STAR-IDAZ
International Research
Consortium on Animal Health

Global Veterinary Vaccinology Research and Innovation Landscape Survey Report

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Executive summary

This paper provides an analysis of the Survey on the Global Veterinary Vaccinology Research and Innovation Landscape conducted by UKRI-BBSRC on behalf of STAR-IDAZ International Research Consortium on Animal Health (STAR-IDAZ) and the veterinary vaccinology research funders and programme owners.

In July 2021, UKRI-BBSRC (BBSRC), in consultation with other animal health funders, conducted a survey on the global veterinary vaccinology landscape to gain insight on the key gaps, priorities and barriers that need to be addressed in the future.

- 122 responses were received.
- 49% of respondents were academic with a small number of responses received from industry, charity, and clinicians.
- The top five disciplines of respondents were vaccinology, immunology, virology, molecular biology, and bacteriology.
- Viruses, followed by bacteria and parasites, were the most common pathogen studied by the survey respondents.
- Large ruminants, followed by swine, poultry and small ruminants, were the most common host species studied by the survey respondents.

Key Finding from the Survey

Respondents were asked to rate the importance of research and innovation gaps within different fields of veterinary vaccinology identified by the BBSRC Veterinary Vaccinology working group and provide any additional gaps. Below is a summary of the key veterinary vaccinology research and innovation needs as identified from this survey:

Key Conclusions

- Sustainable and open access to immunological tools and associated databases.
- Partnership with industry, is a key.
- Developing and validating:
  - new immunological methods and technologies that enable research in the natural host and/or the best model species
  - in vitro tools combined with bioinformatics for testing vaccine antigen efficacy and selection
  - models to reduce, replace and refine the use of animals in research (3Rs)
  - knockout models to decipher different types of immune response
- Discovering and validating adjuvants that generate an optimal immune response in veterinary species (58% very important).
- Incorporation of in silico tools including bioinformatics with wet lab to assist in the development of tools for veterinary vaccine research.

1. Fundamental immunology:

- Need for better understanding of:
  - immune response to pathogens and vaccines including duration of immunity.
  - the role of mucosal, innate, and adaptive immunity.
  - the impact of genetics, microbiome, pathogen evolution etc. on immune and vaccine responsiveness.
  - host-pathogen interactions.
  - species-specific and site-specific immunology.
- Understanding of correlates and surrogates of protection along with defining and developing standardised methods for detecting and measuring correlates and surrogates of protection.

2. Veterinary vaccinology toolbox:

- Developing and validating tools for studying immune response in all veterinary species.
- Supporting databases for development, availability, distribution, and exploitation of lab reagents in collaboration with commercial partners.
- Immunological methods and technologies that enable research in the natural host and/or the best model species – e.g. in vitro tools combined with in silico tools to assist in the development of tools for veterinary vaccine research e.g., testing vaccine antigen efficacy and selection.

3. Model systems:

- Developing and using appropriate model systems for developing and testing vaccines.
- Suitable use and access to animal models to assess safety, including in field settings.
- Knockout models to decipher different types of immune response.

4. Vaccine platform technologies:

- Establish and characterise pipeline of 'plug and play' platforms that can be used for rapid identification of target antigens, vectors, and delivery systems for pathogens.
- Development of mucosal and oral delivery platforms with an understanding of site specific, protective immunity and the ability to target vaccine delivery to these sites.
- Platforms need to be efficacious, economically suitable, scalable, rapid to produce and regulated.
- Developing vaccine platform technologies which can integrate multiple antigens in one vaccine.
- Support for data analytics, bioinformatics, and genomic databases to underpin technology platform.

5. Collaborative working in veterinary vaccinology:

- Developing strong public-private partnership.
- Promoting a One Health approach by aligning veterinary and human vaccine research and innovation, and, supporting joined up capability across veterinary and human research and innovation.
- Coordinated response and knowledge exchange between academia, regulators, and industry to understand the vaccine development landscape, regulation and requirements across species, platforms, and regions.

6. Capability, capacity, and infrastructure:

- Maintaining capacity in veterinary vaccine research across the entire vaccinology research and development career track.
- Strengthening emergency research capacity, manufacturing, and infrastructure (inc. containment facilities) in veterinary clinical practice for emerging epidemic and epizootic diseases.
- Upscaling of vaccine production to Good Medical Practice (GMP) standard.
- Capacity for large scale vaccine field trials.
- Need for improved infrastructure to support post-marketing evaluation of vaccine effectiveness.

Key Recommendations for Funders

- Fund basic research on understanding immunology and host-pathogen interactions.
- Invest in basic research on novel vaccine technology platforms.
- Bridge gaps between regulatory bodies, academia, and industry.
- Promote a One Health working with human vaccinology.
- Provide training and development in an environment which develops vaccines through to commercialisation.
- Foster international collaboration.

The report will be considered by the UKRI-BBSRC's Veterinary Vaccinology Expert Working Group along with other animal health funders and BBSRC Bioscience for Integrated Understanding of Health Strategic Advisory Board. The outputs from the survey will form the basis of the Veterinary Vaccinology Strategy 2022-2027 and provide framework for future research and innovation activities.

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Background

In July 2021, UKRI-Biotechnology and Biological Sciences Research Council (BBSRC), in consultation with other animal health funders and STAR-IDAZ International Research Consortium on Animal Health (STAR-IDAZ), conducted a survey to map the global veterinary vaccinology research and innovation landscape (Annex 1). The aim was to gain insight from researchers and stakeholders on the most important gaps, priorities and barriers that need to be addressed.

The survey was opened throughout July 2021 on the BBSRC website and forwarded to various societies/networks of interest, strategic partner universities/institutions. The survey was also endorsed and advertised by the International Veterinary Vaccinology Network, STAR-IDAZ IRC, British Society of Immunology, Medical Research Council, International Union of Immunological Studies, and the American Association of Veterinary Immunologists.

Context

The BBSRC is a major funder of veterinary vaccinology research and innovation, providing funding for research undertaken both domestically and internationally. Over the last five years (2015-2020) BBSRC has invested £177.2M in Veterinary Vaccinology research and innovation.

BBSRC's research investment in vaccinology are informed by its Veterinary Vaccinology Strategy: 2015-2020 . Now at the end of the lifetime of the original strategy, BBSRC is conducting an exercise to refresh this strategy. Analysis was conducted on the BBSRC Veterinary Vaccinology portfolio to examine how investments have aligned to the initial strategic vision and the Expert Veterinary Vaccinology Working Group (Annex 2) was convened to discuss this.

The Expert Working Group, chaired by Professor Bryan Charleston, agreed that good progress has been made but also highlighted where research and innovation gaps still need to be addressed.

Following the input from the Expert Working Group, BBSRC consulted with the community to seek their views via an online survey and to capture additional priorities, gaps, and barriers within the veterinary vaccinology field. The survey questionnaire is included in Annex 1.

This report presents a narrative of the survey responses through quantitative assessment of the importance of research & innovation and with assessment of underpinning needs to support veterinary vaccinology research and innovation including capability and capacity and skills and training priorities.

Overview

The survey was divided into 3 sections:

Part 1 Introductory Questions

Introductory questions were used to acquire demographics about respondent's research to provide context to answers.

- Region
- Sector
- Discipline
- Pathogen type
- Host species type
- Geographic region of disease focus

Part 2 Research and Innovation for Veterinary Vaccinology

This section includes analysis of the questions asked in the survey. Respondents were asked to rank the importance of research and innovation priorities along with underpinning needs in capacity and skills and training within the veterinary vaccinology field. Respondents were also given additional space to provide additional comments.

This section was divided into nine themes:

- Immune Responses to Vaccines
- Immunological Tools
- Technology Platforms
    i. Underpinning Needs for Technology Platforms
    ii. Unmet Needs
- Vaccine Design and Delivery
- Vaccine Delivery Platforms
- Vaccine Safety, Equity and Uptake
- Epidemiology and Economics
- Capability and Capacity
- Skills and Training

At the end of each theme a key conclusions summary is provided.

Part 3 Overarching Veterinary Vaccine Needs

This section was provided to give respondents an opportunity to acknowledge overarching needs within the field.

Glossary

AMR	Antimicrobial resistance
AI	Artificial Intelligence
BBSRC	Biotechnology and Biological Sciences Research Council
DIVA	Differentiating Infected from Vaccinated Animals
DTPs	Doctoral Training Programmes
ELISA	Enzyme-linked immunosorbent assay
EM	Electron Microscopy
GM	Genetically Modified
GMP	Good Medical Practice
IP	Intellectual Property
LMIC	Low Middle Income Countries
NPVs	Net Present Values
ROIs	Return of Investments
SMEs	Small and medium sized enterprises
SNPs	Single nucleotide polymorphisms
QC	Quality Control

Part 1 Introductory Questions

The survey was launched in July 2021 on the BBSRC website and widely disseminated via STAR-IDAZ IRC, the American Association of Veterinary Immunologist, British Society of Immunology, International Union of Immunological Societies, and the International Veterinary Vaccinology Network.

There were 122 complete responses to the survey. Incomplete responses were not considered. The intended target respondents of this survey were those working in the veterinary vaccinology field globally, this included academics, those working in industry as well as policymakers and funders.

Respondents by Region

Responses were received from 42 countries with the majority responding from the UK (40%) **(Fig 1)**.

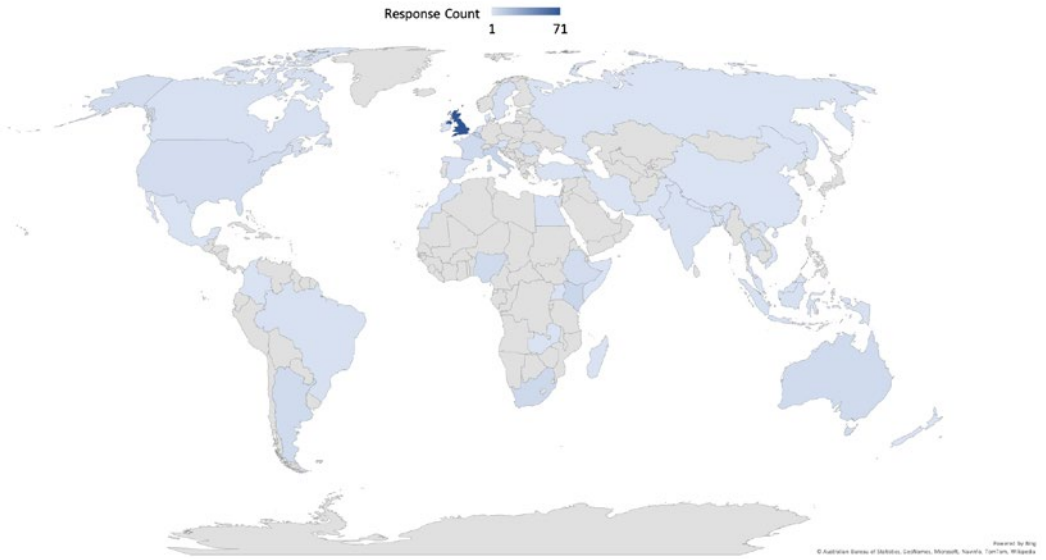

Figure 1 Respondents by region: Americas, Europe, Middle East, Asia, Australia and New Zealand, Africa. Total number of respondents: 122

Respondents by Sector

17. Responses were received from multiple sectors working on veterinary vaccinology **(Fig 2)**, with the majority of respondents working in academia (49%).

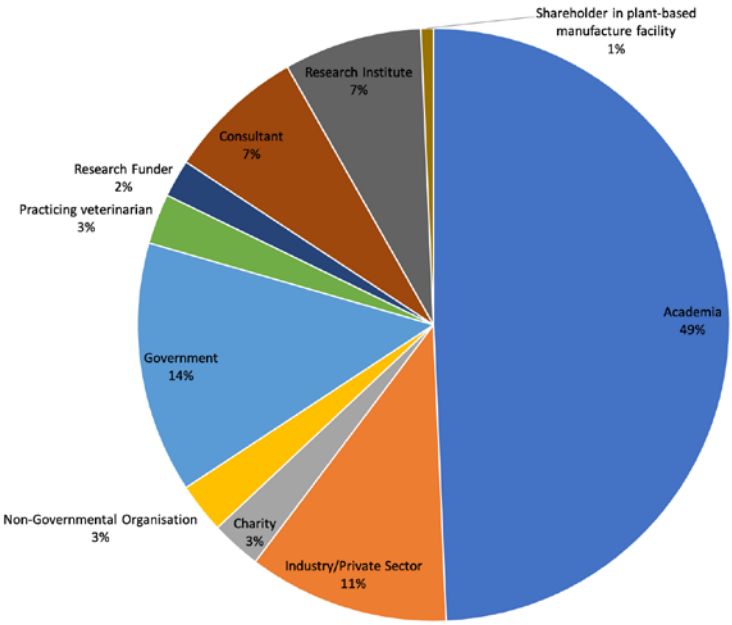

Figure 2 Respondents by sector, multiple options were allowed. Total number of respondents: 122, total number of options selected: 146. Percentages refer to the respondent numbers reporting specific sector divided by total number of options selected.

Respondents by Discipline

Respondents reported a broad range of disciplines and could select multiple options. **Vaccinology was the most common discipline (14%), followed by Immunology (13%), Virology (12%), Molecular Biology (7%) and Bacteriology (7%) (Fig 3)**.

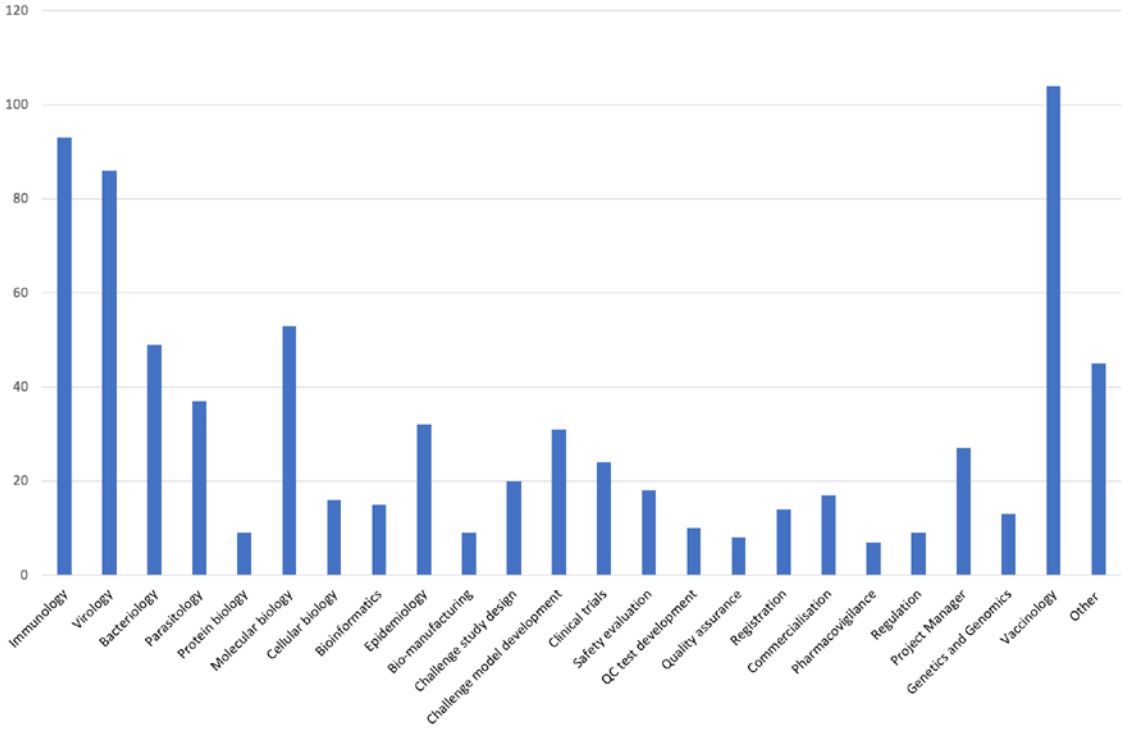

Figure 3 Respondents by discipline, multiple options were allowed. Total number of respondents: 122, total number of options selected: 746.

Respondents by Pathogen-type

The survey results demonstrated that **viruses are the most studied pathogen (41%) followed by bacteria (32%) and parasites (21%)**. The survey showed that little vaccine research is undertaken on prions or fungi **(Fig 4)**.

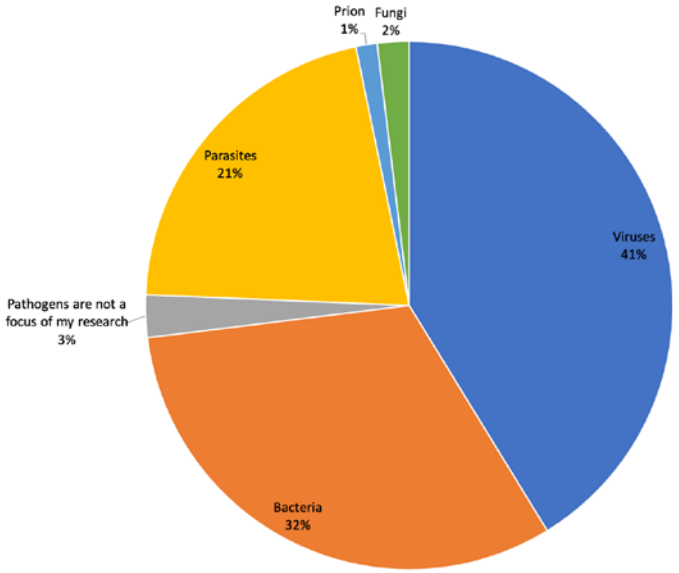

Figure 4 Respondents by pathogen-type, multiple options were allowed. Total number of respondents: 122, total number of options selected: 308. Percentages refer to the respondent numbers reporting pathogen divided by the total number of options selected.

Respondents by Host species type

Respondents reported working on all major animal species with **focus on large ruminants (87%), swine (59%), poultry (59%) and small ruminants (59%) (Fig 5)**. Focus on aquaculture, wild animals, and humans in relation to zoonoses were also reported as species of interest.

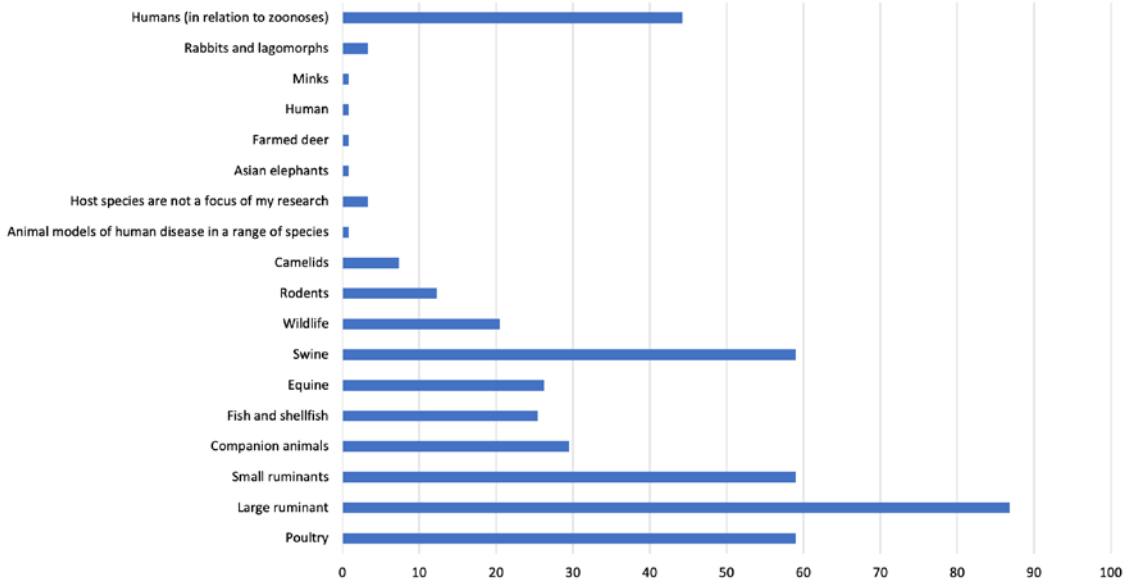

Figure 5 Respondents by Host species type, multiple options were allowed. Total number of respondents: 122, total number of options selected: 537.

Respondents by Geographic Region of Disease Focus

Veterinary vaccine research conducted by respondents focussed on diseases relevant to Europe (including Russia) (49%) followed by Africa (45%) the UK (41%) and Asia (31%) **(Fig 6)**.

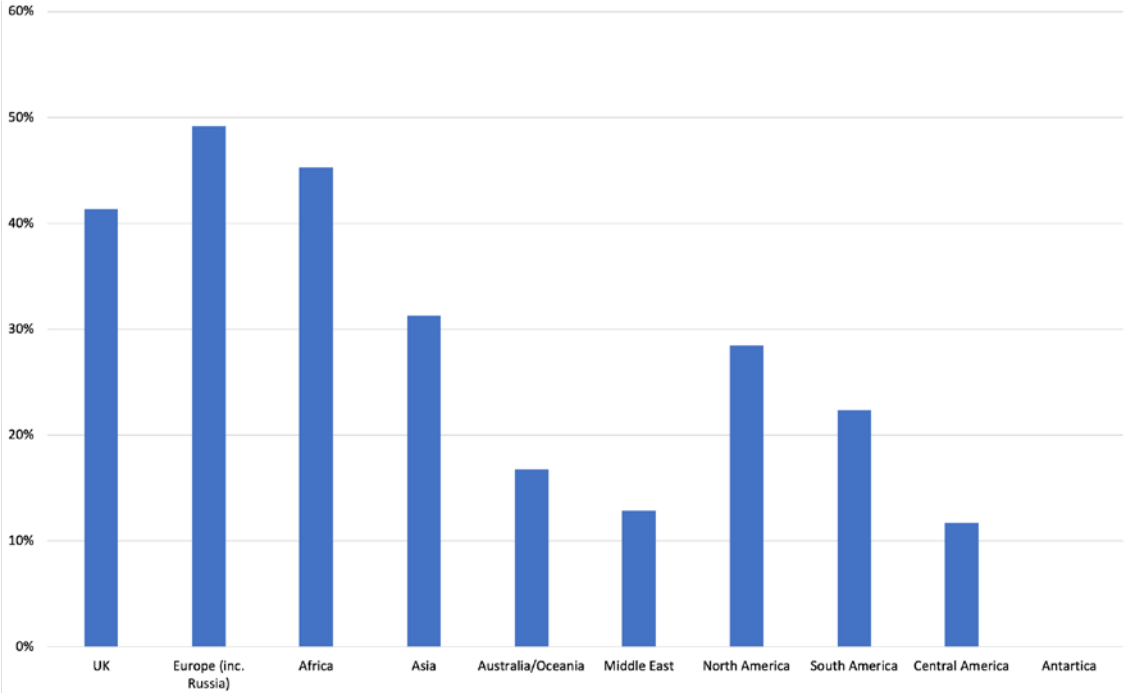

Figure 6 Respondents by geographical region of disease focus, multiple options were allowed. Total number of respondents: 122, total number of options selected: 464. Percentages refer to the respondent numbers.

Key Conclusions:

- 122 responses were received from 42 countries.
- 49% respondents were academic with a small number of responses received from industry, charity, and clinicians.
- The top five disciplines reported by respondents were vaccinology, immunology, virology, molecular biology, and bacteriology.
- Viruses were the most common pathogen studied by survey respondents followed by bacteria and parasites.
- Large ruminants were the most common host species studied, followed by swine, poultry, and small ruminants within the survey.
- Research is mainly focused on diseases which are prevalent in Europe, Africa, Asia, and the UK.

Part 2: Research and Innovations for Veterinary Vaccines

Part 2 of the survey focussed on identifying research and innovation goals within nine different themes of veterinary vaccinology research, development, and innovation. Respondents were asked to rate the importance of research and development gaps within different fields of veterinary vaccinology identified by the BBSRC Veterinary Vaccinology working group and highlight any additional gaps.

Immune Response to Vaccines

The first theme asked about the importance of defined research goals associated with immune responses to vaccines, respondents agreed with the importance of all identified goals **(Fig 7)** with the following being high priority:

- Understanding the **duration of immunity** and need for boosting vaccine responses *(68.2% of respondents reported very important)*.
- Better understanding of **correlates of protection** *(68% of respondents reported very important).*
- **Standardised methods for measuring correlates of protection** *(60% of respondents reported very important)*.
- Knowledge of the role for **trained immune responses in contributing to protective immunit**y *(60% of respondents reported very important).*
- Understanding the **role of mucosal immunity** in infection and vaccine responsiveness *(58% of respondents reported very important).*

How important are the following research goals regarding protective immunity for vaccine research and innovation?

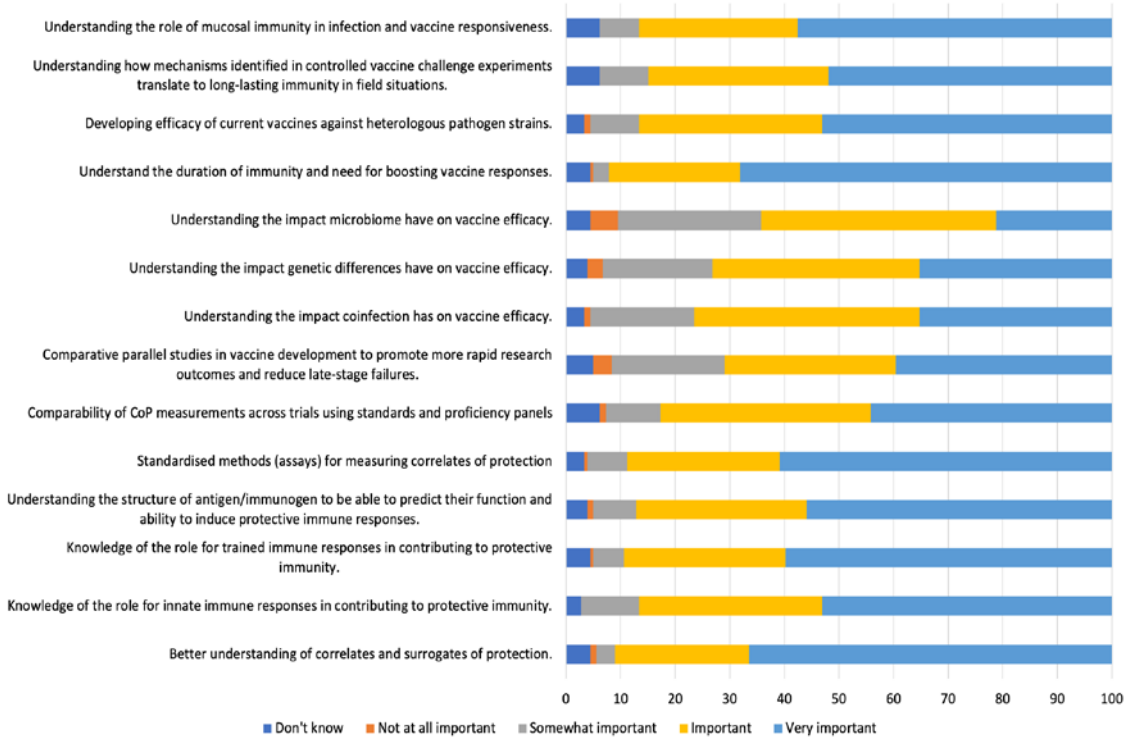

Figure 7 Importance of research goals for immune responses to veterinary vaccines

Respondents also highlighted additional research goals associated with immune response to veterinary vaccines as described below:

Models

- Develop appropriate **organ culture models** to assess immune/vaccine responses *in vitro* to ensure experimental studies are conducted in appropriate target species.
- **Models should be used for multiple organs of a species**, and responses should be assessed using multi-omics approaches to identify the best correlates and surrogates of protection.

Mucosal Immunity

- Understand how **mucosal immunity can be induced by non-living pathogens**.
- Novel platforms to deliver vaccines in the body require further research, especially mucosal vaccines to help improve efficacy.

Adaptive and Comparative Immune Response

- Understanding of **how to enhance adaptive immune responses** in different species.
- Understanding **immunity rather than infection responses**.
- Understanding species specific immune responses: all veterinary species have different cell lineages, different genes associated with immune response and even tissues. Basic immunological principals are not enough to understand the specific veterinary host species response.

Tools

- **Availability of reagents, for multiple species**, to effectively understand the immune responses to veterinary vaccines is a gap.

Key Conclusions

- Better understanding of:
  - immune response to pathogens and vaccines including duration of immunity
  - the role of mucosal, innate, and adaptive immunity
- Understanding the impact of genetics, microbiome etc. on immune and vaccine responsiveness.
- Defining and developing standardised methods for measuring correlates and surrogates of protection.
- Developing and using appropriate model systems for developing and testing vaccines.
- Developing and validating tools for studying immune response in all relevant veterinary species.

Immunological Tools

Immunological tools act as enablers which underpin vaccine research and innovation. Some tools and technologies can have generic application in multiple fields of research and innovation. Respondents agreed with the importance of all suggested research goals **(Fig 8)** with the following being high priority:

- **Developing and validating new immunological methods and technologies** that enable research in the natural host and the best model species *(68% of respondents reported very important).*
- **Development of *in vitro* tools for vaccine antigen efficacy testing and selection** – prior to animal challenge studies (e.g., tissue culture models) *(58% of respondents reported very important).*
- **Discovering and validating adjuvants** that generate an optimal immune response in veterinary species *(58% of respondents reported very important).*

How important are the following research goals regarding tools and technologies for vaccine research and innovation?

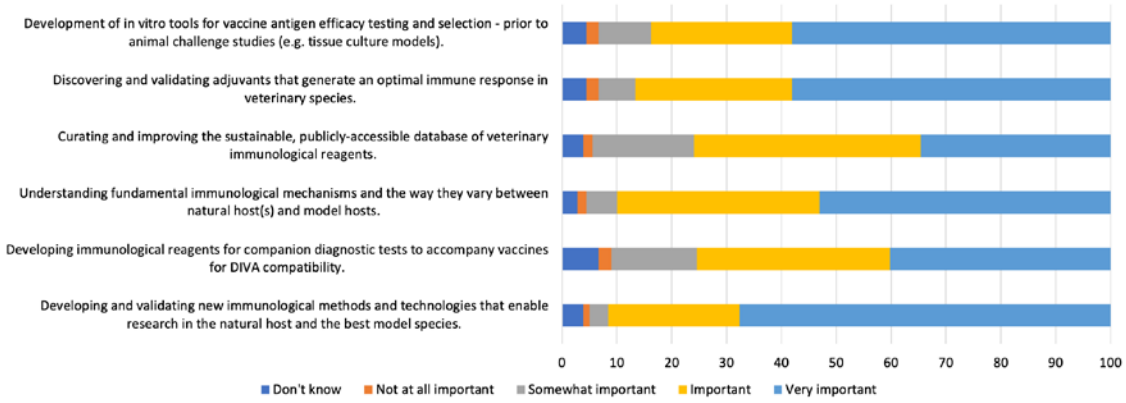

Figure 8 Importance of research goals for immunological tools for vaccine research and innovation.

Respondents also identified additional priorities associated with tools and technologies for vaccine research and innovation. These additional priorities have been separated into common themes and can be found below:

Tools

- Appreciation was given to the BBSRC funded Immunological Toolbox managed by the Pirbright Institute and the Roslin Institute. Comments stressed the need for further sustainable mechanisms to coordinate development, availability, distribution, and overarching databases that provide a whole community approach to development and exploitation of lab reagents, involving commercial partners and alleviating the historic altruistic development and sharing mechanisms for tools.
- Develop guidelines that address development and validation of assays including international assay standards.
- **Incorporation of in silico and predictive tools** for vaccine antigen efficacy testing and selection.
- **Modern tools need to combine bioinformatics with wet lab** to assist in the development of key tools for veterinary vaccine research.

Models

- Develop specific **animal cell lines**.
- Develop **tissue culture models** which translate to good correlates and surrogates of protection *in vivo* to reduce, replace, and refine the use of animals in research (3Rs).
- Develop knockout models to decipher different types of immune responses required for protection.

Comment from respondent "There are no equivalents to B or T cell knockout mice for livestock animals. Often profound differences in the repertoire and function of immune system components exist, such that findings do not always translate across species."

Partnership with Industry

- Translation into commercial products is often an end point of the immunological tool development work, it is important that the **private sector is brought in at the design stage of tool development**. Usually, industries are ahead of academia e.g., adjuvant development.

Technology Platforms

In this theme respondents were asked about the importance of defined research goals, including underpinning and unmet needs for technology platforms.

For the purpose of this survey - a technology is defined as a platform if an underlying, nearly identical mechanism, device, delivery vector or cell line is employed for multiple target vaccines. Such platforms include nucleic acid (RNA, DNA), viral vectors, whole virus (live attenuated, inactivated) and protein (protein subunit, virus-like-particle).

Respondents agreed with defined research goals **(Fig 9)** and highlighted the most important goal is to **establish a pipeline of platform technologies which can be used as 'plug and play' tools for rapid identification of target antigens, vectors, and delivery systems** (*60% of respondents reported very important).*

Survey responses confirmed **systematic evaluation of vaccine efficacy across species and pathogens** is important *(42% and 44% respondents reported respectively).* Comments emphasised that systematic evaluation should be standardised and that evaluation on the specific platform itself is also very important.

How important are the following research goals regarding vaccine platforms for vaccine research and innovation?

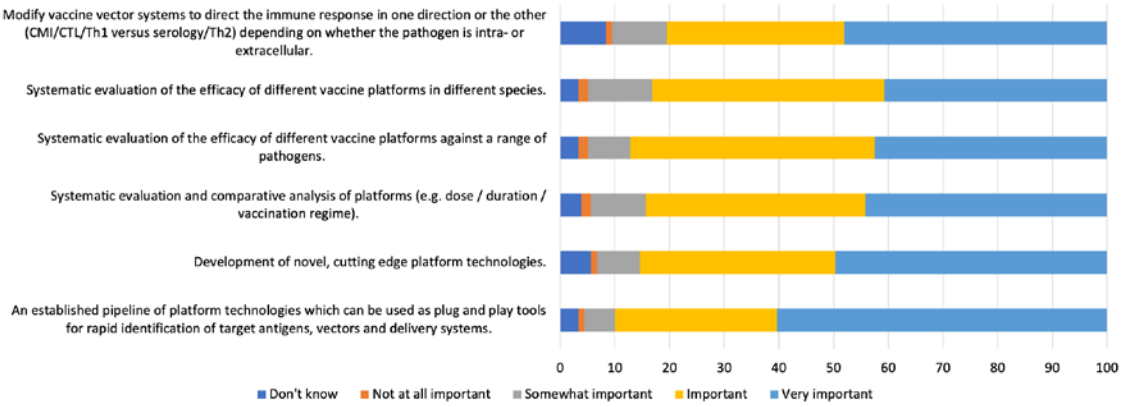

Figure 9 Importance of research goals regarding vaccine platforms for vaccine research and innovation.

Respondents highlighted additional gaps which are separated into common themes and can be found below:

Coordination

- **Capitalise on recent human vaccine platform development** and see how this could be applied in veterinary vaccines.
- Coordination of veterinary vaccinology research platform community to include vaccines for bacteria and parasites as well as viruses.
- Appetite and regulations in place for Genetically Modified (GM) vaccines.

Immune response

- **Understand how different platforms induce immune responses** for effective implementation.
- Develop novel or modify existing systems to elicit protective immunity at the mucosa, specifically eliciting Th17 responses.
- Have a range of technologies, particularly for rapid response to emerging diseases where prior knowledge will accelerate vaccine development to new diseases.
- Define the platforms that would be viable for the target market/populations, for example platforms that would be amenable to mass vaccination and *in ovo* vaccination. These **platforms need to be cost-effective and scalable as well as rapid to produce**. Alongside this, regulations need to be in place for novel platforms, especially as veterinary species are vaccinated with multiple vaccines at the same time.

i. Underpinning Needs for Technology Platforms

This section of the survey focussed on identifying underpinning needs for developing technology platforms. The survey respondents strongly supported the need for these vaccine technology platforms **(Fig 10)**.

Annex 3 provides additional comments on the underpinning needs. Respondents emphasised **the need for accessibility to use platform technologies**; trained personnel and infrastructure; working closely with human vaccinologists; and a general approach that researchers should have a **toolbox of multiple technologies** (multi-omics) that are used together.

Is there a need for:

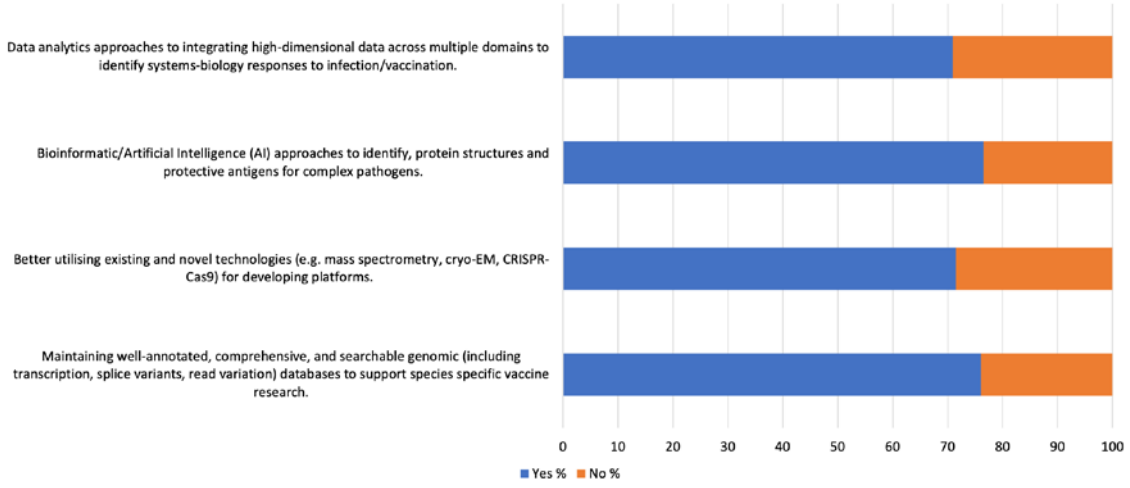

Figure 10 Respondents agreement on research needs for technology platforms for veterinary vaccines

ii. Unmet Needs for Technology Platforms

This section focussed on identifying unmet needs for technology platforms. The survey respondents strongly agreed that these statements remain unmet needs for vaccine technology platforms **(Fig 11).**

Annex 4 provides additional observations made by respondents on the unmet needs. A brief summary is below:

- Developing rapidly deployable vaccine technology platforms for pathogens to combat Antimicrobial resistance (AMR): Along with developing these vaccine technology platforms, **fast-track licencing and the availability of these vaccine** is very important in tackling the AMR problem.
- Developing vaccine platform technology for complex pathogens (anti-parasitic vaccines, including those for large multicellular parasites): requires dedicated pipelines to coordinate research using artificial intelligence, predictions, protein arrays for the design of the vaccines through to testing multiple combinations of the vaccines in the host animal challenge studies to determine if they are effective. **Fundamental research to understand host immune interactions and protective immunity in such pathogens is needed along with genome sequences of pathogens**. Due to the complex nature of these pathogens, it is likely that a plethora of vaccine antigen targets, in their correct structure, will be needed to produce multiple antibody responses to control the disease.
- Developing vaccine technology platforms which can integrate multiple antigens in one vaccine**:** The ability to combine several different antigen types in the same formulation has the potential to change the field completely, supporting animal welfare and cost-effectiveness for farmers. However, the big unanswered question would be **under what variables are vaccines combined e.g., type of species, age, type of production**. The main research gaps include: expression systems, QC tools for monitoring the quality and quantity of each immunogen in the vaccine, assess any additive effects that follow combining of multiple antigens into one vaccine and effect this may have compared to vaccines which target one pathogen type and whether there may be any antigenic competition/ interference if targeting multiple pathogens of the same type.

Comment from respondent “One response noted that the diagnostic test does not necessarily need to be an enzyme-linked immunosorbent assay (ELISA), but highly sensitive and specific point-of-care alternatives are also welcome.”

- Developing vaccine technology platforms and accompanying ELISA tests for serological discrimination, which are DIVA compliant (Differentiating Infected from Vaccinated Animals): Vaccine and diagnostic development need to be run in parallel and there should be a built in DIVA process, this should be highlighted in target product profile of vaccine candidates.
- Developing vaccine technology platforms capable of delivering immunogens effectively across mucosal surfaces to give mucosal and systemic responses**:** A key research aim in this area is **ways to target antigen to key tissues and cell types associated with antigen presentation without mis-priming the immune system** and generating a sufficiently high and targeted immune response. **Support for research on oral vaccines particularly for aquaculture and poultry.**

Is there a need for:

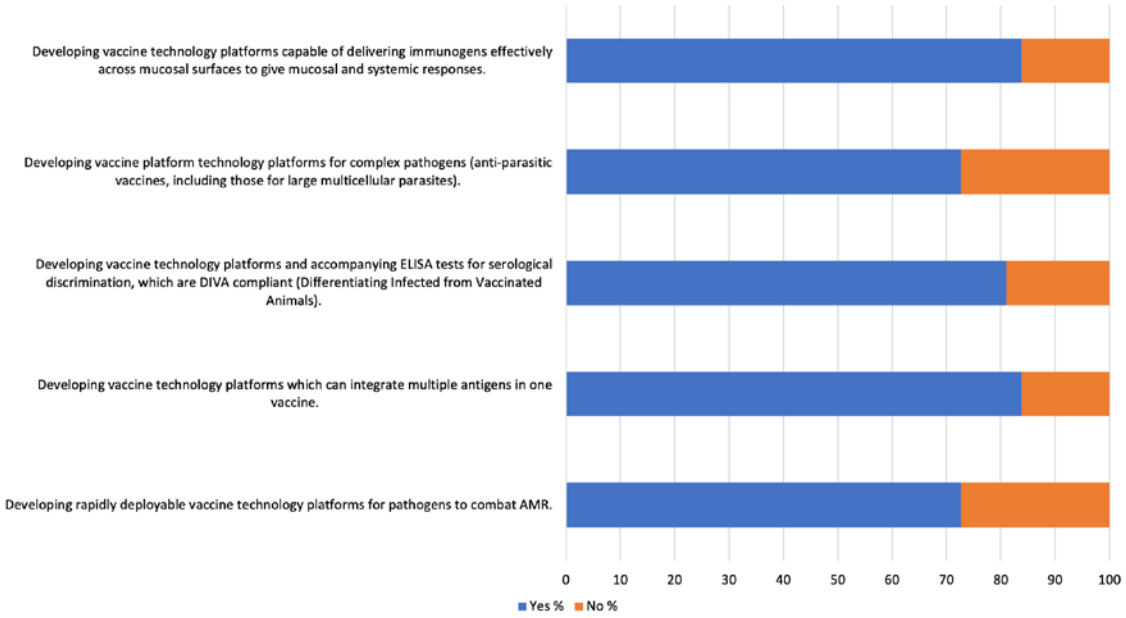

Figure 11 Respondents agreement to unmet needs for vaccine technology platforms

Key Conclusions

- The need to establish and characterise pipeline of 'plug and play' framework platforms that can be used for rapid identification of target antigens, vectors, and delivery systems for viral, bacterial, and parasitic pathogens.
- Platforms need to be cost-effective and scalable as well as rapid to produce.
- Regulations need to be in place for novel platforms, especially as veterinary species are vaccinated with multiple vaccines at the same time.
- Underpinning need for developing vaccine technologies which can integrate multiple antigens in one vaccine.
- Capitalise on human vaccine platform development with application to veterinary vaccines.
- Data analytics, bioinformatics and genomic databases underpin technology platform research and development
- Technologies needed specifically for:
  - Monoclonal antibodies from different species
  - Veterinary pathogen protein/peptide arrays
  - Investigating antigenic variability of parasites
  - Exploiting activity of neutralising antibodies to determine epitope structures
  - Understanding host-pathogen interactions and protective responses at site of infection.
  - Quality Control (QC) testing and antigen characterisation
  - Improving and designing vaccine vectors
  - Toolboxes for genome modification across species

Vaccine Design and Delivery

This section focussed on immunogen design which included questions on thermo-stabilisation, production and scale up, regulatory and delivery systems.

Respondents agreed that all defined vaccine design and delivery goals were considered very important **(Fig 12). Novel vaccines which are efficacious but economically suitable for large-scale production** was the most important goal identified (68% respondent*s reported very important)* followed by **strong public-private partnerships** *(59% respondents reported very important).*

How important are the following research goals for veterinary vaccine design and delivery?

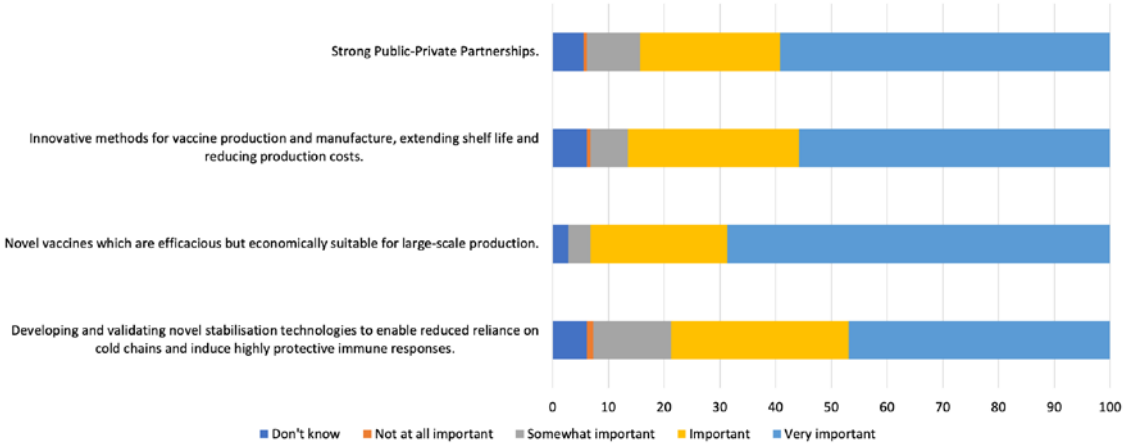

Figure 12 Importance of research goals for veterinary design and delivery

Key Conclusions

- Novel vaccines need to be efficacious and economically suitable for large-scale production.
- Designing new vaccines and delivery systems needs strong public-private partnership.

Vaccine Delivery Platforms

This section focussed on vaccine delivery platforms which included questions on current and novel platforms along with understanding the need for comparative efficacy assessment.

Respondents agreed with further research and innovation on developing novel delivery platforms with a strong focus oral, mucosal and nasal vaccine delivery systems **(Fig 13).**

Respondents highlighted the following novel delivery platforms for the future:

- Aerosols
- Tablet/caplet based as a cold chain free option
- Emulsions
- Immuno-stimulating complexes
- Edible: feed formulation, plant materials
- Immersion vaccines for fish
- Exosomes
- *In ovo* delivery platforms for poultry

- Intra-lymphatic (allergy vaccines)
- Nanotechnology including nanoencapsulation
- Nebulisation
- Needless intradermal application
- Patch technology

Is further research and innovation required for the following delivery mechanisms:

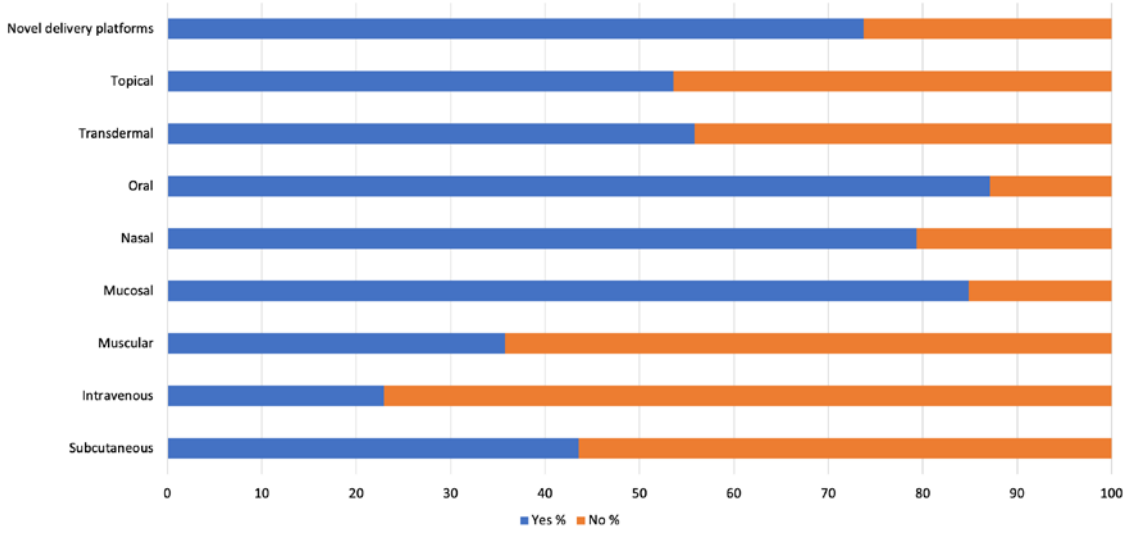

Figure 13 The need for research and innovation for delivery mechanisms

Comparative efficacy assessment of delivery platform technologies

81% of respondents agreed that there is a need for **comparative efficacy assessment of delivery platform technologies** as different delivery platforms may provide route and pathogen specific differences in protective efficacy. Understanding this requires cross-platform and cross-species comparative analyses.

Routes of administration could be critical to improve vaccine efficacy. Immune responses (cellular/humoral) could be stimulated differently by different delivery platforms. There is a need to evaluate the efficacy of vaccines in the field and be able to compare them.

Standardisation of efficacy assessment needs to be accounted for.

Respondents identified following research gaps:

- How oral vaccines translates into local mucosal immune responses at the site of pathogen entry (for respiratory viruses often nasal)?
- How a specific antigen, at a given dose, primes responses of different types when given to age-matched animals *via* different routes. Immunity at the required site and time are key for many pathogens?
- Why mucosal delivered vaccines rarely go to challenge/clinical phases despite promising results in preclinical studies?
- The pros and cons of different delivery routes for the same vaccine.
- The efficacy and safety at the point of vaccination compared to systemic

Key Conclusions

- Need for novel delivery platforms, particularly mucosal, nasal, and oral delivery platforms.
- Comparative efficacy assessment of delivery platform technologies is needed to understand how route and pathogen specific differences in protective efficacy arises from different delivery platforms.

Vaccine Safety, Equity, and Uptake

This section focuses on questions relating to vaccine safety, equity, and uptake along with identifying bottlenecks and barriers to accelerating vaccine development and getting products to market sooner.

71.3% of respondents agreed that **suitable use of animal models** (e.g., target species) to assess vaccine safety is a key unmet need, too often mice are used which does not provide informative data on immune responses **(Fig 14).**

Survey responses also confirmed the need for **better alignment between veterinary and human vaccine research and development (***69.5% agreed*) with comments stressing a lot can be learnt from both fields in terms of vaccine design. Synergies between human and animal vaccines need to be developed further. More direct One Health grants are needed to prove categorically that One Health can work as a concept.

How important are the following research and development goals regarding vaccine safety, equity and uptake for vaccine research and innovation?

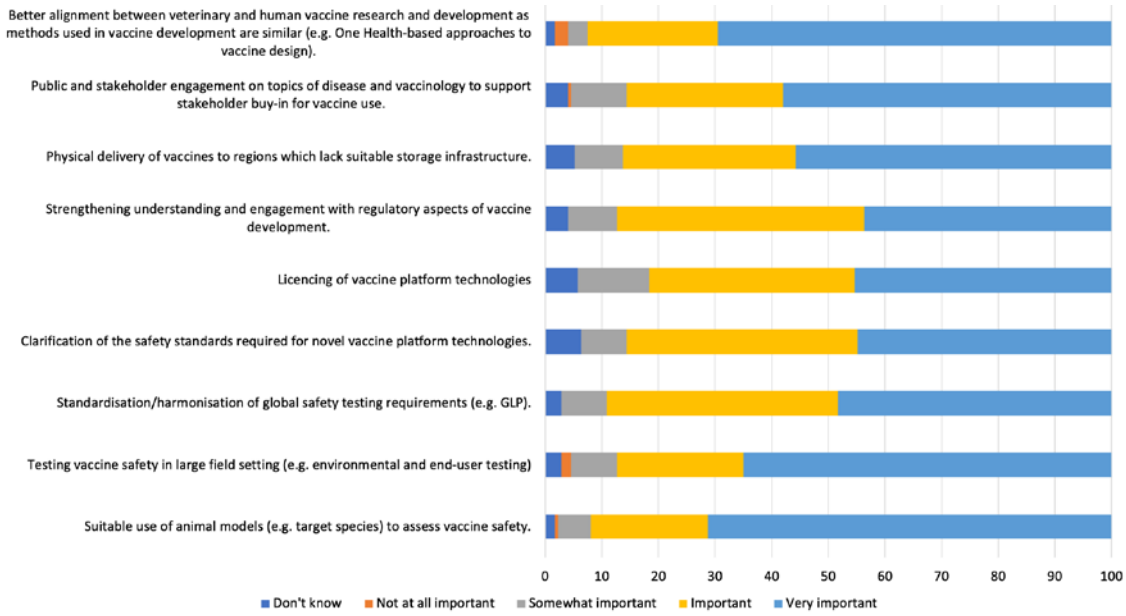

Figure 14 Importance of research and development goals regarding vaccine safety, equity and uptake for vaccine research and innovation

In addition, respondents made the following comments:

Vaccine hesitancy and confidence

- Over the last year issues of vaccine hesitancy and vaccine confidence have emerged as COVID-19 vaccines have been developed at pace. Support is needed to empower researchers as ambassadors, to provide guidance and explanations on the nature and benefits of vaccines to improve vaccine confidence and reduce hesitancy.

Coordination

- Facilitating discussions between researchers, industry and regulators is needed to provide forums to understand and discuss what is needed for registration and commercialisation; producing harmonised testing requirements; safety standards and large-scale testing, with an understanding that there is a marked difference between vaccines given to different species.

Vaccine efficacy and effectiveness

- Differentiating efficacy from effectiveness in all aspects of vaccine discussion.

Market size

- A barrier for development of veterinary vaccines is market size, particularly for zoonoses.

Comment from respondent: "More consideration should be given to public health benefits and how these can be valued."

Bottlenecks/barriers within current pipelines to accelerate vaccine development to get products to market sooner:

Regulation

- Regulation issues are the leading barrier to accelerating vaccine development. The need for collaborations with regulators, researchers, small and medium sized enterprises (SMEs) and industry.
- **Researchers require clearer understanding of the regional and global regulatory landscape, mechanisms and processes including registration**.
- **Regulation process should be harmonised across species, platforms and regions** including consistent models of assessment of immune and protective responses.
- Registering GM vaccines is still a key area that needs development including understanding the regional needs for evidence and what is required for approvals.

Economics

- Understanding of commercial drive, profit margins and uncertainty of market uptake of a significant number of veterinary vaccines specifically those affecting livestock keepers in Low Middle Income Countries (LMICs) is a significant barrier to veterinary vaccine development. Academia needs better understanding of these issues and **consideration of target product profile** in early stages of development.

Commercial involvement is needed at the outset of vaccine research:

- There should be models where industry can advise or have a stake in the research at the earliest opportunity to provide the expertise on development and translation feasibility.
- Academia needs better understanding and consideration of target product profile in early stages of development. It was suggested that the academic curriculum should include industrial aspects e.g., target product profile definition, product development documents, manufacturing, QC/QA, registration, market scoping, Net Present Values (NPVs) & Return of Investments (ROIs) and commercialisation principles.
- There is a need for more upscaling of vaccine production to Good Medical Practice (GMP) standard which is currently lacking in the veterinary field and leads to poor alignment with human health.

Field testing

- Support is required **to test vaccines in field settings**, specifically in the context of where these diseases are found. Large animal testing facilities are still limited globally (e.g., facilities to do vaccine trials on horses).

Key Conclusions

- Suitable use and access to animal models to assess safety, including in field settings.
- A One Health approach aligning veterinary and human vaccine research and development
- Coordinated response and knowledge exchange between academia, regulators, and industry to understand vaccine development landscape and requirements across species, platforms, and regions.
- Barriers to accelerate current vaccine development include: Regulation, Market size, field testing facilities and large animal testing facility

Epidemiology and Economics

This section focuses on veterinary vaccine epidemiology and economics which included questions on epidemiology, transmission and modelling, translation, economics, and social acceptance.

92.3% of respondents agreed with the importance of being able to understand the **impact vaccines have through epidemiological post-introduction evaluation studies and the socio-economic impacts of veterinary vaccine interventions** at different levels (sector, national, global) *(85.7% agreed).* As reported elsewhere in the survey assessing **the need for/feasibility of vaccines in the field context** (including societal need) was considered very important by respondents *(51.2% agreed)* (**Fig 15**).

Survey respondent made following additional comments:

- The need to improve infrastructure to **support post-marketing evaluation of vaccine effectiveness** (inclusive of establishing study design and reporting practices such that study findings will contribute optimally to synthesis of evidence (e.g., living systematic reviews).
- **Undertaking cost: benefit analysis** is critical for manufacturers and end users, producing financing models to understand market demand and service delivery contextual (e.g., LMICs).

In addition, respondents highlighted needs to understand the impact vaccines have on:

- pathogen evolution
- genetic diversity on herd immunity
- in-host transmission dynamics including better understanding of carriership, latency and super-shedding is important in epidemiological and transmission dynamics models
- combined impacts of biosecurity and vaccine use on disease transmission

How important are the following research and development goals regarding epidemiology and economics for vaccine research and innovation?

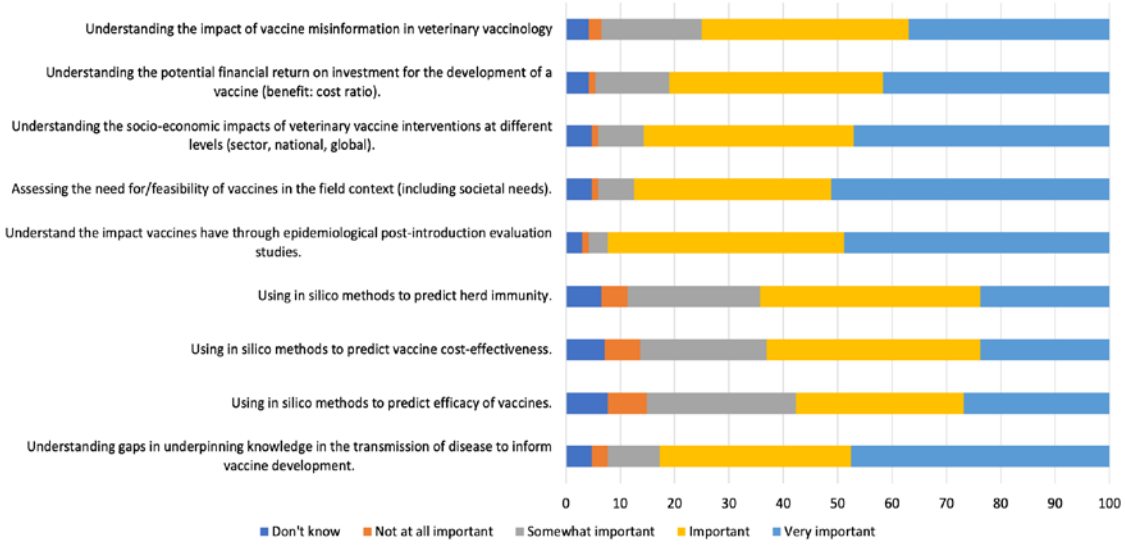

Figure 15 Importance of research goals regarding epidemiology and economics for vaccine research and innovation

Key Conclusions

- Need for epidemiological post-introduction evaluation studies in the field and the socio-economic impacts of veterinary vaccine interventions at different levels.
- Detailed cost-benefit analysis.
- Assessing the need for/feasibility of vaccines in the field context.
- Need for improved infrastructure to support post-marketing evaluation of vaccine effectiveness.
- Current research gaps include the impact vaccines have on:
  - pathogen evolution
  - genetic diversity on herd immunity
  - in-host transmission dynamics
  - combined impacts biosecurity and vaccine use on transmission dynamics

Capability and Capacity

The final two themes focus on underpinning needs to support veterinary vaccinology research and innovation. The first assesses capability and capacity of the veterinary vaccinology field which also includes questions on infrastructure.

As reported elsewhere in the survey, **strengthening knowledge exchange and commercialisation between academia and industry was considered of high importance** by the majority of respondents **(***94.6% respondents reported important and very important)* (**Fig 16**). Likewise **maintaining capacity in veterinary vaccine research across the entire vaccinology research and development career track (***91% respondents reported important and very important***)** and **strengthening emergency research capacity in veterinary clinical practice for emerging epidemic and epizootic diseases** were also reported as a priority **(***91% respondents reported important and very important***)**.

How important are the following research goals regarding capability and capacity to veterinary vaccinology?

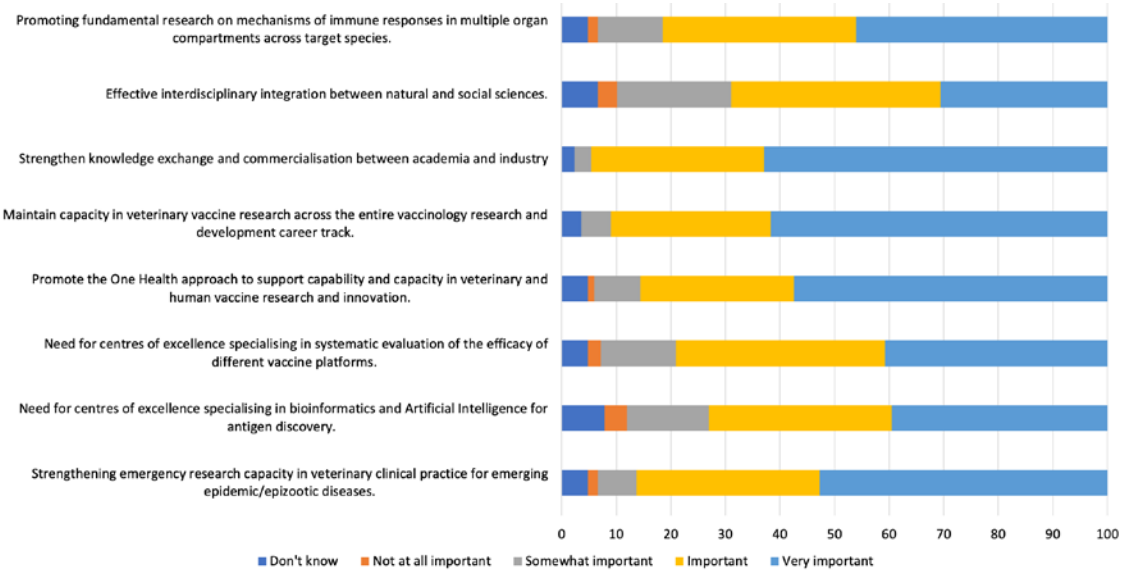

Figure 16 Importance of research goals regarding capability and capacity to veterinary vaccinology.

Respondents also identified additional gaps associated with capability and capacity within the veterinary vaccinology field:

- Establishment of a veterinary vaccine equivalence, or inclusion of veterinary vaccine research as a specialty area within the Cochrane Collaboration (Evidence Based Medicine) to promote methods and use of research synthesis. Synthesizing evidence from the field, particularly to highlight gaps in understanding or unnecessary 'waste' of research (i.e., due to unknown risk of bias, incomplete reporting, otherwise avoidable heterogeneity in study design and reporting).
- **Development of a national database** for pathogen, disease, and vaccination surveillance, and accompanying statistical and mathematical modelling tools to assess vaccine efficiency (in the field) and potential impact on pathogen spread and evolution.
- **Exploitation of AI/Systems biology and knowledge-sharing** is crucial for accelerated vaccine development and uptake.
- BBSRC-sponsored Institutes and selected veterinary schools with the requisite infrastructure and critical mass have a critical role to play in addressing this vulnerable capacity.

Comment from respondent: "Treatment of endemic diseases is a major cause or antibiotic metaphylaxis and treatment. Responsibility for endemic disease has historically fallen at the interfaces of BBSRC, DEFRA and industry, with gaps as a consequence. Only a handful of UK researchers work on mastitis vaccines for example, which should be viewed in the context of a £200M/annum problem."

Key Conclusions

- Maintaining capacity in veterinary vaccine research across the entire vaccinology research and development career track.
- Strengthening emergency research capacity in veterinary clinical practice for emerging epidemic and epizootic diseases.
- Strengthening knowledge exchange and commercialisation between academia and industry.
- One Health approach to support capability across veterinary and human vaccinology research and innovation.

Infrastructure

All the gaps identified for infrastructure related to veterinary vaccinology were identified as being important issues that need to be addressed (**Fig 17**). As reported previously in the survey analysis, **support for containment facilities for challenge studies to evaluate vaccine efficacy for pathogens including zoonoses** (*respondents reported 73.3% very important*) **along with support for large scale vaccine trials in animals** were considered of high importance (*respondents reported 61.8% very important*). Similarly **manufacturing capability** to be able to produce vaccines including those that can rapidly respond to pandemic threats were also of high importance (*respondents reported 67.9% very important*).

Respondents made the following comments:

- There is a real need for manufacturing facilities in veterinary and human vaccine development as has been shown over the COVID-19 pandemic. It was suggested that **infrastructure investment be made in multiple sites** within the UK for resilience and safety and to support vaccine research in endemic and epidemic diseases.
- Large scale **vaccine trials should be conducted in collaboration with industry**.
- There is a particular **bottleneck for containment facilities for research on notifiable pathogens of fish and shellfish**.

Comment from respondent: "In the UK there are fantastic facilities available (PHE, DSTL, University of Liverpool, DEFRA) however these are not always easy to access."

How important are the following objectives regarding infrastructure to veterinary vaccinology?

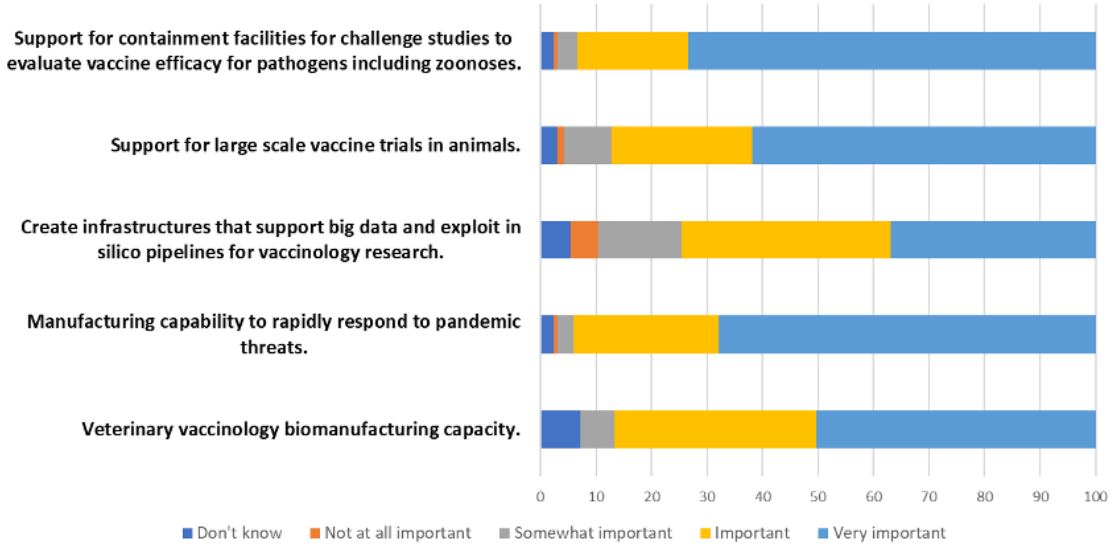

Figure 17 Importance of objectives regarding infrastructure to veterinary vaccinology

Key Conclusions

- Support for containment facilities for challenge studies to evaluate vaccine efficacy for pathogens including aquaculture and zoonoses.
- Vaccine manufacturing capability to rapidly respond to pandemic threats.
- Need for Veterinary vaccinology biomanufacturing capacity.
- Bottleneck for containment facilities for notifiable diseases of fish and shellfish

Skills and Training

Skills are training questions were asked within each of the seven research theme sections in the survey. For the purposes of this report the skills and training section has been grouped into a separate section due to similar reporting across themes.

Respondents were asked: *where are the skills and training gaps in the research area?* The options given included: Graduate, Postgraduate, Postdoctoral and Fellowship. Skills and training gaps were reported equally across the career track.

Respondents were asked: *what are the main issues for skills and training in the research area?* The options given were lack of retention, recruitment challenges, lack of workforce. In most research themes, the three issues were given equal weighting whilst **lack of workforce was reported as a bigger issue** (*43% of respondents reported lack of workforce*) within epidemiology and economics of veterinary vaccinology.

Respondents identified additional needs associated with skills and training within the veterinary vaccinology field:

Training

- **Training and retaining expertise in *in vivo* work** with target hosts.
- **Specialised training** in vaccinology is needed including topics relating to immune responses to vaccines, differentiated by the type of response needed (mucosal, systemic, antibody mediated, etc).
- More training including courses that combine understanding of development of vaccines along with immunological tools as well as more specialised areas including cellular aspects of immunological tools.

Workforce

- Incentives are needed to attract and keep skilled staff working on immunological tools and toolboxes in position. Reagent/tool development is not seen as a viable focus of career for many people.
- As the field of vaccine technology platform is rapidly evolving due to the recent COVID-19 pandemic, **more expertise will be needed for example joint roles between research and industry**. The workforce will also require more up to date skills and training in the technologies as well as accessibility to these technologies.

Comment from respondent: "It is a challenge to get PhD students in particular working on the sort of interdisciplinary projects that are needed for technology platforms in this area. There would be a lot of value in having a multi-student project supported by one or two postdoctoral researchers, but these are difficult to get funded in a coordinated way."

Resources

- The lack of resources and consumables for lab work for PhD students and early career researchers.

Part 3: Overarching Veterinary Vaccine Needs

The final section of the survey asked respondents to report on overarching veterinary vaccine needs in terms of research, capacity, discipline gaps and recommendations to be made to animal health funders.

Research gaps

Respondents were asked to identify any other additional gaps in veterinary vaccinology research. The major gaps identified were:

Immune Response to Vaccines

Understanding fundamental immunology remains a priority: the nature of protective immunity; understanding host-pathogen interactions; species specific and site-specific immunology; tools and tool evaluation to study the immune response.

Understanding of correlates and surrogates of protection remains a large challenge for many veterinary pathogens: the need for advanced technologies as an enabler to be able to detect correlates and surrogates of protection.

Mucosal vaccinology: site specific, protective immunity, ability to target vaccine delivery to these sites.

Vaccine Technology Platforms

Developing novel vaccine technology platforms with the ability to be adapted for different pathogens; undertake field trials; reduce reliance on cold chain.

Capability and Capacity

Capacity for large scale vaccine field studies: Conducting vaccination studies in target species under field conditions and understanding the factors in the field that affect vaccine efficacy. Vaccine failures in the field are poorly understood. Monitoring real field efficacy including post-authorisation. The need to collaboratively work with personnel and institutes in the study areas (for example LMICs).

Basic and specific training for graduates and postgraduates which included fundamental vaccinology principles; in silico methods; training in target species; training for fish and shellfish immunologists and epidemiologists; product use, diagnostics, and manufacturing

Translation of vaccine research to commercialisation: specific gaps identified were understanding the routes to market; knowledge in upscaling manufacturing; regulatory compliance, involvement of industry at early stages; vaccine testing pipelines, vaccine production; manufacturing facilities for commercialisation and access to them; vaccine evaluation post licensure; the technology commercialisation process

Other notably priority gaps identified were early collaborations between academia, industry, and regulators, recruiting graduates into veterinary vaccinology and researcher retention.

International perspective

Throughout the survey responses emphasised the need to work with and support research and capacity building in the countries where diseases are most prevalent and cause the most impact.

Research gaps

Veterinary vaccines and associated tests need to be tested in the right context early on: different genetic pools of cattle/fish/pigs/chickens are found in different regions of the world which may have a significant effect on vaccine efficacy.

Vaccines need to be tested in contextual field settings where the disease is present.

Better understanding of barriers to veterinary vaccine uptake and access in LMICs.

Making a business case for diseases affecting livestock keepers in LMICs, especially epizootic diseases.

Supporting IP and production of vaccines in LMICs.

Support awareness within local authorities in LMICs to budget for and allocate sufficient funds to science and technology, more so vaccinology in general.

Develop financing models, market demand and service delivery in LMICs.

Capacity

Direct interactions and collaborations are needed with LMIC institutes and governments to coordinate research in the field.

Sustained long-term funding on veterinary vaccinology research in multiple geographies is a major issue. The human vaccinology field in LMICs benefits from long-term investment in centres of excellence by funders, meaning there is always a large pool of early-to late-postdoc level personnel for vaccine R&D programmes. For instance, many vets in Kenya find themselves pursuing human research (which is good) in centres such as the Kenya Medical Research Institute (KEMRI). Sustained long-term funding to support capacity development would help address the current skills and training gaps.

Affordable tools (vaccines and diagnostics) that could be used in LMIC developing countries.

Research on endemic neglected diseases (LMIC focus).

Retention of qualified personnel in veterinary vaccinology is a key capacity gap in LMICs.

The need for GMP production in LMICs.

Supporting, knowledge exchange and vaccine development in LMICs.

Key Recommendations for Funders

Fund basic research on understanding immunology and host-pathogen interactions.

Invest in basic research on novel vaccine technology platforms.

Multi-disciplinary groups:

- Bridge gaps between regulatory bodies, academia, and industry so that innovative ideas for vaccine development can progress smoothly from bench to animal testing to large scale production.
- **Promote a One Health working** with human vaccinology: focus on production of antigens that can be used as reagents for detection / characterisations, and vaccines, and which could be used as human vaccines too. Leverage One Health approaches in vaccine development to benefit both animal and human health and in doing so reduce on working in 'silos' mentality for those involved in animal and human vaccine development

Provide training and development in an environment which develops vaccines through to commercialisation.

Foster international collaborations between researchers (western/northern hemisphere) and stakeholders/growers (eastern/southern) are essential to ensure that the development of research knowledge has applicability in the context of low-income farming countries.

Annex 1 Veterinary Vaccinology Landscape Survey

Veterinary Vaccinology landscape Survey

UKRI- BBSRC on behalf of the veterinary vaccinology research funders and programme owners are consulting the community (including academic, funders, industrial, and other key stakeholders) on the current knowledge, research gaps and barriers within the veterinary vaccinology field as well as identifying future research and innovation priorities to inform a five year Veterinary Vaccinology Strategy 2021-2026.

This survey has three parts: Part 1 Introductory questions, Part 2 Research and Innovation and Part 3 Overarching Vaccinology needs. There are 47 questions in total however, you may not need to answer them all depending on your situation and background. It will take approximately 30 minutes to complete. We thank you in advance for your input.

All information submitted to UKRI-BBSRC will be treated in confidence. Nonattributable comments from the survey may be used in subsequent activities e.g., included in internal and external publications on this topic. If you have any questions about this survey, or experience any problems filling it out, please contact: **bfh@bbsrc.ukri.org**

We would also welcome joint Institution response.

PART 1: Introductory questions

In this first section you will be asked to provide general information about your role within the veterinary vaccinology field to provide context.

UKRI-BBSRC carries out the processing of personal data in accordance with the General Data Protection Regulation (GDPR). The information you provide as part of this survey will only be used by UKRI-BBSRC and its partner, Survey Monkey, for the purpose of informing the review of this area. If you decide to include your contact details, we would like to use these to:

- Provide updates on the review, including requesting further community input and provision of a copy of the final report.

The personal data you have provided will be collated and made non-attributable prior to analysis. Information gathered will be used by UKRI-BBSRC, alongside data gathered through other exercises, to provide a dialogue that facilitates strategy development.

The personal data provided will be retained on our systems for as long as is required to carry out processing for the purposes outlined above. By providing your information you are consenting to its use as detailed above. You can access a copy of the UKRI Data Protection Policy at: **https://www.ukri.org/files/termsconditions/ukri-data-protection-policy-pdf/**

1. Would you be willing to be contacted again for these purposes?

- Yes, I would be happy to be contacted again for these purposes, including to provide additional information.
- Yes, I would be happy to be contacted again, but only to receive a copy of the final report
- No, I do not wish to be contacted further.

2. Please provide your details below

- First Name
- Last Name
- Organisation
- Email Address
- Country

3. Please state if providing responses as an individual or as an institution.

4. Which of these options best describes your workplace?

- Academia
- Industry/Private Sector
- Charity
- Non-Governmental Organisation
- Government
- Practicing veterinarian
- Research Funder
- Other (please specify)

5. What is your discipline (Multiple options allowed)?

- Immunology
- Virology
- Bacteriology
- Parasitology
- Mycology
- Protein biology
- Molecular biology
- Structural biology
- Cellular biology
- Systems biology
- Bioinformatics
- Economics
- Epidemiology
- Formulation technology
- Genetics and Genomics
- Bio-manufacturing
- Challenge study design
- Challenge model development
- Clinical trials
- Safety evaluation
- QC test development
- Quality assurance
- Registration
- Commercialisation
- Deployment
- Ethics
- Pharmacovigilance
- Regulation
- Project Manager
- Policymaker
- Other (please specify)

6. Which pathogen(s) is/are the main focus of your research and innovation investigation? (Multiple options allowed)

- Viruses
- Bacteria
- Parasites
- Prions
- Fungi
- Others
- Pathogens are not a focus of my research

7. Which host species are the primary focus of your research and innovation investigation? (Multiple options allowed)

- Poultry
- Large ruminants
- Small ruminants
- Companion animals
- Fish and shellfish
- Equine
- Swine
- Wildlife
- Rodents
- Camelids
- Humans (in relation to zoonoses)
- Other, please specify
- Host species are not a focus of my research

8. In which geographical region(s) does your research have the most impact? (Multiple options allowed)

- UK
- Europe (inc. Russia)
- Africa
- Asia
- Australia/Oceania
- Middle East
- North America
- South America
- Central America
- Antarctica

PART 2: Research and Innovations for Veterinary Vaccinology

This second section contains questions on how important research and innovations goals are within different themes of veterinary vaccinology research, development, and innovation. The answers to these questions will help us understand the importance of these goals within the veterinary community and guide us in developing a five-year veterinary vaccinology strategy.

Questions span vaccinology research, development and innovation as well as include questions focused on capacity and capability, skills and training and infrastructure.

The following section will focus on eight themes in veterinary vaccinology research, development, and innovation:

- Immune response to vaccines
- Immunological Tools
- Technology Platforms
- Vaccine Safety
- Vaccine Design and Delivery
- Epidemiology and Economics
- Capability and Capacity
- Infrastructure
- Overarching vaccinology needs

Immune response to vaccines

9. On a scale of 1-5 How important are the following research goals regarding protective immunity for vaccine research and innovation?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Better understanding of correlates and surrogates of protection.
- Knowledge of the role for innate immune responses in contributing to protective immunity.
- Knowledge of the role for trained immune responses in contributing to protective immunity.
- Understanding the structure of antigen/immunogen to be able to predict their function and their ability to induce protective immune responses.
- Standardised methods for measuring correlates of protection
- Establish comparability of correlates of protection measurements across trials using standards and proficiency panels.
- Comparative parallel studies in vaccine development (e.g., multiple animal models), rather than relying on single target species to promote more rapid research outcomes and reduce late-stage failures.
- Understanding the impact coinfection has on vaccine efficacy.
- Understanding the impact genetic differences have on vaccine efficacy.
- Understanding the impact microbiome have on vaccine efficacy.

- Understand the duration of immunity and need for boosting vaccine responses.
- Developing efficacy of current vaccines against heterologous pathogen strains (e.g., FMDV).
- Understanding how mechanisms identified in controlled vaccine-challenge experiments translate to long-lasting immunity against pathogens (e.g., parasitic) in field situations.
- Understanding the role of mucosal immunity in infection and vaccine responsiveness.

If you would like to raise other areas of interest or objectives regarding topics relating to protective immunity, please use the text box.

10. Does your work focus on the Immune response

- Yes
- No

If your work focuses on protective immunity:

11. Where are the skills and training gaps in the area of immune response to vaccines?

- Graduate level
- Postgraduate level (PhD)
- Postdoctoral level
- Fellowships
- Other, please specify

12. What are the main issues?

- Recruitment challenges
- Lack of workforce
- Lack of retention
- Other, please specify

13. If you would like to make any further comment on skills and training needs and challenges in protective immunity please use the text box.

Immunological Tools

Tools and technologies act as enablers which underpin vaccine research and innovation. Some tools and technologies can have generic application in multiple fields of research and innovation. This section focuses on immunological reagents, adjuvants, and vectors.

14. On a scale of 1-5 How important are the following research goals regarding tools and technologies for vaccine research and innovation?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Developing and validating new immunological methods and technologies that enable research in the natural host and the best model species.
- Developing immunological reagents for companion diagnostic tests to accompany vaccines for DIVA compatibility.
- Understanding fundamental immunological mechanisms and the way they vary between natural host(s) and model hosts.
- Curating and improving the sustainable, publicly accessible database of veterinary immunological reagents.
- Discovering and validating adjuvants that generate an optimal immune response in veterinary species.
- Development of *in vitro* tools for vaccine antigen efficacy testing and selection – prior to animal challenge studies (e.g., tissue culture models)

If you would like to raise other areas of interest or objectives regarding topics relating to immunological tools please use the text box.

15. Does your work focus on Immunological Tools?

- Yes
- No

If your work focuses on immunological tools:

16. Where are the skills and training gaps in the area of immunological tools?

- Graduate level
- Postgraduate level (PhD)
- Postdoctoral level
- Fellowships
- Other, please specify

17. What are the main issues?

- Recruitment challenges
- Lack of workforce
- Lack of retention
- Other, please specify

18. If you would like to make any further comment on skills and training needs and challenges for immunological tools please use the text box.

Technology Platforms

A technology is defined as a platform if an underlying, nearly identical mechanism, device, delivery vector or cell line is employed for multiple target vaccines. Such platforms include nucleic acid (RNA, DNA), viral vectors, whole virus (live attenuated, inactivated) and protein (protein subunit, virus-like-particle).

19. On a scale of 1-5 How important are the following research goals regarding tools and technologies for vaccine research and innovation?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- An established pipeline of platform technologies which can be used as 'plug and play' tools for rapid identification of target antigens, vectors, and delivery systems.
- Development of novel, cutting edge platform technologies
- Systematic evaluation and comparative analysis of platforms (e.g., dose / duration / vaccination regime).
- Systematic evaluation of the efficacy of different vaccine platforms against a range of pathogens.
- Systematic evaluation of the efficacy of different vaccine platforms in different target species.
- Modify vaccine vector systems to direct the immune response in one direction or the other (CMI/CTL/Th1 versus serology/Th2) depending on whether the pathogen is intra- or extracellular

If you would like to raise other areas of interest or objectives regarding topics relating to Technology platforms, please use the text box.

Underpinning Needs for Technology Platforms

20. Is there a need for (Yes/No):

- Maintaining well-annotated, comprehensive, and searchable genomic (including transcription, splice variants, read variation) databases to support species-specific vaccine research.
- Better utilising existing and novel technologies (e.g., mass spectrometry, cryo-EM, CRISPR-Cas9) for developing platforms.
- Bioinformatic/Artificial Intelligence (AI) approaches to identify protein structures and protective antigens for complex pathogens.
- Data analytics approaches to integrating high-dimensional data across multiple domains to identify systems-biology responses to infection/vaccination.

If Yes, what is required?

Unmet Needs:

21. Is there a need for (Yes/No):

- Developing rapidly deployable platforms for pathogens to combat AMR.
- Developing vaccine platform technology for complex pathogens (anti-parasitic vaccines, including those for large multicellular parasites).
- Developing vaccine technology platforms which can integrate multiple antigens in one vaccine.
- Developing vaccine technology platforms and accompanying ELISA tests for serological discrimination, which are DIVA compliant (diagnostics tests that can differentiate between infected and vaccinated animals).
- Developing vaccine technology platforms capable of delivering immunogens effectively across mucosal surfaces to give mucosal and systemic responses

If Yes, what is required?

22. If you would like to raise other areas of interest or objectives regarding topics relating to platform technologies please use the text box.

23. Does your work focus on Technology platforms?

- Yes
- No

If your work focuses on technology platforms:

24. Where are the skills and training gaps in the area of technology platforms?

- Graduate level
- Postgraduate level (PhD)
- Postdoctoral level
- Fellowships
- Other, please specify

25. What are the main issues?

- Recruitment challenges
- Lack of workforce
- Lack of retention
- Other, please specify

26. If you would like to make any further comment on skills and training needs and challenges for technology platforms, please use the text box:

Vaccine Design and Delivery

This section focuses on immunogen design which includes questions on thermostabilisation, production and scale up, regulatory and delivery systems.

27. On a scale of 1-5 how important are the following research and development goals regarding immunogen design for vaccine research and innovation?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Developing and validating novel stabilisation technologies to enable reduced reliance on cold chains and induce highly protective immune responses.
- Novel vaccines which are efficacious but economically suitable in terms of large-scale production.
- Innovative methods for vaccine production and manufacture, extending shelf life and reducing production costs.
- Strong Public-Private Partnerships.

Vaccine Delivery Platforms

28. Is further research and innovation required for the following delivery mechanisms:

- Subcutaneous
- Intravenous
- Muscular
- Mucosal
- Nasal
- Oral
- Transdermal
- Topical
- Novel delivery platforms (examples if possible)

29. Is there a need for comparative efficacy assessment of delivery platform technologies (e.g., subcutaneous, intravenous, muscular, mucosal, nasal, oral etc.)?

Vaccine Safety, Equity and Uptake

30. On a scale of 1-5 how important are the following research and development goals regarding vaccine safety, equity and uptake for vaccine research and innovation?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Suitable use of animal models (e.g., target species) to assess vaccine safety.
- Testing vaccine safety in large field setting (e.g., environmental and end-user testing)
- Standardisation/harmonisation of global safety testing requirements.
- The EU/other global requirements to conduct safety studies to GLP.
- Clarification of the safety standards required for novel vaccine platform technologies
- Licencing of vaccine platform technologies
- Strengthening understanding and engagement with regulatory aspects of vaccine development.
- Physical delivery of vaccines to regions which lack suitable storage infrastructure.
- Public and stakeholder engagement on topics of disease and vaccinology to support stakeholder buy-in for vaccine use.
- Better alignment between veterinary and human vaccine research and development to enable switching between human and animal regulatory regimes as methods used in vaccine development are similar (e.g., One Health-based approaches to vaccine design).

If you would like to raise other areas of interest or objectives regarding topics relating to vaccine design and delivery, please use the text box.

31. What are the bottlenecks/barriers within current pipelines to accelerate vaccine development to get products to market sooner?

32. Do you work on vaccine safety, equity, and uptake?

- Yes
- No

If your work focuses on vaccine design and delivery:

33. Where are the skills and training gaps in the area of vaccine design and delivery?

- Graduate level
- Postgraduate level (PhD)
- Postdoctoral level
- Fellowships
- Other, please specify

34. What are the main issues?

- Recruitment challenges
- Lack of workforce
- Lack of retention
- Other, please specify

35. If you would like to make any further comment on skills and training needs and challenges for vaccine design and delivery please use the text box:

Epidemiology and Economics

This section focuses on the epidemiology and economics of veterinary vaccinology including questions on epidemiology, transmission and modelling, translation, economics, social acceptance.

36. On a scale of 1-5 How important are the following research and development goals regarding epidemiology and economics for vaccine research and innovation?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Understanding gaps in underpinning knowledge in the transmission of disease to inform vaccine development.
- Using in silico methods to predict efficacy of vaccines.
- Using in silico methods to predict vaccine cost-effectiveness.
- Using in silico methods to predict herd immunity.
- Understand the impact vaccines have through epidemiological post-introduction evaluation studies.
- Assessing the need for/feasibility of vaccines in the field context (including societal needs).
- Understanding the socio-economic impacts of veterinary vaccine interventions at different levels (sector, national, global).
- Understanding the potential financial return on investment for the development of a vaccine (benefit: cost ratio).
- Understanding the impact of vaccine misinformation in veterinary vaccinology

If you would like to raise other areas of interest or objectives regarding topics relating to epidemiology and economics, please use the text box.

37. Do you work on epidemiology or economics of veterinary vaccines?

- Yes
- No

If your work focuses on veterinary vaccine epidemiology and economics:

38. Where are the skills and training gaps in the area of veterinary vaccine epidemiology and economics?

- Graduate level
- Postgraduate level (PhD)
- Postdoctoral level
- Fellowships
- Other, please specify

39. What are the main issues?

- Recruitment challenges
- Lack of workforce
- Lack of retention
- Other, please specify

40. If you would like to make any further comment on skills and training needs and challenges for epidemiology and economics please use the text box:

Capacity and Capability

41. On a scale of 1-5 How important are the following research goals regarding capability and capacity to veterinary vaccinology?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Strengthening emergency research capacity in veterinary clinical practice for emerging epidemic/epizootic diseases.
- Need for centres of excellence specialising in bioinformatics and Artificial Intelligence for antigen discovery.
- Need for centres of excellence specialising in systematic evaluation of the efficacy of different vaccine platforms.

- Promote the One Health approach to support capability and capacity in veterinary and human vaccine research and innovation.
- Maintain capacity in veterinary vaccine research across the entire vaccinology research and development career track.
- Strengthen knowledge exchange and commercialisation between academia and industry.
- Effective interdisciplinary integration between natural and social sciences.
- Promoting fundamental research on mechanisms of immune responses in multiple organ compartments across target species

If you would like to raise other areas of interest or objectives regarding topics relating to capability and capacity, please use the text box.

Infrastructure

42. On a scale of 1-5 How important are the following objectives regarding infrastructure to veterinary vaccinology globally?

(1. not at all important, 2. somewhat important, 3. important, 4. very important, 5. don't know)

- Veterinary vaccinology biomanufacturing capacity.
- manufacturing capability to rapidly respond to pandemic threats.
- Create infrastructures that support big data and exploit *in silico* pipelines for vaccinology research.
- Support for large scale vaccine trials in animals.
- Support for containment facilities for challenge studies to evaluate vaccine efficacy for pathogens including zoonoses.

If you would like to raise other areas of interest or objectives regarding topics relating to infrastructure, please use the text box.

PART 3: Overarching vaccinology needs

These final eight questions provide a chance for you to comment on any overarching needs within veterinary vaccinology research, development, and innovation.

43. In your opinion, please list the top three research gaps in veterinary vaccinology research and innovation?

44. In your opinion, please list the top three gaps in veterinary vaccinology capability, capacity, skills, and development? This may include gaps in knowledge exchange and commercialisation.

45. What research disciplines (e.g., immunology, virology) are not represented well in Veterinary Vaccinology research and innovation? (list 3 at most)

46. Please state any key strategic recommendations you may have for funders?

47. Do you have any further comments that you would like veterinary vaccinology funders to consider?

Annex 2 BBSRC Veterinary Vaccinology Working Group

The BBSRC Veterinary Vaccinology Working Group provides advice to UKRI-BBSRC on strategic direction of veterinary vaccinology research and innovation.

Working Group Members:

Name	Affiliation
Professor Bryan Charleston (Chair)	The Pirbright Institute
Professor Mick Bailey	The University of Bristol
Dr Tim Connelley	The University of Edinburgh, Roslin Institute
Professor Gary Entrican	The University of Edinburgh, Roslin Institute
Dr Mike Francis	BioVacc Consulting Ltd
Professor Jayne Hope	The University of Edinburgh, Roslin Institute
Dr Theo Kanellos	Zoetis Ltd
Professor Jacqui Matthews	The Moredun Research Institute
Professor Helen McShane	The University of Oxford, Jenner Institute
Dr Sean Monaghan	The University of Stirling
Professor Fiona Tomley	The Royal Veterinary College
Professor Vish Nene	International Livestock Research Institute (ILRI)
Professor Rowena Hoare	The University of Stirling

Other Stakeholders

Jeremy Salt – The Vaccine Group

Nick Juleff – The Bill & Melinda Gates Foundation

Annex 3 Detailed gaps on Underpinning Needs for Technology Platforms

Maintaining well-annotated, comprehensive, and searchable genomic databases to support species specific vaccine research:

1. Accessible internationally including searchable tools that could be used by non-bioinformaticians.
2. Requirement for high performance supercomputing facilities, servers, and technical personnel to manage it.
3. Databases that specialise in identified vaccine candidate antigens.
4. Genomic resources for fish and shellfish lag behind other species.
5. Complete genome scaffolds for many species do not exist and are needed to permit identification of genomic differences between closely related species with differential susceptibility to pathogens. This will support breeding programmes as well as vaccine development.
6. Breadth of coverage and resources that capture the global genetic diversity within species, including representation of pathogens, breeds, lines, and genes from traditionally neglected areas (Africa, Asia).

Survey respondents highlighted the need for capacity building, training, accessibility, and availability for better utilising existing and novel technologies (e.g., mass spectrometry, cryo-Electron Microscopy EM, CRISPR-Cas9) including centralised access, multidisciplinary working between research institutes, universities, and industry:

1. Access to staff with skills in protein chemistry and mechanisms for exposure and supportive working between fields
2. Multiple structural vaccinology approaches to identify antigen subunits that provide long-lasting immune responses against challenging pathogens that often escape successful vaccine design (e.g., parasites).
3. Public support for the implementation of such technologies in vaccine research would be powerful to remove negative stigma.

Bioinformatics/Artificial Intelligence (AI) approaches to identify protein structures and protective antigens for complex pathogens:

1. Bioinformatics and AI is a rapidly expanding area that has the potential to radically change how candidate vaccine antigens are identified, produced, and assessed for protective efficacy.
2. Accessible training is required for graduate students and research groups to be able to programme; handle large datasets; interpret the meaning of the information; and turn it into real application evidence.

3. Competent and sustainable involvement of bioinformatics staff is needed.
4. The human health field is ahead with these technologies, fostering collaborations between human and veterinary bioinformatic research will be hugely beneficial.
5. Integrate of multi-omics data through bioinformatics pipelines to inform antigen selection, such data includes conservation on candidate antigens, roles in virulence, expression data, subcellular localisation.
6. Data from multiple sources should be brought together on curated databases.
7. Coordination at an institute/regional level is required including structural bioinformatics/antigen discovery networks and centres of excellence with the development of veterinary specific software.

There is a specific need for bioinformatics for:

1. Understanding zoonotic spillover.
2. Prediction of immunogenic epitopes/antigens or protein structural requirements.
3. Analysis of various biological responses at single cell/tissue and whole animal levels.
4. High throughput methods of screening.

Data analytics approaches to integrating high-dimensional data across multiple domains to identify systems-biology responses to infection/ vaccination:

1. This is still a new field for veterinary vaccinology so requires training and collaboration across research groups, institutes, and industry. Similar to bioinformatics and AI research, human vaccinology is ahead of veterinary vaccinology systems biology and data analytics, there is therefore need to foster collaborations by applying systems immunology in human and veterinary vaccinology.
2. Understanding the benefits of vaccination at herd or population levels and to assess pharmacovigilance data.
3. Uniform standards of data collection, reporting and access to raw data are needed to be able to conduct in-depth and systematic research, this could include use of government databases.
4. Centralised databases and analysis pipelines for assessing integrated responses to infection and vaccination, including memory responses are warranted.
5. Integration of genomic, transcriptomic, proteomic and epigenomic datasets will require high dimensional data analytics.
6. Data analytics, along with bioinformatics and AI will require significant capability and capacity support including supercomputer facilities, servers and technical roles.

The use of data analytics was specifically highlighted for:

1. Identifying vaccine antigens.
2. Immune-profile of parasite-resistant individuals for further vaccine design
3. 3Rs refinement prior to pre-clinical testing.
4. Identify disease resistant animals which can open up new avenues for veterinary vaccine development.
5. Development of mathematical models for multi-omics analysis.
6. Combining omics datasets for syndromic disorders in livestock and aquaculture research.
7. A global and systematic systems serology analysis to understand what the target protective profile is.
8. Analysis of signatures in complex datasets. Single-cell RNAseq is already revealing huge complexity in immune cell subsets and their responses but is in its infancy in farmed animals.

Annex 4 Unmet Needs for Technology Platforms

Developing rapidly deployable vaccine technology platforms for pathogens to combat Antimicrobial resistance (AMR):

1. In many regions of the world diagnostic kits for veterinary disease are not easily accessible, antibiotics are freely administered which leads to a lot of antibiotic residues in the environment leading to an increase in resistance in both veterinary and human diseases.
2. AMR is a significant problem in swine, poultry, and aquaculture. Cross strain protection will be very important in combatting resistance to pathogens where multiple drug resistance is a problem.
3. Along with developing these vaccine technology platforms, fast-track licencing and the availability of these vaccine is very important in tackling the AMR problem.
4. Further research is need to
   - understand risk factors contributing to AMR (i.e., production, trade, housing, transport practices, population sizes, how other interventions are used).
   - Develop pen-side tests and AMR diagnostic tools that are reliable, user friendly and cost effective.

Developing vaccine platform technology for complex pathogens (anti-parasitic vaccines, including those for large multicellular parasites):

1. To help develop suitable vaccine platform technology for complex pathogens, multiple approaches are needed, **combining systems serology, parasite genomics/bioinformatics and proteomics to identify potential vaccine candidates**. Dedicated pipelines need to be in place that coordinate research using artificial intelligence, predictions, protein arrays for the design of the vaccines through to testing multiple combinations of the vaccines in the host animal challenge studies to determine if they are effective.
2. There is a lot of diversity within the species of complex pathogens (parasite, helminths) which means it is likely to need detailed research on specific parasites, specific stages of life cycle and vaccine strategies may require presentation of multiple antigens.
3. **Fundamental research to understand host immune interactions and protective immunity in such pathogens is needed**. Due to the complex nature of these pathogens, it is likely that a plethora of vaccine antigen targets, in their correct structure, will be needed to produce multiple antibody responses to control the disease. Targeting the early larval stage is the optimum control strategy to block growth of the parasite to the adult stage but developing vaccines at this stage has historically been harder.
4. Foundational datasets and genomes of these pathogens are needed, many genomes of these pathogens have yet to be sequenced. Sequencing pathogens from diverse geographical regions will be critically for epitope mapping. Protein expression facilities and challenge facilities are needed to produce validated challenge models.

Developing vaccine technology platforms which can integrate multiple antigens in one vaccine:

1. The ability to combine several different antigen types in the same formulation has the potential to change the field completely, supporting animal welfare and cost-effectiveness for farmers. However, the big unanswered question would be **under what variables are vaccines combined e.g., type of species, age, type of production**.
2. The main research gaps include:
   - expression systems
   - QC tools for monitoring the quality and quantity of each immunogen in the vaccine
   - assess any additive effects that follow combining of multiple antigens into one vaccine
   - what effect this may have compared to vaccines which target one pathogen type and whether there may be any antigenic competition/interference if targeting multiple pathogens of the same type.
3. Developing polyvalent vaccines for pathogens that have multiple strains are also important as is including antigens that target the humoral and cellular responses.
4. 'Plug and play' platforms capable of combining and switching is a key research aim. Being able to quickly adapt vaccines to the field situation (evolving pathogens such as Covid in humans, Influenza in animals and humans) would be highly beneficial.

Developing vaccine technology platforms and accompanying ELISA tests for serological discrimination, which are DIVA compliant (Differentiating Infected from Vaccinated Animals):

1. Vaccine and diagnostic development need to be run in parallel and there should be a built in DIVA process, this should be highlighted in target product profile of vaccine candidates. One response noted that the diagnostic test does not necessarily need to be an enzyme-linked immunosorbent assay (ELISA), but highly sensitive and specific point-of-care alternatives are also welcome.
2. Understanding of immune responses and ability to discriminate correlates of infection from correlates of protection and the design and delivery of subunit vaccines.
3. Tests need to be validated in a standardised way, so they are accepted globally. Platforms to be able to express purified proteins are needed, particularly for large scale production.
4. DIVA is particularly important for animal movement and transboundary and emerging diseases as well as for elimination and eradication programmes. It could also be used to assess different variants/strains of pathogen exposure.

Developing vaccine technology platforms capable of delivering immunogens effectively across mucosal surfaces to give mucosal and systemic responses:

1. Developing vaccines that are easy to administer and are still efficacious is always beneficial, especially for livestock/wildlife and an animal welfare perspective.
2. Antigen delivery systems including adjuvants can play an important role in effectively delivering vaccines across the mucosa hence the importance of developing novel delivery systems as well as standardising methods to assess so that the data can be compared between studies involving different systems for different vaccines to stimulate mucosal responses.
3. A key research aim in this area is how to target antigen to key tissues and cell types associated with antigen presentation without mis-priming the immune system and generating a sufficiently high and targeted immune response.

4. Species specific understanding of innate mucosal immunity is required to avoid immune imbalance in the mucosal site, alongside better technology is needed to measure mucosal immunity in target species.
5. Most veterinary pathogens have a mucosal surface component, this area is in its infancy compared to humans therefore One Health multidisciplinary coordination would be supportive to develop this area further.
6. Support for research on oral vaccines particularly for aquaculture and poultry.

Further technological needs were highlighted, these included developing technologies specifically for:

1. Monoclonal antibodies from different species
2. Veterinary pathogen protein/peptide arrays
3. Investigating antigenic variability of parasites
4. Exploiting activity of neutralising antibodies to determine epitope structures
5. Understanding host-pathogen interactions and protective responses at site of infection.
6. Quality Control (QC) testing and antigen characterisation
7. Improving and designing vaccine vectors
8. Toolboxes for genome modification across species

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