as a satellite meeting within the 14th International Veterinary Immunology Symposium (IVIS), hosted in Vienna, Austria. It was convened to examine some of the scientific and practical barriers to developing effective bacterial vaccines for use in the veterinary sector by sharing examples of challenges in vaccine development in veterinary hosts. To do this, illustrative presentations were given that focused on bacteria that i) have the potential to cause disease in both animals and humans (*Salmonella)*; ii) do not cause disease in their veterinary host, but can cause serious disease in humans (*Escherichia coli* O157: H7) or iii) are pathogens only in their veterinary hosts (*Mycoplasma* spp). For each pathogen, discussions include existing and potential vaccine strategies.

Introduction

There is a pressing need for improved veterinary vaccines. Both zoonotic and non-zoonotic bacterial infections in animals contribute to significant health, societal, and economic costs worldwide. Different animal immune systems and models must be considered within a framework that allows comparison of immune functions and vaccine responses across species but also incorporate the length of time vaccine-mediated protection may be needed for specific animal species.

Veterinary vaccinology is confronted with multiple complex challenges. These include a limited range of research tools and reagents, funding constraints, the diversity of host–pathogen interactions, complex regulatory requirements, the role of reservoirs, the distinction between colonisation and disease, and the absence of established correlates of protection. All these points need to be addressed in the ultimate design and delivery of a vaccine that is economically viable, particularly for low-middle income countries (LMICs).In many respects, these issues, present a greater combination of obstacles than encountered in settings more relevant to human health. A fundamental principle of vaccine development is that no vaccine can be effective without eliciting an appropriate immune response. A deeper understanding of specific animal host immunity is essential to optimise the design and evaluation of new bacterial vaccines and understand how they may work.

Organisations such as BactiVac, IVIS, and their partner institutions play a vital role in advocating for increased investment and policy support from governments, non-governmental organisations, and the farming industry. Advancing veterinary vaccines provides benefits that reach far beyond animal health. By improving the control of zoonotic infections, these vaccines help safeguard both animals and people, while also contributing to reduced antibiotic use and reducing the development of antimicrobial resistance.

To illustrate these challenges, the Workshop examined a series of case studies. *Salmonella* was presented as an example of a pathogen that can cause disease in many, but not all animal species, and in humans. This provided the basis for discussion on *Salmonella* pathogenesis, antigen identification, and vaccine development strategies. The programme then shifted to *Escherichia coli* O157:H7 (*E. coli* O157:H7), a pathogen with limited impact on animal health but significant implications for human health. The final pathogen discussed was *Mycoplasma mycoides*, which is highly relevant to animal health but poses no direct threat to humans, and whose disease burden falls disproportionately on LMICs.

Tackling *Salmonella* Through Vaccines: From Livestock to One Health

Salmonella in Livestock: Interventions to Protect Animal and Public Health

Overview

Salmonella is both an animal pathogen and a zoonotic

agent. Complicating this further, in some animals (species and individual hosts) it can colonise but not cause disease. Based on host specificity, *Salmonella enterica* subsp. *enterica* can be classified into three main groups: host-specific, host-restricted and generalist serovars. Its antigenic structure is central to its characterisation, classification, and influence on an immediate immune response. The bacterium possesses somatic (O) carbohydrate antigens within the lipopolysaccharide (LPS) antigen of the outer membrane, as well as proteinaceous flagellar (H) antigens. Different combinations of these antigens result in a high level of diversity within the genus with approximately 2,500 serovars recognised. Despite this diversity, most infections within a given country are caused by only around 30 serovars (Figure 1). Cross-protection between serotypes expressing different O-antigens is limited, presenting a significant challenge for vaccine development.

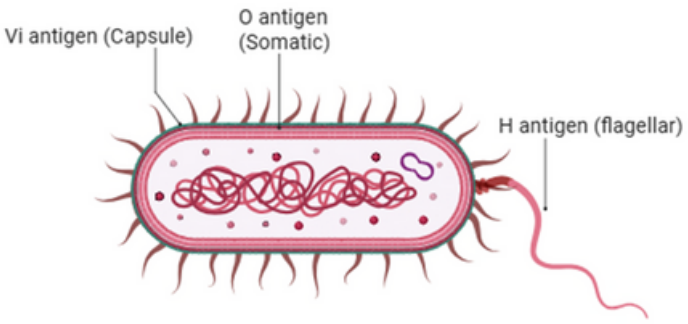

Figure 1: Structure of *Salmonella*
The White-Kauffmann-Le Minor scheme classifies S*almonella* serovars. The serovars are identified by their somatic (O) antigens within the lipopolysaccharide (LPS) of the outer membrane. It categorizes and flagellar (H) antigens, with additional consideration for the capsular (Vi) antigen.

These characteristics make *Salmonella*, and its infections, a valuable case study for vaccine research. Its antigenic diversity, host adaptation, and zoonotic potential illustrate many of the scientific and practical challenges facing veterinary vaccinology, while highlighting the importance of targeted strategies to control both animal and human disease.

Epidemiology and Public Health Importance

The EU One Health 2023 Zoonoses Report identified *Salmonella* as the leading cause of foodborne outbreaks of known origin in the EU. Reported cases are underestimated, representing only a fraction of the true incidence. In the UK, the underreporting factor is estimated to be by a factor of 4.7. The report includes a Sankey diagram (Figure 2) illustrating the distribution of the EU's top five *Salmonella* serovars in human infections, linking cases to food and animal sources.

Salmonella is highly successful in both host and non-host environments. It survives passing through the stomach, colonises the intestines, resists desiccation and heat stress, forms robust biofilms, and shows relative resistance to disinfectants, enhancing its persistence on farms and the environment.

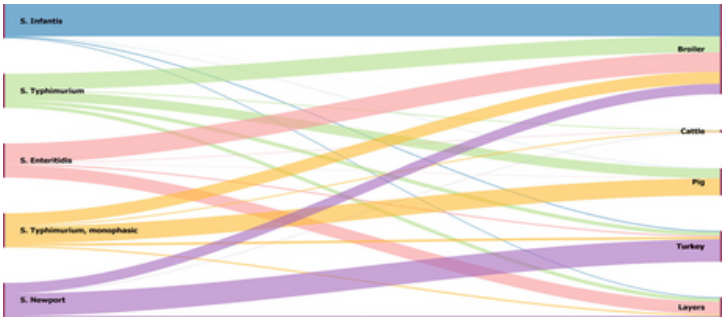

Figure 2: Sankey diagram of the distribution of the top five *Salmonella* serovars in human salmonellosis acquired in the EU
The left side of the diagram shows the five commonest reported *Salmonella* serovars from human salmonellosis cases acquired in the EU The right side shows the five sources considered (broiler, cattle, pig, turkey and layers). The width of the coloured bands linking sources and serovars is proportional to the percentage of isolation of each serovar from each source[1].

Introduction and Persistence on Farms

Zoonotic transmission is bi-directional. Multiple pathways exist for farm introduction, including vertical and horizontal transmission. Vertical transmission can occur, for example, with *Salmonella* Gallinarum (*S*. Gallinarum) in poultry when contaminated embryos carry bacteria from the ovary or oviduct. Horizontal transmission occurs at all stages of production, including exposure to litter, faeces, feed, water, dust, or contact with people, livestock, and wild animals. Rodents can amplify environmental contamination by shedding high numbers of bacteria. Effective rodent control is therefore critical to reducing the spread of bacteria.

High levels of environmental contamination must be addressed before vaccination can be most effective. Thorough cleaning, drying, and appropriate disinfection are essential to reduce bacterial loads. The UK Department for Environment, Food & Rural Affairs' (Defra) disinfectants approval scheme provides guidance for selecting correct disinfectants and concentrations to target pathogens effectively.

Table 1: Key Farm Persistence Factors and Control Measures

Persistence Factor	Control Measures
Survival in faeces, litter, dust	Thorough cleaning, drying & approved disinfectants
Rodent reservoirs	Rodent monitoring & control programmes
Contaminated feed & water	Quality assurance, regular testing & hygiene management
Vertical transmission via eggs	Breeder flock vaccination, egg hygiene & monitoring
Resistance to desiccation & heat	Use of correct disinfectants at proper concentrations
Biofilm formation on surfaces	Deep cleaning, surface disinfection & drying between flocks

Vaccination Stratergies

Vaccination is an important tool for controlling *Salmonella* but cannot replace biosecurity measures. Practices vary globally and the UK, poultry vaccination targets *Salmonella* Enteritidis (*S.* Enteritidis) and *Salmonella* Typhimurium (*S.* Typhimurium) to protect public health. Vaccines are administered during the rearing phase before the onset of lay, using either injection of inactivated vaccines or live vaccines applied orally through spray or drinking water. In flocks with high environmental bacterial loads, a combination of live and inactivated vaccines are often used. Live vaccines can inhibit colonisation, stimulate secretory IgA responses, and induce cellular immunity, while inactivated vaccines are primarily associated with enhancing humoral immunity.

Case studies demonstrate that vaccination in breeder and layer flocks reduces their *Salmonella* levels, which correlates with a decrease in human infections. Current UK strategies can include two doses of killed vaccine in broiler breeders to provide maternal immunity, and three doses of live vaccine in high-risk layer breeders. Duration of immunity is typically 50 to 60 weeks, though layers may be kept up to 80 weeks, raising questions about long-term protection. More studies are required to determine the long-term protection afforded by these vaccines in different species.

Pigs can be vaccinated against *S*. Typhimurium. For example, a live auxotrophic mutant ST DT9 vaccine has been successfully used. The vaccination protocol typically involves two subcutaneous doses in sows, with an additional booster before farrowing to confer maternal antibody protection to piglets. This vaccine is commercially available in some European countries. However, even with vaccination, environmental contamination remains a key factor in overall herd infection levels.

Salmonella infection also provides an informative model for vaccine research, as multiple vaccine platforms have proven effective. These include live attenuated bacterial vaccines such as Ty21a and capsular polysaccharide vaccines based on the Vi antigen, both of which are licensed for human typhoid prevention. Two additional candidates for invasive non-typhoidal *Salmonella* (iNTS), the Generalised Modules for Membrane Antigens (GMMA) outer membrane vesicle vaccine and a flagellin O-antigen conjugate, have progressed into human clinical trials. These platforms show promise for use in animal species, and additional antigen targets may offer further opportunities.

General considerations for vaccine use include the logistics surrounding administration, duration of immunity, cost-effectiveness, compatibility with other vaccines, and potential residues in food products. Field studies in target species are essential, as many vaccines are initially developed in specific pathogen-free animals or alternative models such as mice. Tests for Differentiating Infected from Vaccinated Animals (DIVA) are critical where control programmes exist.

Overall, *Salmonella* control in livestock requires a holistic approach. Vaccination is a key tool but must be integrated with stringent biosecurity, disinfection, cleaning, environmental management and rodent control.

Opportunities and Challenges in the Development of *Salmonella* Vaccines for Farmed Animals

Genetic Complexity and Vaccine Design

Millions of human non-typhoidal salmonellosis cases occur each year, with chickens, pigs, and cattle acting as major reservoirs. In farmed animals, *Salmonella* can cause severe enteric and systemic disease, depending on both bacterial and host factors. Current vaccines offer only partial control of these infections, and even when protection is observed, it is often limited to specific serovars. Further complicating control efforts, *Salmonella* is not genetically static. Although O-antigen usage is relatively conserved, the pathogen evolves through the emergence and decline of epidemic variants.

Over 702,000 *Salmonella* genomes have been sequenced (at the time of workshop delivery), providing a powerful resource for studying this pathogen. However, genome data alone cannot explain how these genes contribute to colonisation, pathology, or transmission. Gene expression and function vary across host species, anatomical niches, and stages of infection, complicating interpretation of genetic variation and limiting efforts to identify universal vaccine targets.

High-Throughput Screening Approaches

Early gene-by-gene studies revealed specific virulence factors, but this is impractical given *Salmonella* typically has around 4,500 genes. Signature-tagged mutagenesis (STM) allows the screening of pools of random transposon mutants, where attenuated mutants can be identified based on negative selection in the host. Newer methods such as transposon-directed insertion-site sequencing (TraDIS) enable simultaneous screening of thousands of mutants with massively parallel sequencing of transposon-flanking regions being used to simultaneously identify the insertion sites and relative abundance of the cognate mutants. This approach has uncovered both conserved and host-specific virulence determinants while minimizing the number of animals required for studies. For example, a TraDIS screen of 8,550 *S*. Typhimurium mutants in chickens, pigs, and calves identified approximately 600 genes with conserved roles in gut colonisation.

Host and Serovar-Specific Outcomes

Different serovars show distinct outcomes across hosts. For example, *S*. Typhimurium causes acute diarrhoea in calves, *Salmonella* Dublin (*S*. Dublin) leads to systemic typhoid-like disease, and *S*. Gallinarum is avirulent in calves but highly virulent in poultry. These differences limit universal vaccine approaches.

A conserved virulence system that is consistently required for infection across different hosts is the Type III Secretion System-1 (T3SS-1), which enables rapid invasion and survival across the gut and within host cells. However, the speed with which this system functions (as short as 90 seconds) means it may be difficult to target with antibody-based vaccines.

Table 2: Key Opportunities and Challenges in *Salmonella* Vaccine Development

Opportunities	Challenges
Around 702,000 sequenced genomes (at the time of workshop delivery)	Large genome with redundancy can complicate target identification
Conserved and surface-exposed antigens can be predicted from genome data	Virulence factors can be host- or niche-specific
High-throughput tools (TraDIS, STM) systematically identify virulence genes with minimal animal use	Humoral responses to the O antigen can dominate & lead to serovar-specific protection
Hundreds of genes critical for colonisation in key animal species are known	Challenging to predict effective B & T cell epitopes
Rational design of live-attenuated vaccines is feasible as *Salmonella* is genetically tractable	For live vaccines, difficult to predict which mutations will give the desired balance of persistence, safety & immunogenicity
Function and mode of action of some virulence factors is well understood	
	Achieving antibody responses at the right place, level & time to be effective can be challenging
	In vivo studies are required for validation of vaccines & can be expensive in farmed animals

Harnessing *Salmonella* Porins for Vaccine Development: A One Health Strategy

Diseases caused by bacteria of the genus *Salmonella* (including typhoid fever, paratyphoid fever, non-typhoidal *Salmonella* (NTS) and its invasive form iNTS) remain a major global health challenge, particularly in LMICs, where they disproportionately affect children and immunocompromised adults. Licensed vaccines exist only for typhoid fever (the live oral Ty21a, the Vi polysaccharide, and the Vi–TT conjugate). There are currently no licensed vaccines for paratyphoid fever or for NTS caused mainly by *S*. Typhimurium and *S*. Enteritidis.

Studies using patient sera have identified outer membrane proteins, especially porins, as promising protective antigens. In mice, immunization with purified porins confers protection against *S*. Typhimurium and *Salmonella* Typhi (*S*. Typhi) in challenge models, eliciting robust T-cell proliferation, strong antibody responses, and an expansion of IgM memory B cells. Immunized animals develop long-lived germinal centres in which T follicular helper cells are essential for sustaining IgM responses. Porins promote Th1-skewed $CD4^+$ T-cell differentiation and induce type-I T follicular helper cells, supporting durable bactericidal antibody production.

The OmpD porin from non-typhoidal *Salmonella* has emerged as a key target, although a single amino acid substitution can disrupt antibody-mediated protection. Importantly, studies in HIV-infected patients in sub-Saharan Africa revealed that while these individuals produced high antibody levels against *Salmonella*, anti-LPS antibodies blocked the bactericidal activity of anti-porin antibodies, highlighting the challenge of LPS shielding.

Evidence from poultry supports the protective role of porins. Subcutaneous vaccination of breeder hens with purified *S*. Gallinarum porins generated robust IgY responses, conferring passive immunity to offspring against virulent, drug-resistant strains. Cross-reactivity between porins of *S*. Gallinarum and *S*. Typhi underscores their potential as broadly protective antigens.

Human studies further support the translational potential of porins. *S*. Typhi porins induce long-lasting IgM and IgG responses in humans, persisting for up to 11 years. These porins contain conserved T cell epitopes across clinically relevant strains and function as TLR2 and TLR4 agonists, enhancing antibody responses to co-administered vaccines. A single low dose (10 µg) can induce durable immunity, making porins strong candidates for multivalent vaccines with both human and veterinary applications.

Summary of *Salmonella* Research and Vaccine Development

Collectively, the workshop discussions highlighted *Salmonella* as an exemplar of both the challenges and opportunities in bacterial vaccine development. Its epidemiological importance as the leading cause of foodborne outbreaks in Europe, coupled with its remarkable ability to persist in hosts, the environment, and farm settings, underscores the complexity of controlling this pathogen. Vaccination has proven valuable in managing low-level environmental

contamination and reducing zoonotic transmission from poultry, but current approaches remain limited by serovar specificity and changing epidemiology. Genomic and high-throughput functional studies have identified hundreds of genes critical for colonisation and virulence, yet translating these into cross-protective vaccine antigens is difficult due to host- and serovar-specific variation and the difficulty of predicting which antigens or genes to target for subunit or live-attenuated vaccines, respectively. Recent advances in vaccine technologies and approaches including porin-based vaccine research offer a promising One Health solution. Porins are highly conserved across *Salmonella* serovars and maintain high levels of homology within serovars, are strongly immunogenic, and capable of eliciting durable antibody and T cell responses in both animal models and humans. Together, these insights illustrate why *Salmonella* continues to be a pivotal model for understanding bacterial pathogenesis and for guiding the rational design of next-generation veterinary and human vaccines.

Field Evaluation of a Prototype Subunit Vaccine to Control *Escherichia coli* O157:H7 in Cattle

Disease Overview

A key challenge with *E. coli* O157:H7 is that it causes severe disease in humans but no clinical disease in cattle, its principal reservoir. This serotype belongs to the group of Shiga toxin-producing *E. coli* (STEC), which produce Shiga toxins that bind human endothelial cells.

Human infections can involve haemorrhagic colitis that manifests as bloody diarrhoea. In severe cases, endothelial damage in the kidneys results in haemolytic uraemic syndrome (HUS), a life-threatening condition associated with significant morbidity, resulting in dialysis, or the need for kidney transplantation. Children and the elderly are particularly vulnerable, making outbreaks a major public health concern.

Transmission occurs through direct or indirect contact with ruminant faeces, often via contaminated food. Among the STEC serotypes, O157:H7 accounts for approximately 50% of human clinical cases. Two major Shiga toxin types exist: Stx1 and Stx2 (with subtypes a–g). The Stx2a subtype, particularly in combination with the *eae* gene encoding the adhesin intimin is strongly associated with severe human disease.

Epidemiology

Cattle are the major reservoir of *E. coli* O157:H7, though other ruminants can also carry these bacteria. Importantly, ruminants show no clinical disease or production losses, making it difficult to persuade farmers to adopt costly multi-dose vaccines.

While O157:H7 remains the dominant serotype in human disease, non-O157 infections are rising. For example, in 2024 the UK experienced a large outbreak of O145 linked to contaminated lettuce. Between 25 May and 24 June 2025, 275 cases were confirmed: 81% developed bloody diarrhoea, seven developed HUS, two adults died, and 49% required hospitalisation. This outbreak strain carried stx2a and *eae*, markers of high virulence.

Current Control Measures

At present, no on-farm control measures exist. Instead, food safety relies on hazard analysis and critical control point (HACCP) systems in slaughterhouses and on appropriate handling and cooking practices in the household. These measures have reduced cross-contamination from infected carcasses, and in the US, packed meat is subject to active microbiological surveillance.

Attempts at vaccination have faced obstacles. Two commercial products Econiche™ (Bioniche) and Vaxxon® SRP® *E. coli* O157:H7 (Epitopix/Vaccinova®), failed commercially due to insufficient efficacy and high cost. While farmers recognise their role in on-farm control, they remain highly cost-sensitive.

High-Shedding Cattle as a Vaccine Target

Modelling studies show that approximately 80% of cattle-to-cattle transmission originates from around 20% of animals, known as super-shedders, which excrete large amounts of bacteria in faeces. Targeting this minority of highly shedding cattle could have a disproportionate positive impact. By vaccinating just 3–6% of the highest shedders, the basic reproduction number (R_0) could be reduced below 1, effectively interrupting transmission.

Vaccine Design and Mechanism

Colonisation of the bovine gut is central to STEC persistence. The process begins with motility and adhesion via H7 flagella, followed by colonisation through the action of a Type III secretion system (T3SS). This comprises a needle-like structure composed of EspA filaments which injects effector proteins into cells lining the gut, including the translocated intimin receptor (Tir) which then binds to the intimin protein on the bacterial surface. This leads to intimate adherence of STEC to the surface of host cells (Table 3, Figure 3). A subunit vaccine was therefore designed to block this stage of colonisation.

Formulations containing EspA, Intimin-531, and H7 showed the most promise, significantly reducing colonisation and faecal shedding. Cross-protection was also investigated. Antibody cross-recognition of additional serotypes have been observed, but whether these antibodies are functionally protective remains to be determined.

Table 3: *E. coli* O157:H7 Vaccine Antigens and Their Roles in Colonisation

Antigen	Function in Colonisation	Impact of Vaccine-induced responses
H7 flagellin	Motility and initial adhesion	Blocks early attachment to epithelial cells
EspA	Needle-like structure of T3SS	Prevents effector protein injection
Intimin	Bacterial surface adhesin	Disrupts adhesion to host cells
Tir	Host-injected receptor enabling binding	Blocks stable intimin–Tir interaction

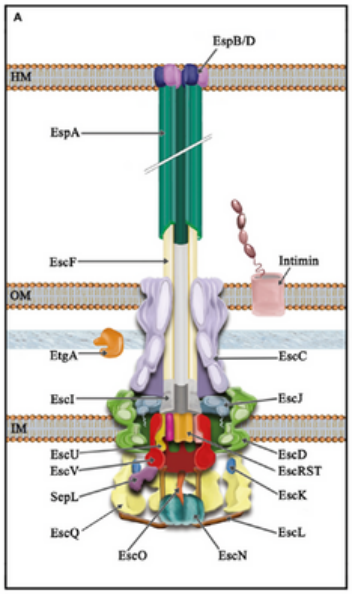

Figure 3: Schematic representation of the type III secretion system
The T3SS is divided into three main parts, from top to bottom extracellular appendages, translocation pore filament and needle. The needle-like structure is composed of EspA filaments which inject effector proteins, including the translocated intimin receptor (Tir), into host cells, enabling stable bacterial attachment via intimin[2].

Field Evaluation

A Good Manufacturing Practice (GMP) vaccine of the subunit vaccine formulation containing EspA, Intimin-531 and H7 has now been tested under feedlot conditions in the US. The vaccine reduced colonisation and daily bacterial shedding compared with unvaccinated controls, with evidence of immune memory. However, short duration of effect, combined with economic and logistical barriers, highlights the challenges of deploying such a vaccine in livestock.

Tackling Bacterial Livestock Diseases in sub-Saharan Africa – Spotlight on Contagious bovine pleuropneumonia and Contagious caprine pleuropneumonia

Disease Overview

Contagious bovine pleuropneumonia (CBPP) is caused by *Mycoplasma mycoides* subsp. *mycoides* (Mmm). It is a World Organisation for Animal Health (WOAH) listed disease that is transmitted via aerosol droplets through close contact between infected and susceptible animals. Mortality in naïve cattle herds can reach 50%, with variable incubation periods. Clinical signs include fever, respiratory distress, anorexia, and unilateral lung lesions with pleural fluid. The disease may present in acute, subacute, or chronic form and is widespread across much of sub-Saharan Africa.

Contagious caprine pleuropneumonia (CCPP) is caused by *Mycoplasma capricolum* subsp. *capripneumoniae* (Mccp). It is widespread in Central and East Africa, the Middle East, and Asia, affecting domestic goats and wild ruminants. CCPP is transmitted via aerosol droplets during close contact in herds and can cause up to 80% mortality. Clinical signs are similar to CBPP.

Both diseases are epidemiologically related, as they belong to the *Mycoplasma mycoides* cluster. The closest relative to Mmm is *Mycoplasma mycoides* subsp. *capri* (Mmc) (Figure 4).

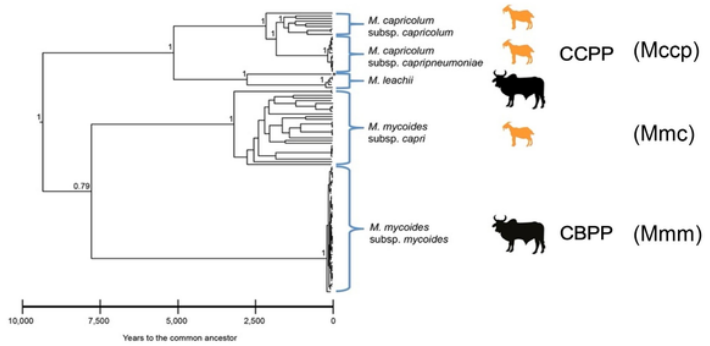

Figure 4: The *Mycoplasma mycoides* clusters
A Maximum Clade Credibility tree resulting from the combined BEAST analysis of 110 strains. CBPP is caused by *Mycoplasma mycoides* subsp. *mycoides* (Mmm) while CCPP is caused by *Mycoplasma capricolum* subsp. *capripneumoniae* (Mccp). Both diseases are epidemiologically related, as they belong to the *Mycoplasma mycoides* cluster. The closest relative to Mmm is *Mycoplasma mycoides* subsp. *capri* (Mmc)[3].

Vaccines against CBPP and CCPP

CCPP: A lyophilised Mccp vaccine (0.15 mg/dose, suspended in saponin) is available. It has a shelf life of at least 14 months and is recommended every 6–12 months. Protection can be up to 100%.

CBPP: A live attenuated vaccine (mainly T1/44 strain) is used. Efficacy is variable (20–80%) depending on infection dynamics and measurement methods, with no harmonised standard. Protection typically lasts for one year, but some animals can develop severe injection-site reactions (Willems' reactions), which discourage vaccination and often require antibiotic treatment. More attenuated strains may provide improved safety but lower protection, necessitating vaccination roughly every six months. The vaccine is prepared at 10^7 cfu, sold in 50–100 dose vials, and must be used within one hour of reconstitution.

Research is ongoing to identify novel vaccine targets,

study host–pathogen interactions to improve efficacy, and develop better policy and control programmes. The current CBPP control options include four strategies: vaccination, movement restriction, test and slaughter and antibiotic treatment.

Vaccination reduces burden but modelling shows it is currently insufficient to eliminate CBPP. Movement restriction and test-and-slaughter were used in Europe when the disease was introduced to Africa. Antibiotics are not recommended, as treatment could induce a chronic CBPP carrier state which could play a role in new outbreaks (although this hypothesis has not been proven) and can make animals more susceptible to secondary infections and contribute to antimicrobial resistance (AMR).

Challenges in Sub-Saharan Africa

CBPP remains endemic and disease management varies by country. Strict vaccination campaigns place heavy financial burdens on national veterinary services. Because of cost, preventive vaccination is uncommon; most vaccination occurs during outbreaks, often too late to stop transmission. Movement restrictions are only partly implemented and farmers frequently act independently, as slaughter is too expensive and compensation is lacking. These challenges have ripple effects on trade and livelihoods.

Pilot CBPP Control Programme in Kenya

A Kenyan project is developing a scalable control programme in pastoral farming systems, combining vaccination with antibiotic treatment of breakthrough infections. A scoping study confirmed CBPP on farms, with estimated herd mortality of 30%. The disease caused major economic losses from drug costs and animal deaths. Self-treatment by farmers is common, with veterinarians sometimes initiating treatment before leaving drugs for farmers to continue.

The project aims to:

- Conduct controlled on-farm vaccine efficacy trials
- Use mathematical modelling to test combinations of control options
- Carry out cost benefit analyses
- Improve vaccine quality control
- Establish AMR monitoring, which is currently lacking

Advances in CCPP and CBPP Research

A robust challenge model for CCPP has been established, yielding reproducible results, which can now be used for *in vivo* testing of prototype vaccines. For CBPP, a nebuliser-and-mask vaccine delivery model has recently been developed. After initial antigen discovery used *in silico* methods, followed by pooled immunogenicity testing and vaccine efficacy trials four recombinant antigens were selected for further evaluation and induced protection of ~50% based on lesion scoring.

Mmm itself is not amenable to site-directed mutagenesis, but its close relative Mmc can be genetically modified via genome transplantation, a system to transfer the entire bacterial genome into yeast cells, modify it, and then reinsert it into the bacterium. Using this methodology, the polysaccharide pathway has been identified as a virulence factor in Mmc. Today, also whole-genome saturated transposon mutagenesis is being used to discover additional virulence factors as potential vaccine targets.

CBPP and CCPP continue to impose heavy health and economic burdens across sub-Saharan Africa, with limited vaccine options and control measures. While CCPP vaccines offer relatively high protection, CBPP vaccines remain less effective and carry safety concerns, discouraging widespread adoption. Current research is focusing on novel antigen discovery, improved challenge models, and genetic tools to identify virulence factors, while policy studies explore sustainable control strategies. Progress in these areas is essential to developing next-generation vaccines and integrated control programmes that can reduce transmission, protect livelihoods, and mitigate the broader impacts of these neglected livestock diseases.

Market, Regulatory and Translational Challenges in Bacterial Vaccine Development

This Workshop highlighted a wide spectrum of bacterial pathogens, using *Salmonella*, STEC, and *Mycoplasma* as case study examples. While biologically distinct, they all share a common reality. Vaccine development for veterinary animals is not pursued purely as a scientific or welfare exercise alone but must be undertaken in the context of an appreciation of market forces, trade implications, and regulatory frameworks. Frequently, the greatest need for vaccines is in LMICs, where the market is weakest, while in high-income countries where markets exist, difficult policy questions arise about who should shoulder the costs. This conflict between where vaccines are needed most and where they are economically viable is at the heart of many challenges in livestock vaccine development.

A central theme is the role of DIVA. Importing countries rely on antibody tests to screen animals and products, but these tests cannot always distinguish between natural infection and vaccine-induced immunity. If antibodies triggered by vaccination reflect those induced by infection, then products may be prohibited from export into international markets, even when animals are healthy. Vaccines that contain DIVA, paired with diagnostic tests approved by WOAH, therefore provide a

vital solution. However, approval of such diagnostics is slow and highly regulated, adding other layers of complexity and cost.

Regulation of live-attenuated vaccines further illustrates how scientific solutions meet practical constraints. Live vaccines remain among the most effective tools against bacterial diseases, yet their use in food-producing animals raises unique issues, particularly where they are genetically modified and may enter the environment. To ensure safety, regulatory authorities require withdrawal periods, during which animals or their products cannot enter the food chain, to ensure clearance of the vaccine from meat, milk, or eggs. This safeguard exists because consumers have not consented to ingesting vaccine material, even if harmless. Thus, withdrawal periods add cost, logistical hurdles, and influence whether a vaccine is ultimately marketable.

Beyond safety, the process of translating a candidate vaccine to a field trial is filled with regulatory hurdles. Many academic researchers are unfamiliar with what regulators require, leading to studies that must be repeated or redesigned at a significant expense. For example, proving efficacy in the intended host species is essential as immune systems can differ greatly between animals, with data from small laboratory models often not extrapolated in other challenge models or systems. Chickens, as a key reservoir species for *Salmonella*, illustrates this point. The regulation of immune responses can be different, not least because they lack lymph nodes found in mammals and the basis of immune priming is less well understood. Additionally, deeper assessments of immune responses in chickens can be restricted by the relative paucity of reagents Moreover, tools such as B and T-cell knockout chickens are currently lacking, which makes it harder to identify protective immune responses.

Regulatory expectations vary across regions, shaping the strategies used in vaccine development. As a result, identical vaccines may encounter very different pathways to approval and adoption depending on the markets developers target. An additional challenge arises in countries with less developed regulatory systems, which are often the same regions where the need for vaccines is greatest, making progress even more difficult.

To guide developers through this complexity, Target Product Profiles (TPPs) are an essential tool. A TPP is essentially a blueprint that outlines the desired characteristics of a vaccine, including the number of doses, expected duration of protection, side effect profile, cost, and ease of administration. By forcing innovators to think early about what the market and regulators will demand, TPPs help ensure that promising laboratory findings can be translated into products that meet real-world needs. Industry, regulators, and funders alike rely on TPPs when assessing whether to support or license new vaccines.

Ultimately, successful vaccine development requires collaboration across multiple sectors. Academia often generates innovation, but can lack insight into production constraints, regulatory expectations, or market dynamics. Industry, in contrast, has expertise in these areas but can benefit from academic research on host-pathogen interactions and their outcomes. Regulators cannot dictate product design but are increasingly open to early dialogue, and many now have dedicated teams to guide developers. Funders also play a role by mandating early engagement with regulators and sometimes even providing access to regulatory consultants for grantees. Initiatives like BactiVac have reinforced the importance of early academic–industry partnerships to avoid costly missteps later.

The Workshop also highlighted a persistent mismatch in communication and expectations. Researchers, regulators, industry, and funders often speak different “languages,” which can lead to misunderstandings or delays. Encouragingly, progress is being made: regulatory authorities are engaging more with developers, funders are embedding translational support into grants, and training opportunities are beginning to equip scientists with the tools to navigate regulatory and commercial landscapes. These are reasons to be optimistic and potentially reinforce the role of networks and networking to facilitate progress, help derisk projects and bring development costs down. Nevertheless, all activities need to be underpinned by significant investment, which is absolutely crucial to help vaccines reach where needed.

Taken together, the discussions made clear that the obstacles to vaccine development go far beyond the laboratory bench. Issues such as DIVA compatibility, regulatory approval, withdrawal periods, TPPs, and the need for cross-sector collaboration are common threads linking work on *Salmonella*, *E. coli*, and *Mycoplasma*. Addressing these cross-cutting challenges will be essential if promising scientific discoveries are to translate into effective vaccines, reduce reliance on antibiotics, and ultimately improve both animal and human health.

Conclusions and takeaways

The success of a vaccine candidate ultimately requires it to progress into a viable product. Scientific discovery, preclinical studies, and field testing provide the foundation, but translation into real-world impact requires collaboration with industry. Industry brings expertise in large-scale manufacturing, regulatory navigation, quality assurance, and market delivery. These capabilities are essential for overcoming hurdles such as regulatory

approval and production scale-up.

A central tool in guiding this process is the TPP. The TPP serves as both a strategic framework and a roadmap for vaccine development. It defines the intended use, target population, and key product features, ensuring that research remains aligned with practical requirements and market expectations. By setting clear goals from the outset, the TPP helps focus scientific and clinical efforts, shape trial design, support regulatory submissions, and increase the likelihood that the final vaccine will be both scientifically robust and commercially viable.

The workshop highlighted the importance of studying pathogens in their natural host. For example, *Salmonella* deploys host- and niche-specific virulence factors and may elicit different responses in different hosts, meaning that a vaccine that is effective for one species may not be effective in another. This underlines the need to conduct discovery research in the intended target animal, supported by robust animal models and appropriate reagents. Pen and field trials, while challenging, are essential to advance vaccine development and to deepen understanding of immunopathology and immunoprotection.

There is also a pressing need for stronger surveillance systems and harmonised experimental protocols to ensure comparability across studies. Such standardisation would accelerate the identification of correlates of protection but requires reliable funding and access to reagents, which are particularly difficult to secure in low-resource settings. In addition, vaccine candidates must demonstrate sufficient protection to be valuable in the marketplace. If vaccines are costly but only moderately effective, uptake is likely to be limited, especially in resource-constrained regions.

Vaccines remain a powerful tool to reduce the severity of infections, bacterial shedding, and overall bacterial burden. Effective vaccination can also reduce antibiotic use, thereby helping to lessen the global challenge of AMR.

Access to expertise and resources is essential throughout this pathway, and networks play a critical role by connecting researchers with the knowledge and tools needed to address key gaps. The journey from academic discovery to licensed product is complex, and setbacks are inevitable. It is important to learn from shared experiences. By fostering open dialogue, strengthening collaborations, and building on collective lessons, product developers can avoid repeating missteps and accelerate progress toward successful vaccines.

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References

1. Control, E.F.S.A.a.E.C.f.D.P.a. & ECDC), E.a. The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2017. *EFSA Journal 16* (2018).
2. Gaytan, M.O., Martinez-Santos, V.I., Soto, E. & Gonzalez-Pedrajo, B. Type Three Secretion System in Attaching and Effacing Pathogens. *Front Cell Infect Microbiol* 6, 129 (2016).
3. Fischer, A. et al. The origin of the '*Mycoplasma mycoides* cluster' coincides with domestication of ruminants. *PLoS One* 7, e36150 (2012).

Abbreviations	Full description
AMR	Antimicrobial resistance
APHIS	Animal and Plant Health Inspection Service
CBPP	Contagious Bovine Pleuropneumonia
CCPP	Contagious Caprine Pleurpneumonia
CFU	Colony forming units
B/T cell	B and T lymphocyte
Defra	Department for Environment, Food & Rural Affairs
DIVA	Differentiating Infected from Vaccinated Animals
E. coli O157	*Escherichia coli* O157
EU	European Union
EMA	European Medicines Agency
EspA	Enteropathogenic *Escherichia coli* secreted protein
FDA	Food and Drug Administration
GMMA	Generalised Modules for Membrane Antigens
GMP	Good Manufacturing Practice
H7	H7 flagellin
HACCP	Hazard analysis and critical control point
HIV	Human immunodeficiency virus
HUS	Haemolytic uraemic syndrome
Ig	Immunoglobulin
IgM	Immunoglobulin M
IgG	Immunoglobulin G
IgY	Immunoglobulin Y
iNTS	invasive non-typhoidal *Salmonella*
IVIS	International Veterinary Immunology Symposium
LMIC	Low- and Middle-Income Country
LPS	Lipopolysaccharide
Mccp	*Mycoplasma capricolum* subsp. *capripneumoniae*
Mmc	*Mycoplasma mycoides* subsp. *capri*
Mmm	*Mycoplasma mycoides* subsp. *mycoides*
NTS	Non-typhoidal *Salmonella*
OmpD	Outer Membrane Protein D
S. Dublin	*Salmonella* Dublin
S. Enteritidis	*Salmonella* Enteritidis
S. Gallinarum	*Salmonella* Gallinarum
STEC	Shiga toxin-producing
S. Typhimurium	*Salmonella* Typhimurium
STM	Signature-Tagged Mutagenesis
T3SS	Type III Secretion System
Tfh	T Follicular Helper cell
Th1	T helper type 1
Tir	Translocated intimin receptor
TLR2	Toll-Like Receptor 2
TLR4	Toll-Like Receptor 4
TPP	Target Product Profile
TraDIS	Transposon-directed insertion-site sequencing
UK	United Kingdom
US	United States
Vi-TT	Vi polysaccharide–tetanus toxoid
WOAH	World Organisation for Animal Health

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This report seeks to capture the knowledge and perspectives shared during the Workshop, making these rich discussions accessible to a wider audience and supporting ongoing efforts to address the bottlenecks and challenges in developing vaccines for veterinary infections.

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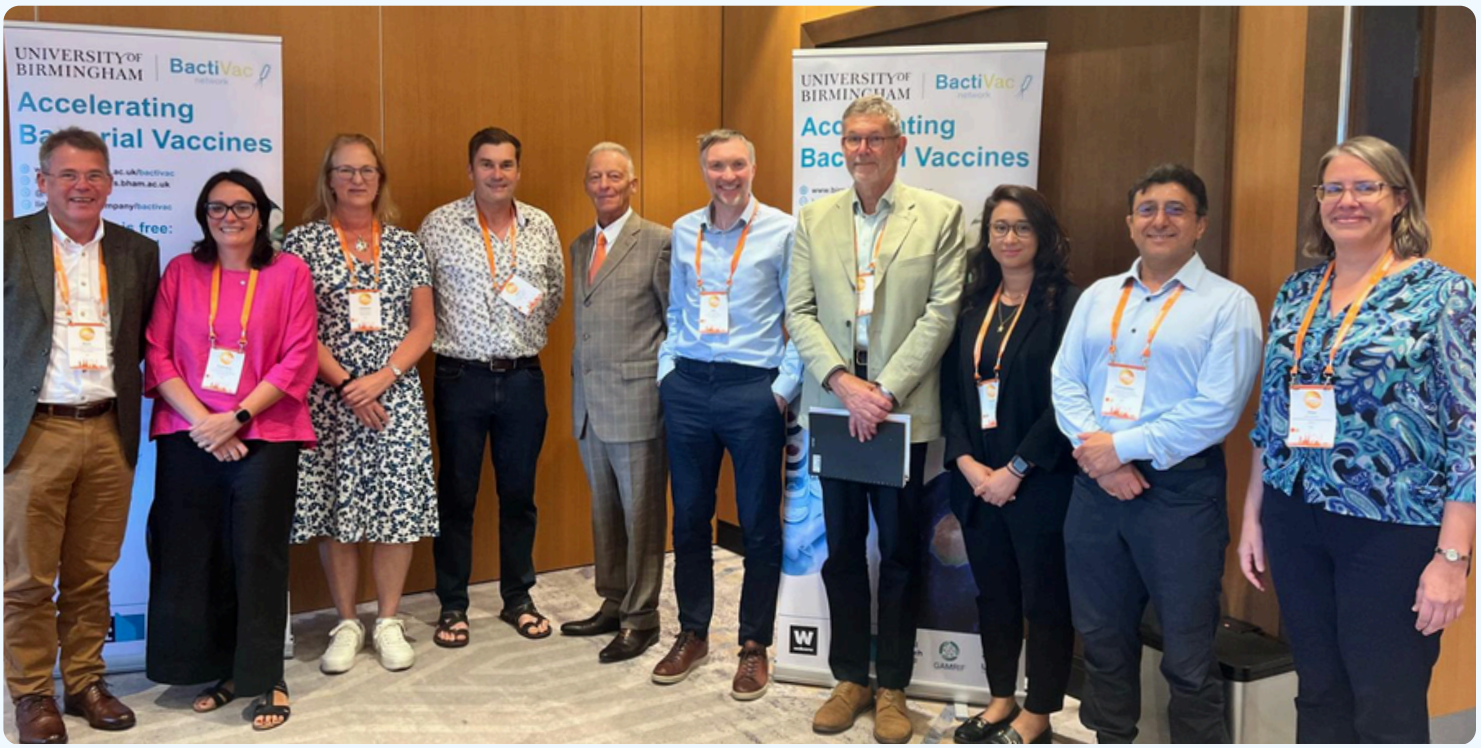
We would appreciate it if you could complete a brief survey on the report *Considerations for Developing Bacterial Vaccines for Veterinary Infections*. Your feedback will help us understand how the report is being used and how it can be improved. Please scan the SLIDO QR code or enter the survey code # 1552856 to take part.



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