STAR-IDAZ WORK PACKAGE 4 VETERINARY VACCINOLOGY SURVEY REPORT

BACKGROUND

The EU FP7 funded Global Network, STAR-IDAZ[1] – Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses, aims to coordinate the research on the major infectious diseases of livestock and zoonoses at both research funders and programme owners level.

As a part of Work package 3 (Analysis of and responding to global, regional and industry sector priorities) STAR-IDAZ consortium identified 10 priority diseases and three cross-cutting issues for collaborative activities at a global level.

Diseases:
Influenza, Bovine Tuberculosis and other mycobacterial diseases, Foot and Mouth Disease, Salmonella, helminth parasites, Porcine Reproductive and Respiratory Syndrome Virus, Brucellosis, African Swine Fever and Rabies

Three cross-cutting issues:
Alternatives to Antibiotics; Vaccinology; and Reducing GHG Emissions through Disease Control)

STAR-IDAZ Consortium Meeting: 2012

The STAR-IDAZ consortium at the Bangkok meeting in 2012 held a workshop in veterinary vaccinology to identify and agree priority areas that would benefit from international research collaboration and methods for taking these forward. The workshop looked at:

- Expectation from an ideal vaccine
- Technological developments
- Challenges needing to be addressed

The group identified some vaccine research challenges and recommended that to progress global coordination in vaccinology research there is a need to establish

- what problems have STAR-IDAZ partners identified;
- what is being funded (see One Health questionnaire); and
- where are gaps in vaccinology research?

To establish a preliminary understanding of vaccine research challenges, the DISCONTOOL[2] database was analysed.

[1] http://www.star-idaz.net/
[2] http://www.discontools.eu/Diseases

DISCONTOOL Database Analysis

The analysis of the animal diseases included in the DISCONTOOLS[3] database illustrates three main categories (**Annex 1**) of diseases in terms of vaccines need:

- Diseases for which there are no vaccines (e.g. African Swine Fever, Campylobacteriosis, Cryptosporidiosis, Liver fluke, Nematodes, Nipah Virus, Swine Vesicular Disease, Trypanosomiasis, Varroa mite).
- Diseases for which there are vaccines but not well controlled (e.g. African Horse Sickness, Avian Influenza, Foot and Mouth Disease, Salmonellosis).
- Diseases for which there are vaccines, and are well controlled but not eradicated (e.g. Anthrax, Blue Tongue, Rabies).

In most cases the lack of vaccine is because either classical methods of developing vaccine have failed or the immunological response is not sufficiently well understood to develop a vaccine using available technologies.

Further analysis of the database showed that there are some common generic vaccinology research areas/gaps for various diseases e.g.

BlueTongue

- Currently there is not a one shot application of an inactivated vaccine that gives long-lasting protection from viraemia and clinical signs;
- No subunit vaccines commercially available as yet;
- No efficacious and safe DIVA vaccines available.

Influenza

There is a need for:

- Safer adjuvant/adjuvant system(s);
- Improving the efficacy of the vaccines.

It is evident from the analysis that even though vaccine research is mostly done in the context of a particular disease, there are generic vaccinology research areas/gaps that would benefit from coordinated research efforts. There is need for improved understanding of immunology, novel tools and generic technologies for producing novel and/or improved vaccines.

BBSRC, as a leader of the **Work Package 4 -Networking of on-going research activities on major animal health issues** designed and conducted a survey to map the current research landscape of vaccinology in the member countries of the STAR-IDAZ consortium.

[3] http://www.discontools.eu/Diseases

VETERINARY VACCINOLOGY SURVEY

The aims of the survey are:

- map the current research activities and identify key players in veterinary vaccinology;
- identify current research gaps and needs with the vision of developing a coordinated global research Network in veterinary vaccinology; and
- identify the aims and objectives of such a Network

The survey was aimed at both:

- Science Policy or Administration Professionals (**Annex 2**);
- Active researchers (**Annex 3**).

The survey was sent to all STAR-IDAZ partners and associate members. Also, the partners were encouraged to widely circulate the survey to their research community and other funders within their country.

Response to the survey

100 responses from 19 countries were received as shown in Figure 1 below. These includes

- 21 responses from Science Policy or Administration Professionals; and
- 79 from Researchers.

Figure 1: Vaccinology Survey Response by Country

Table 1 below provides the number and types of responses received from each country. In general, responses were received from most STAR-IDAZ consortium countries but there was no response from the African sub-continent. Also, other than Ella Foundation in India there were no responses received from Industries.

Table 1: Number and Type of Vaccinology Survey Responses by Country

Name of the Country	Responses from Science Policy or Administration Professional	Responses from Researchers
Argentina		1
Australia	3	6
Belgium	2	1
Brazil	1	2
China		1
Denmark	1	2
France		1
Germany	1	1
India	1	4
Indonesia		1
Italy	1	10
Ireland		1
Mexico	1	1
New Zealand	3	2
Russia	1	
Spain		6
Sweden	1	
United Kingdom	2	38
United States of Americas	3	1

SECTION I: CURRENT RESEARCH ACTIVITIES IN VETERINARY VACCINOLOGY

SECTION 1A: CURRENT RESEARCH LANDSCAPE

Responses from Science Policy or Administration Professionals

The science policymakers or administration professionals identified top diseases of various livestock sectors for which they are providing funding for vaccinology research. Table 2 below provides a summary of results received and the most funded diseases in each livestock species.

The USDA-ARS has vaccine research programmes for all of the major diseases of cattle, farmed fish, poultry and pigs.

Table 2: Funded Diseases of Various Livestock Sectors

Species	Diseases Funded	Names of Diseases	Most Funded Disease(s)
Large Ruminants (Cattle, Buffalo)	20	Bluetongue, Bovine Respiratory Disease Complex, Bovine Respiratory Syncytial Virus, Bovine Tuberculosis, Brucellosis, Contagious Bovine Pleuropneumonia (CBPP), Cooperia, Dictyocaulus viviparous, Digital dermatitis, East Coast Fever, Ephemeral fever, Fasciola; Foot and Mouth Disease, Haemorrhagic Septicaemia, Johne's Disease, Ostertagia, Parasites, Rift Valley Fever, Tick-borne diseases, Udder Infections	Bovine Tuberculosis/Foot and Mouth Disease
Small Ruminants (Sheep and Goats)	17	Bluetongue, Brucellosis, Contagious Caprine Pleuropneumonia, Enterohaemorrhagic Escherichia coli, Foot and Mouth Disease, Influenza, Johne's disease, Lynphadenitis, Mannheimia hemolytica, Malignant Catarrhal Fever, Parasites, Pasteurella, Peste-des-Petits Ruminants, Rift Valley Fever, Schmallenberg Virus, Sheep and Goat Pox, Sheep scab	Bluetongue/Foot and Mouth Disease
Pigs	9	African Swine Fever, Classical Swine Fever, Foot and Mouth Disease, Lawsonia, Pneumococcal, Porcine cysticercosis, Porcine Reproductive and Respiratory Syndrome, Swine Fever, Swine Influenza	Swine Fever (African and Classical)
Poultry	12	Avian Influenza, Campylobacter, Coccidiosis, Chlamydia Psittaci, Clostridium Perfringens, , Enteric viruses, Infectious Bronchitis, Infectious Bursal Disease, Marek's Disease, Newcastle Disease, Fowlpox, Salmonella	Influenza and Newcastle disease
Equines	7	African Horse Sickness, Equine Herpes Virus-1, Equine infectious anaemia, Equine Influenza, Equine Piroplasmosis, Hendra, Rhinopneumonia	African Horse Sickness/Hendra virus
Aquatic Species	10	Aquabirnavirus, aquareovirus, Edwardsiella ictaluri, Flavobacterium columnare, Herpesvirus inf. of sturgeon; Infectious Pancreatic Hepatitis; Spring	Edwardsiellosis

Species	Diseases Funded	Names of Diseases	Most Funded Disease(s)
		viraemia of carps; Streptococcus iniae; Viral haemorrhagic septicaemia; White Spot Syndrome	

The science policymakers or administration professionals also identified major diseases/threats in their country for which a vaccine is needed. Table 2 below shows, in order of the number of times mentioned, diseases which were mentioned multiple time and the reasons for the need for new vaccines:

Table 2: Funders' Perspective: Top Threats for which VACCINE is Needed

Disease	Species	Issues
African Swine Fever	Pigs	• No vaccine available • Disease threat is increasing with it currently spreading in Eastern Europe
Bovine Tuberculosis	Cattle, farmed deer and possums (Trichosurus vulpecula)	• No DIVA vaccine • A major problem for the livestock industry and nationally and Internationally • International commerce • Wildlife hosts • Control/eradication/export markets
Foot and Mouth Disease	All ruminants	• Need vaccines designed for control and eradication • Speed of onset of protection • Emergency vaccines
Avian Influenza	Poultry	• To contain outbreak if the disease becomes endemic • Universal vaccine • Length of immunity
Porcine Reproductive and Respiratory Syndrome	Pigs	• Current vaccines are not efficacious and contributing to strain diversity • New emerging strains

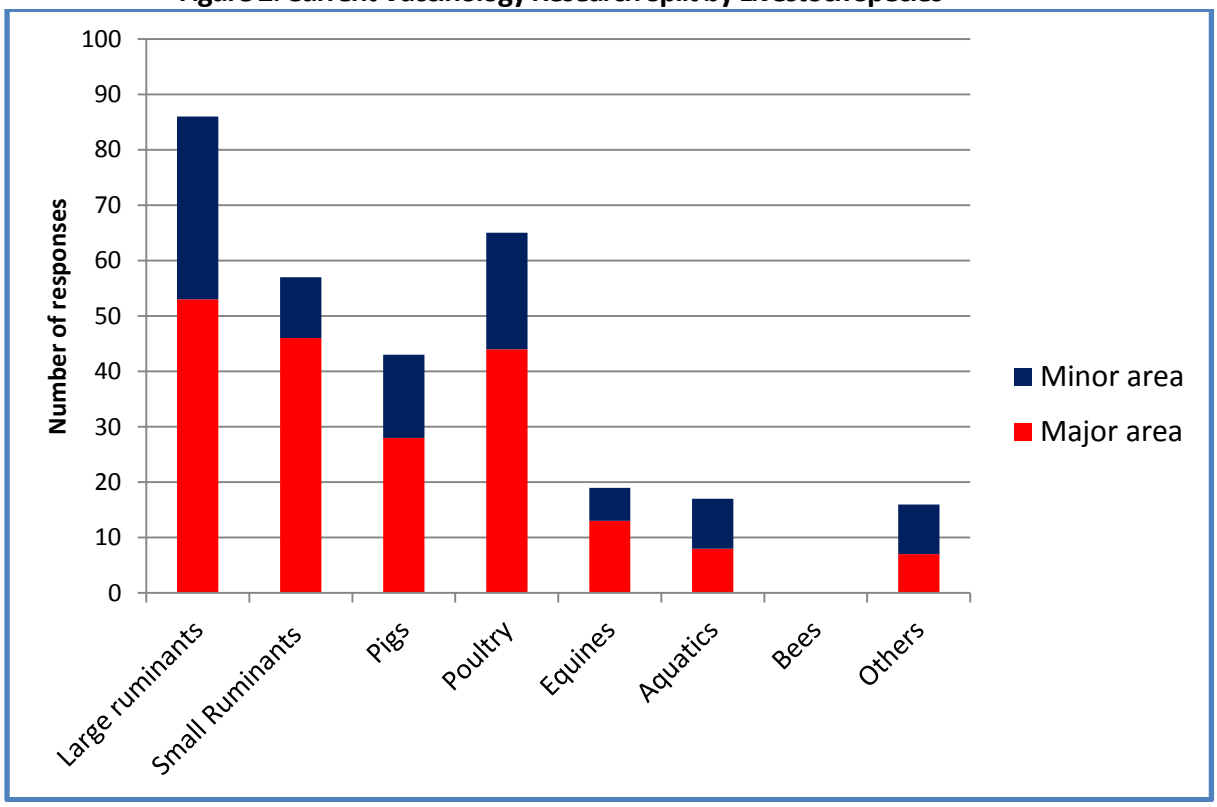
A number of other diseases for which there is need for improved vaccines were also mentioned including:

- Brucellosis: new programme to eliminate disease.
- Newcastle disease as the current vaccines do not prevent transmission/viral shedding
- Johne's Disease: a major production disease

Responses from Active Researchers

Each researcher identified the top (up to five) diseases of various livestock sectors which is the major or the minor focus of their vaccinology research. Figure 2 shows that vaccinology research is carried out on all major livestock species and in many cases it is a major focus of their research.

Figure 2: Current Vaccinology Research Split by Livestock Species

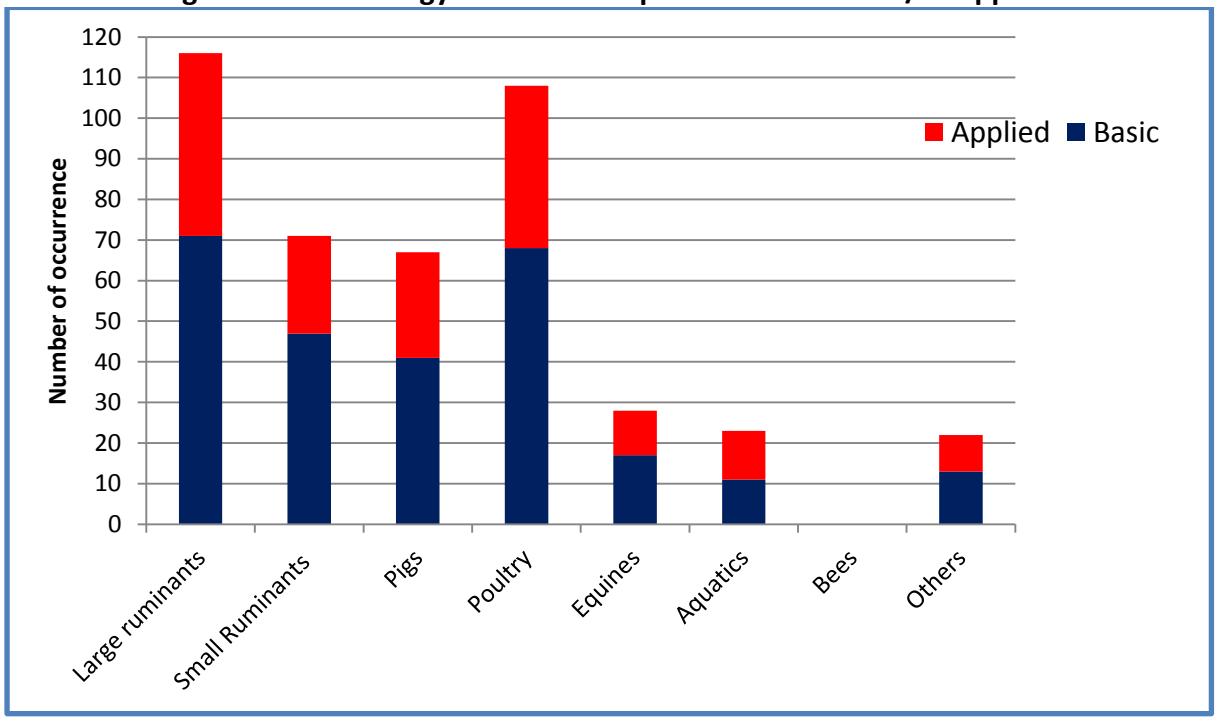


In general, the major focus of vaccinology research is on large ruminants. However, the research is not focused on any one disease in any species, there being a number of diseases for which vaccine research is carried out and these are shown in Annex 4.

Active researchers also identified if their research was either applied research that includes vaccine development, production, or testing etc. or basic research focussing on underpinning immune responses, host-pathogen interaction, pathogen biology etc. Responses received are presented in Figure 3.

The results show that both applied and basic vaccinology research is undertaken but there is more focus on basic research (62%) compared to applied research (38%).

Figure 3: Vaccinology Research: Proportion of Basic and/or Applied



Summary of the section 1a: Current Research Landscape

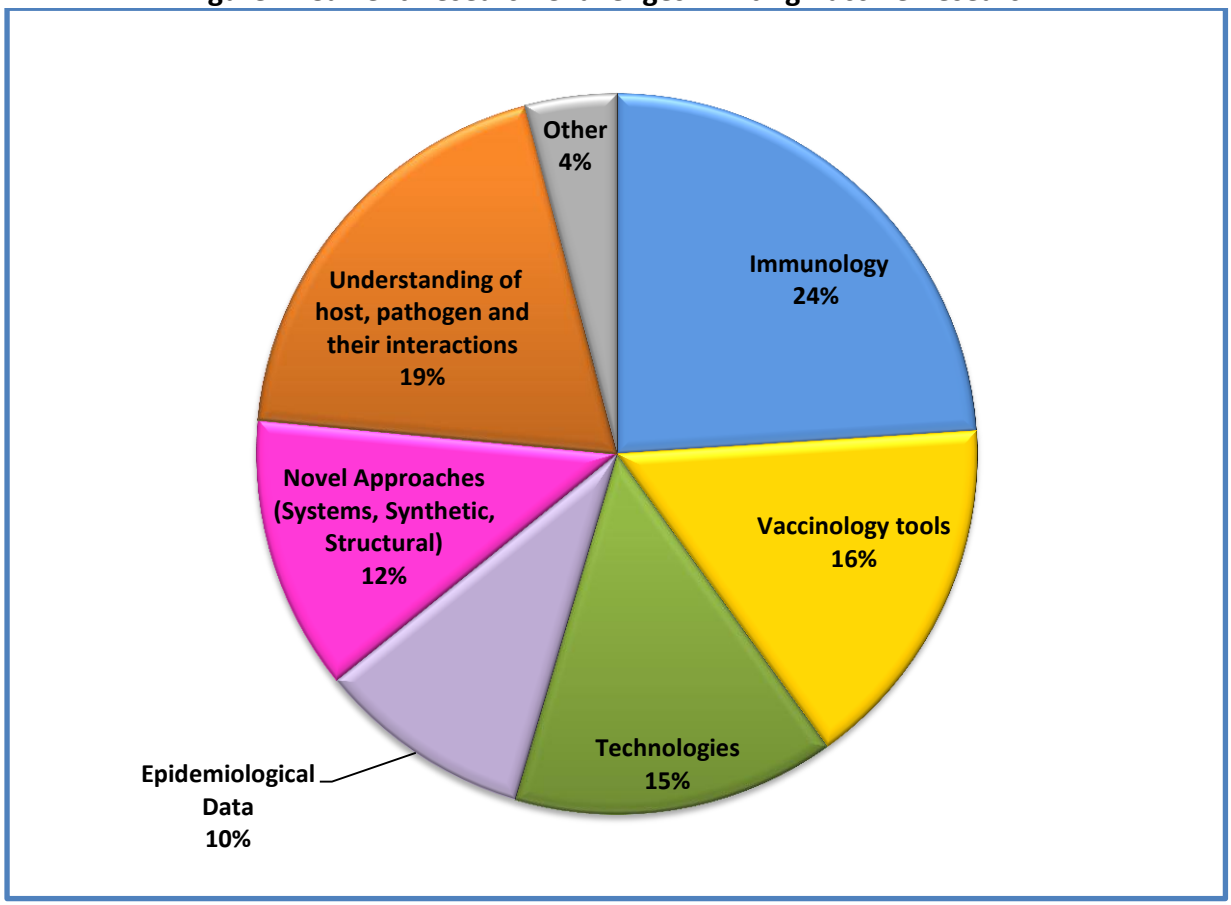
- Both basic and applied vaccinology research is done on number of diseases of various livestock species
- Vaccinology research funding is available for number of diseases of various livestock species
- Large ruminants vaccinology research dominates the landscape
- African Swine Fever is the most common identified threat but the need for vaccines for Bovine TB, Avian Influenza, Foot and Mouth Disease and Porcine Reproductive and Respiratory Syndrome was also identified.

SECTION 1B: CHALLENGES, GAPS AND FUTURE NEEDS

Current Research Challenges Identified by Active Researchers

A number of research challenges that could potentially limit current vaccinolgy research were identified based on discussion with STAR-IDAZ consortium and analysis of DISCONTOOL database. Active Researchers were then asked if these challenges were limiting the progress of current veterinary vaccinology research in diseases and animal species that are major focus of their research. The overall response received which covers diseases and species is represented in Figure 4:

Figure 4: Current Research Challenges Limiting Vaccine Research



Further analysis of data based on major livestock species and some of the major disease threats is shown in Figure 5 a and b respectively. There are some species and disease-specific differences in the challenges but overall need for immunology and technologies is evident.

Figure 5a: Challenges based on livestock species

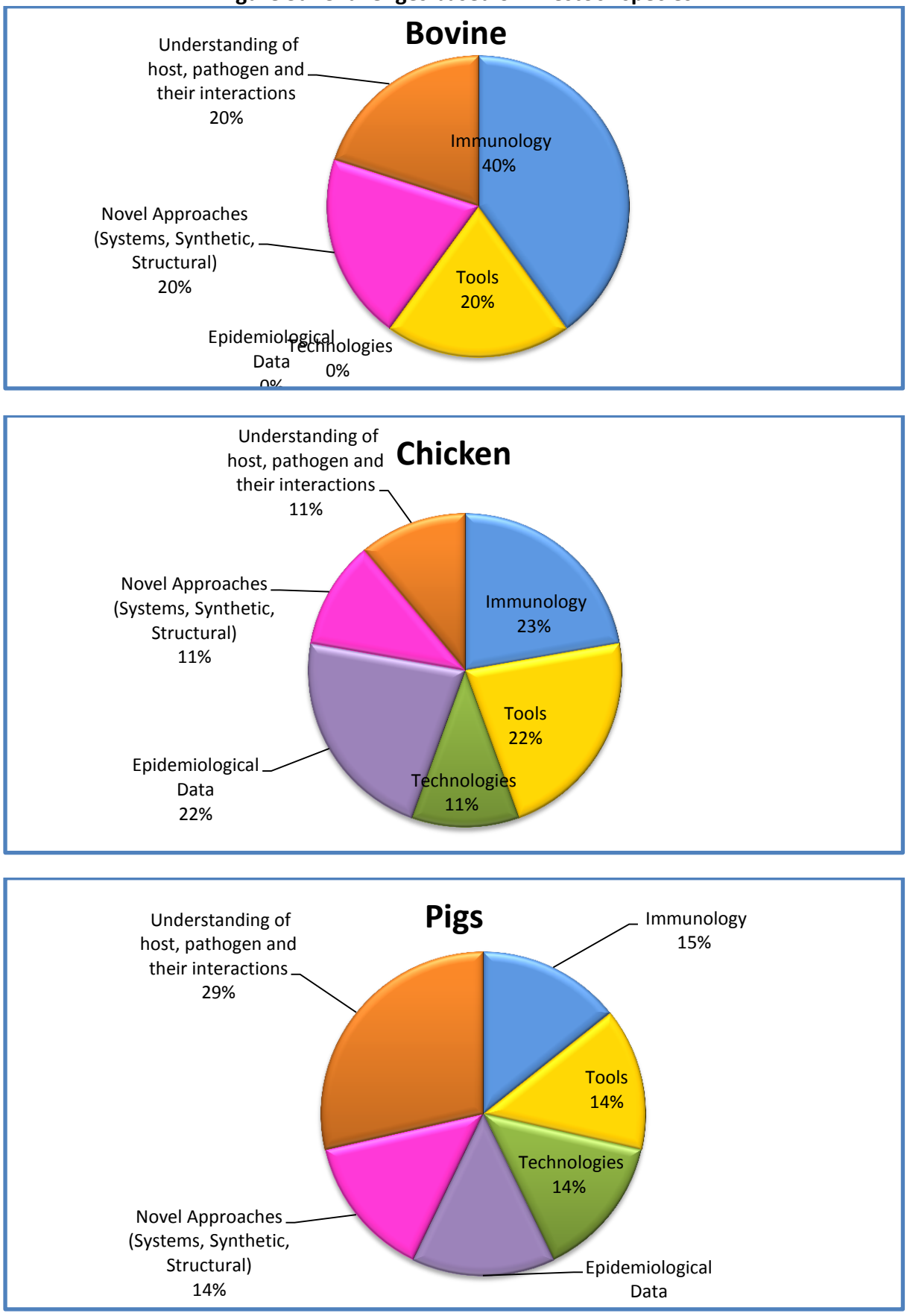
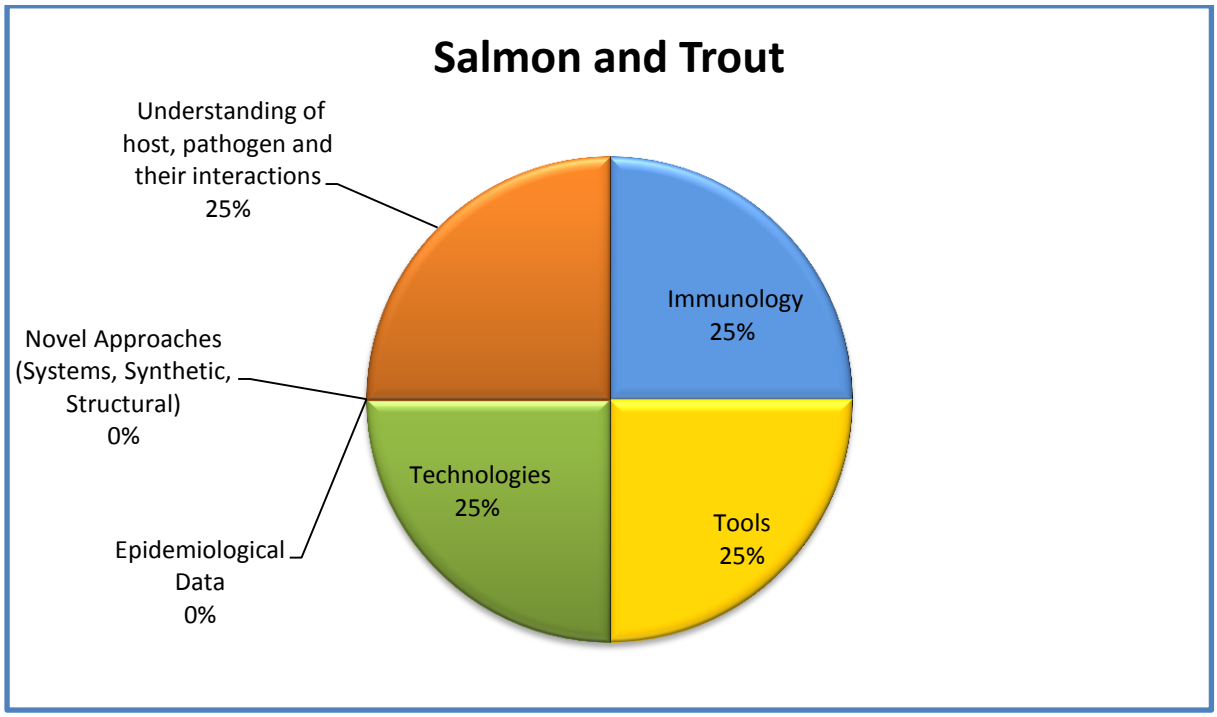
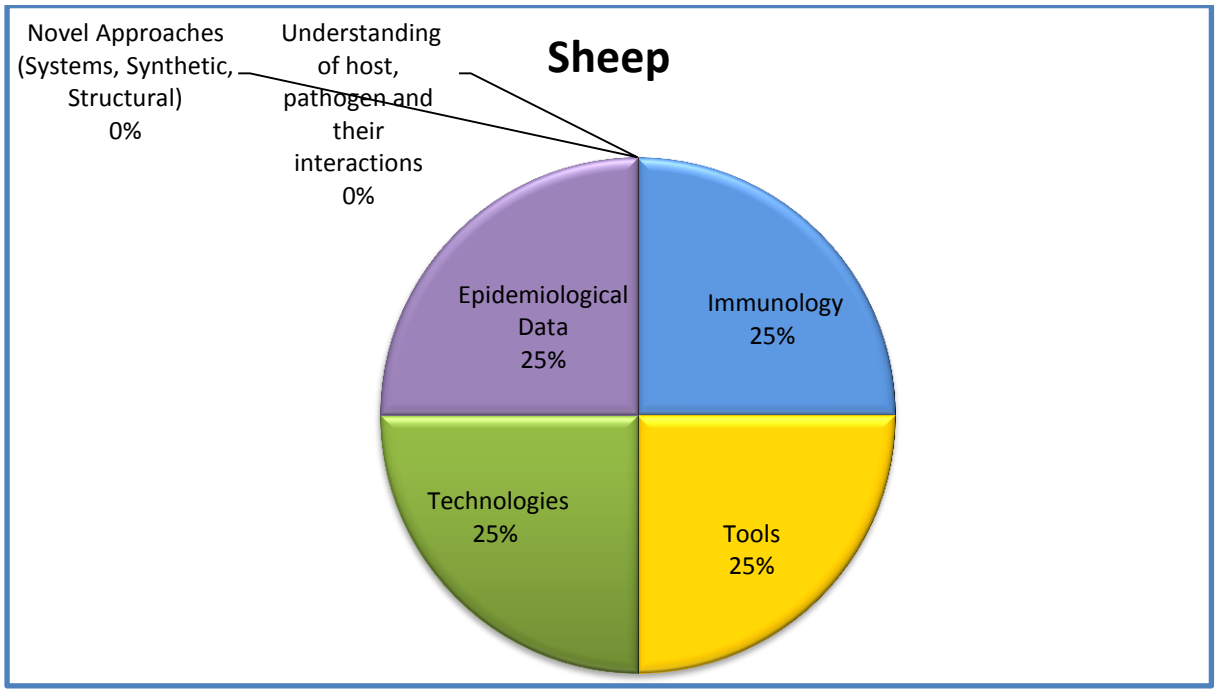
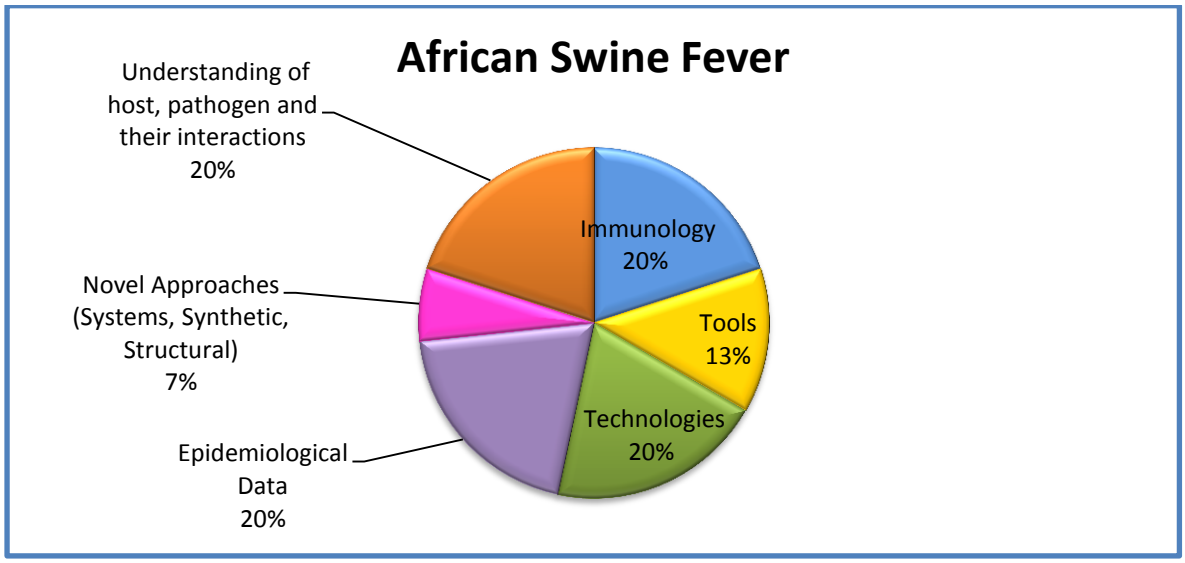
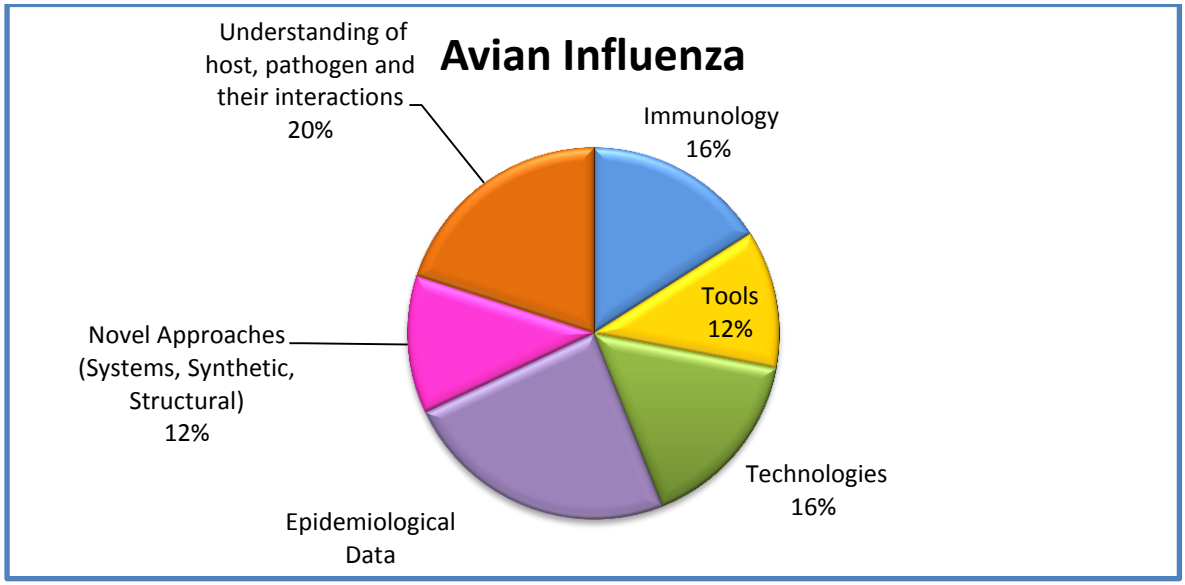


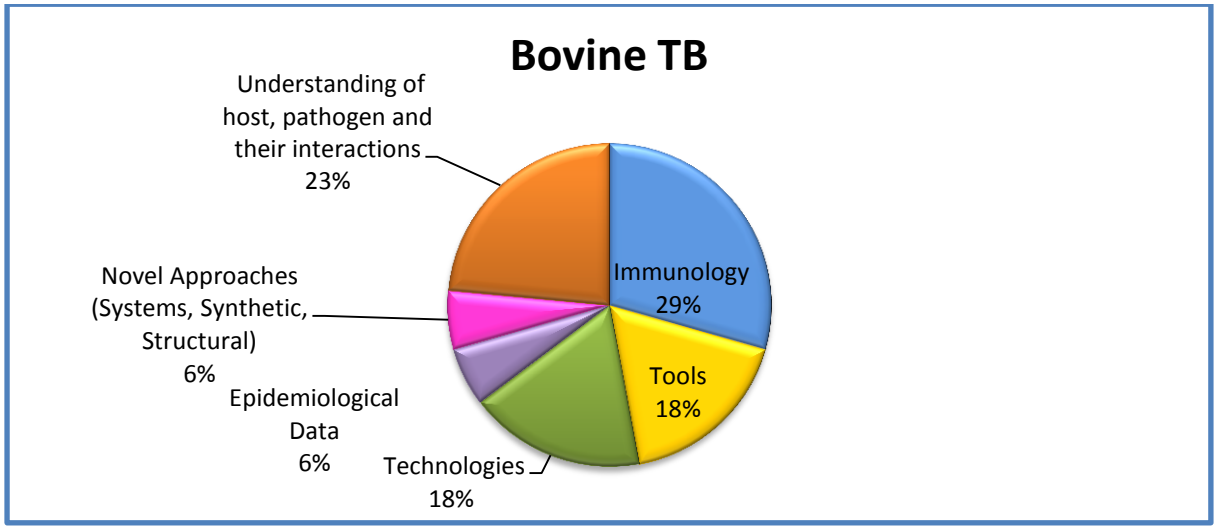
Figure 5a: Challenges based on livestock species






African Swine Fever
Understanding of host, pathogen and their interactions 20%
Immunology 20%
Tools 13%
Technologies 20%
Epidemiological Data 20%
Novel Approaches (Systems, Synthetic, Structural) 7%


Avian Influenza
Understanding of host, pathogen and their interactions 20%
Immunology 16%
Tools 12%
Technologies 16%
Epidemiological Data
Novel Approaches (Systems, Synthetic, Structural) 12%


Bovine TB
Understanding of host, pathogen and their interactions 23%
Immunology 29%
Tools 18%
Technologies 18%
Epidemiological Data 6%
Novel Approaches (Systems, Synthetic, Structural) 6%

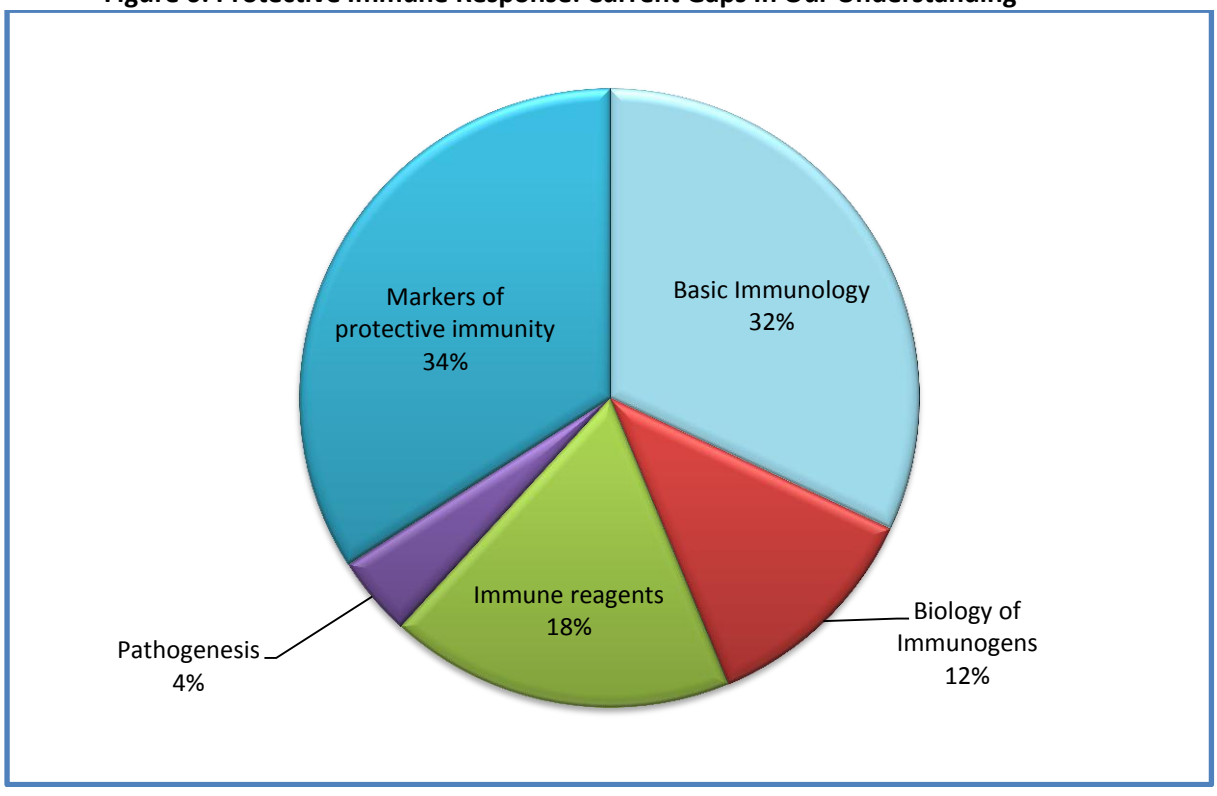
SUMMARY OF THE SECTION IA: CURRENT RESEARCH CHALLENGES IDENTIFIED BY ACTIVE RESEARCHERS

1. **Immunology** including understanding the protective immune response; **Tools (**e.g. safe adjuvants, vectors that are able to express multivalent antigens) **and Technologies** (e.g. vaccine delivery system, thermostablization technologies, challenge models) are the major research challenges that are currently limiting the progress of vaccine research.
2. There are some species and disease-specific differences in the challenges but overall need for immunology, and tools is evident.

Gaps in Understanding of Protective Immune Response

Active researchers were asked to identify further the specific gaps in our understanding of the protective immune response which impact on vaccine research. The responses received were divided under the heading shown in Figure 6.

Figure 6: Protective Immune Response: Current Gaps In Our Understanding



The respondent identified gaps in basic immunology along with specific gaps in

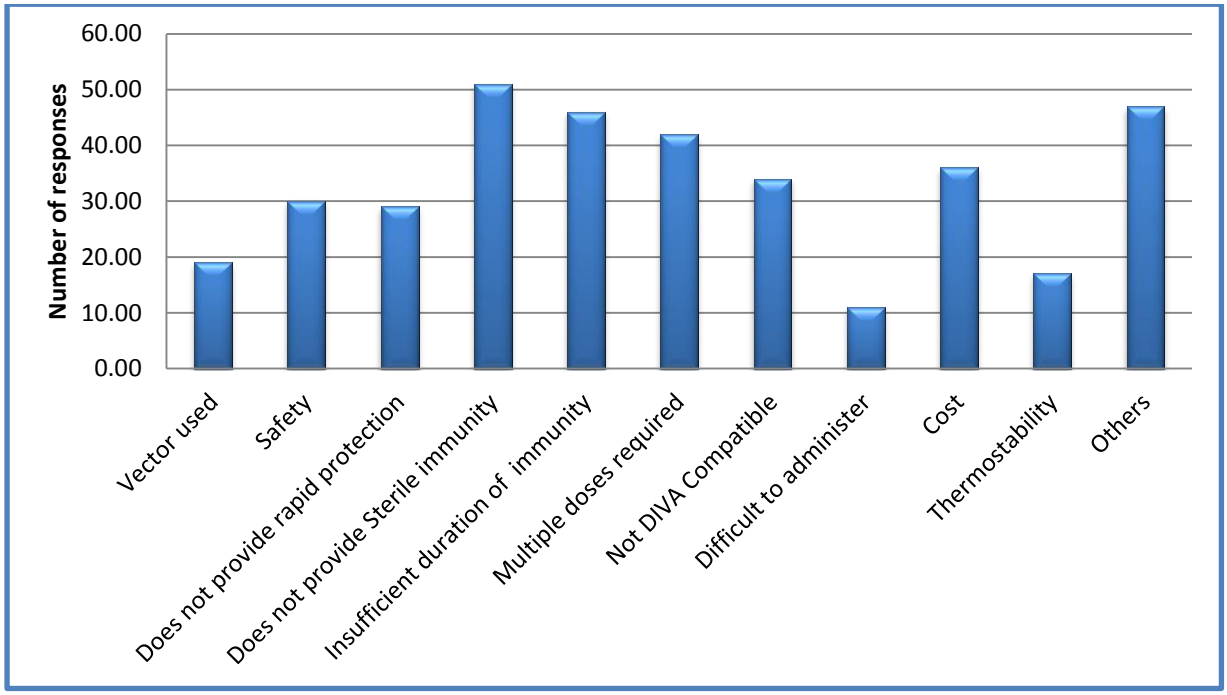
understanding of protective immunity. The need for better methods to identify protective antigens and tools to study protective immunity was also highlighted. The main gaps identified under each heading are in Annex 5.

Scientific and Technical Factors Currently Preventing Candidate/Prototype Vaccines from Practical Field Use

Active researchers were further asked if there are any potential vaccine candidates where there are scientific and technical factors are currently preventing them from practical field use. There were 55 diseases mentioned and the major factors that prevent vaccines from practical field use are shown the Figure 7a and are

- Current vaccines do not provide sterile immunity;
- Current vaccines have insufficient duration of immunity.

Figure 7a: Scientific and Technical Factors that are *Currently* Preventing Candidate Vaccines from Practical Field Use

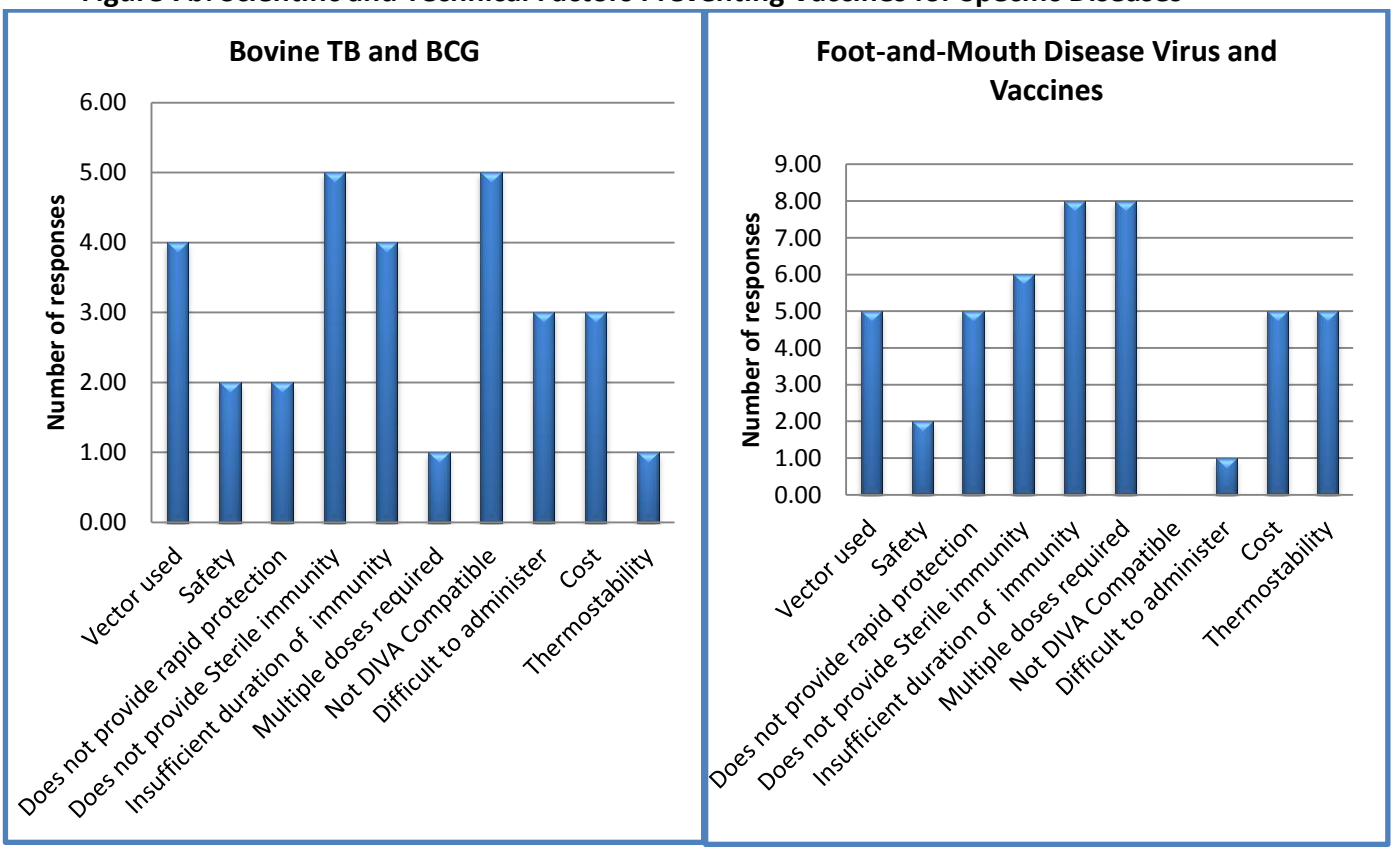


Some of other factors highlighted includes:

- current regulation;
- availability of containment facilities;
- scale-up production facilities;
- need for field testing/efficacy; and
- lack of cross-protection.

From the responses received subtle differences, based on particular disease/current vaccines, were seen as shown in Figure 7b but the overall need for vaccines that provide sterile and long-lasting immunity seems important.

Figure 7b: Scientific and Technical Factors Preventing Vaccines for Specific Diseases

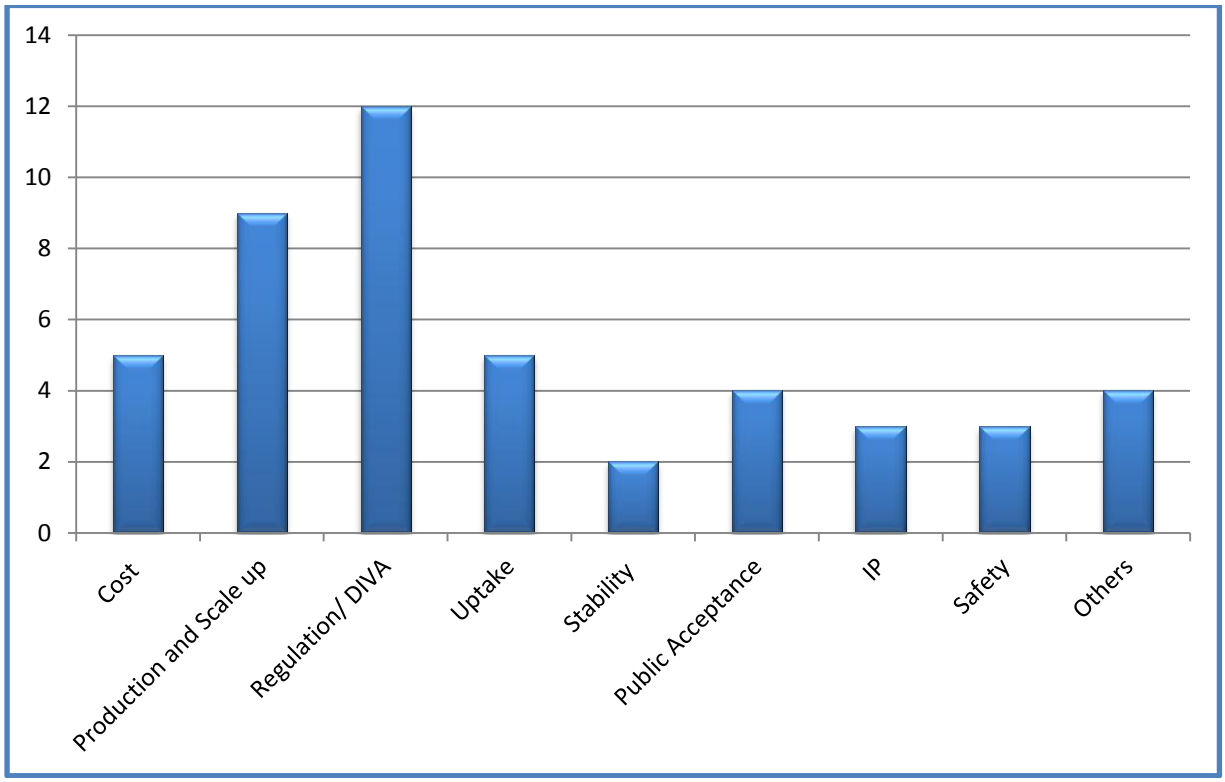


Post-discovery Issues

Active researchers were asked for any post-discovery issues that have prevented specific vaccines becoming available for use. Responses received are shown in Figure 8. The issues such as regulation, uptake of vaccines by Industry, scale-up and production facilities were highlighted.

The respondents also highlighted a number of issues including regulatory and diagnostic interference especially with regards to vaccine against TB, Johne's disease, and Contagious agalactia. Industrial uptake, cost, scale-up, including lasck of scale-up facilities and safety are other limiting factors.

Figure 8: Post-Discovery Issues that have Prevented Specific Vaccines becoming Available for Use



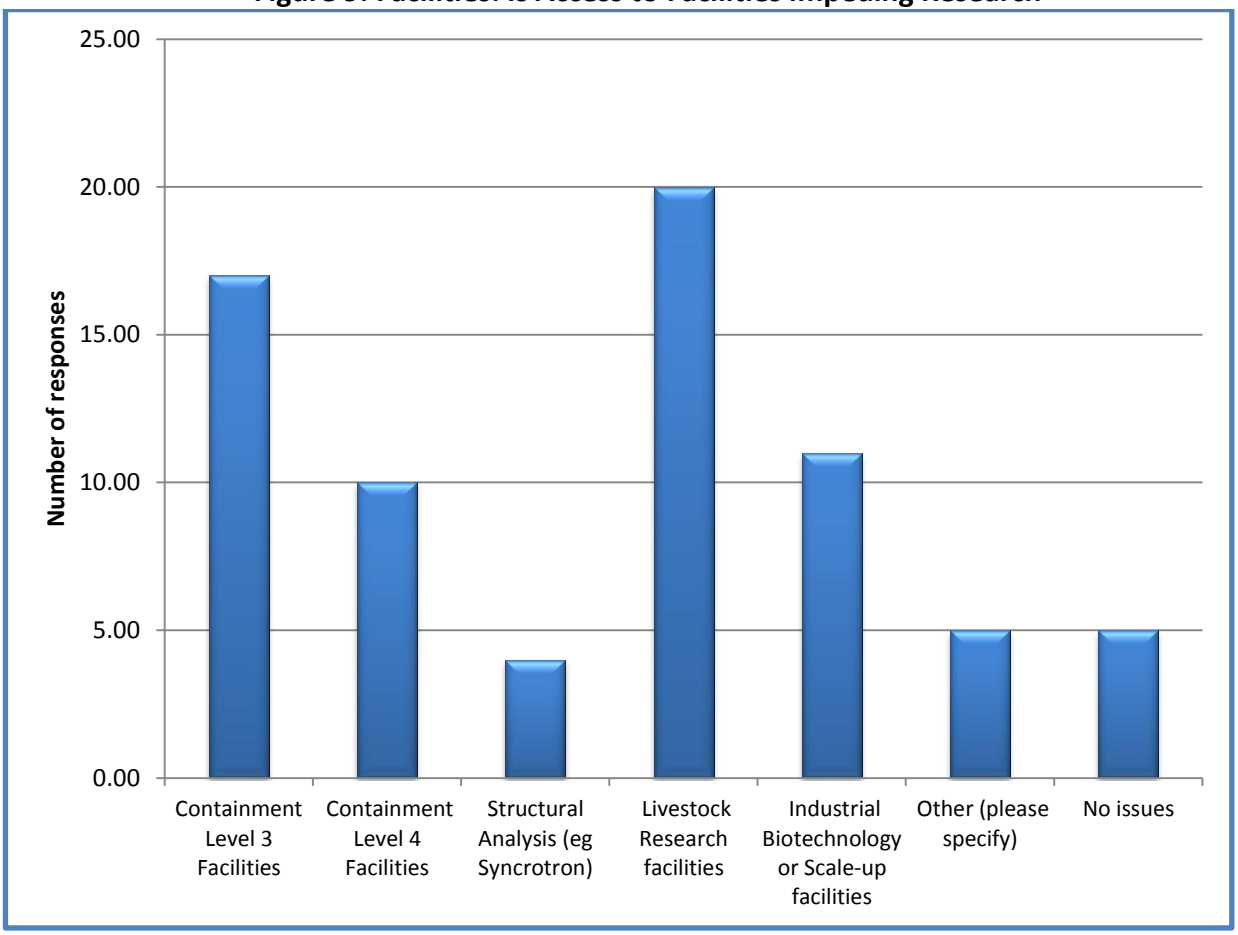
Facilities

Active researchers were asked if lack of access to particular facilities is directly impacting their research. The responses received are summarised in Figure 9. There are four main facilities impacting vaccine research:

- Livestock research
- Containment level 3
- Scale-up
- Containment level 4

Also, highlighted was that in some cases facilities are available but access is highly limited by legal/political reasons. Cost, funding support and trained staff to run these facilities were also an impediment.

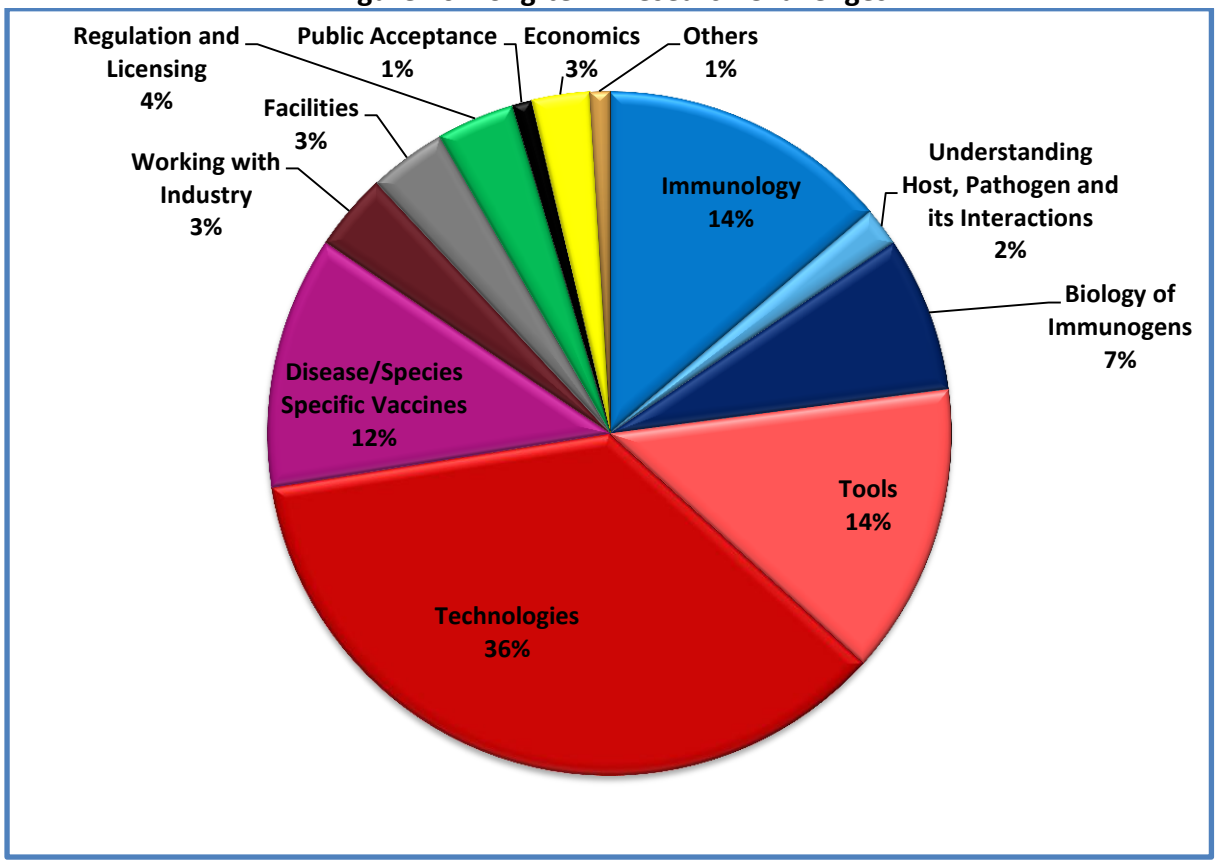
Figure 9: Facilities: Is Access to Facilities Impeding Research



LONG-TERM RESEARCH CHALLENGES

Both science policy/administration professionals and active researchers were asked to identify long-term research challenges for vaccine research. The challenges were then classified under various headings as shown in Figure 10.

Figure 10: Long-term Research Challenges



The three main long-term challenges are in the following areas and described in detail in Annex 6.

- Technologies: It is highlighted as a major future research challenge and the need for omics technologies, delivery systems, novel vaccine development technologies; scale-up and production technologies were all highlighted.
- Immunology: It remains as one of the research challenges of the future with focus on the need for better understanding of the basic host immune response, protective immunity, immunogenetics and proteomics of various animal species.
- Tools: Need for immunological reagents, novel adjuvants, vectors and need for animal models was highlighted.

SUMMARY OF THE SECTION IB: CHALLENGES, GAPS AND FUTURE NEEDS

- Immunology of the protective immune response
- **Long term** research challenge: developing **new tools and technologies**

Others

- Industry engagement
- Facilities

SECTION II: KEY PLAYERS

Some of the key vaccine research institutes/centres/industry identified by the survey are shown below in Table 3.

TABLE 3: Key Vaccine Research Institutes/Centres/Industry

Name	Web address	Expertise
Africa		
International Livestock Research Institute	www.ilri.org	upstream vet vaccinology
Argentina		
Australia		
Australian Animal Health Laboratory	http://www.csiro.au/aahl	Vaccines of diseases exotic to Australia
Bioproperties Pty Ltd	http://www.bioproperties.com.au/	Manufacturing
Australian Animal Health Laboratory	www.csiro.au	Pathogenesis studies, product development and testing
Melbourne University		Veterinary vaccines
WEHI	http://www.wehi.edu.au/	Immunology
Bioproperties Australia	http://www.bioproperties.com.au/	
Belgium		
PROVAXS	www.provaxs.com	Veterinary vaccines
Laboratory of Immunology	http://www.vetimmunology.ugent.be	Mucosal immunisations in pigs, sheep, calves, poultry, Viral infections in pigs and cats
Brazil		
Embrapa Beef Cattle	www.cnpgc.embrapa.br	Vaccines for Cattle
China		
Harbin Vet Res Inst, CAAS	www.hvri.ac.cn/	
Shanghai Vet Res Inst	www.shvri.ac.cn	
Denmark		
State serum institute	www.ssi.dk	Human vaccine, TB Specialist
National Veterinary institute	www.vet.dtu.dk	innate immunity, cellular

Name	Web address	Expertise
		immunity
France		
Vallée Agronegócios	www.vallee.com	Manufacturing
ANSES		
Germany		
FLI	http://www.fli.bund.de/	All kind of infections
Paul-Ehrlich-Institut	www.pei.de	vaccines for human and veterinary use
India		
Indian Veterinary Research Institute	http://www.ivri.nic.in/	Almost all the diseases of Farmed animals (Large and Small ruminants, Pigs), Poultry)
Indian Immunological Limited, Hyderabad	https://www.indimmune.com/	Toxoid vaccines; Contraceptive vaccines; Parasitic vaccines; Viral vaccines; Glyco-conjugate vaccines
MSD Animal Health, Pune	http://www.msd-animal-health.co.in/	Veterinary vaccines: Live and inactivated
Hester Biosciences, Ahmadabad	http://www.hesterbiosciences.co.in/	Veterinary vaccines: Live
Indovax Private Limited, Hisar	http://www.indovax.com/	Biologics
Biovet Pvt. Limited	http://www.biovet.in/	
Ella Foundation	www.ellafoundation.org	Bluetongue, Foot and mouth disease
TANUVAS	http://www.tanuvas.ac.in/	Veterinary vaccines
Indian Veterinary Research Institute	http://www.ivri.nic.in/	Premier institute for biological products and their standardization
Venkateshwara Hatecheries	http://www.indiamart.com/venkateshwara-hatcheries-limited/	
Veterinary Biologicals & Research institute, Hyderabad		Vaccine production
Indonesia		

Name	Web address	Expertise
PUSVETMA	https://www.facebook.com/pusvetma	Government Vaccine production
Italy		
Ministero della Salute	www.salute.gov.it/	Public Veterinary health and drugs/food traceability
Direzione Generale della sanità animale e dei farmaci veterinari Dipartimento della sanità pubblica veterinaria, della sicurezza alimentare e degli organi collegiali per la tutela della salute Ministero della Salute	http://www.salute.gov.it/	
Istituto Zooprofilattico della Lombardia e dell'Emilia Romagna	www.izsler.it	
Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise	www.izs.it	
INTA, Instituto de Virologia	www.inta.gob.ar/unidades/235000/	Virology
Istituto Zooprofilattico Sperimentale delle Venezie	http://www.izsvenezie.it	Rabies, Avian flu
Istituto Superiore di Sanità	http://www.iss.it/	Research, control and consultation
Ireland		
Mexico		
SENASICA, SAGARPA	http://senasica.gob.mx/	National authority and quality control
INIFAP	www.inifap.gob.mx	Bacteriology, Parasitology
New Zealand		
AgResearch	www.agresearch.co.nz	Infectious Diseases/Parasitology/Mastitis
Spain		
Ouro Fino Abronegócios	www.ourofino.com	Animal health
INIA	www.inia.es	
IREC	http://www.uclm.es/irec/	Wildlife vaccines

Name	Web address	Expertise
NEIKER	http://www.neiker.net/default.asp	
VISAVET		
CRESA	www.cresa.es/	pig and ruminant diseases
Sweden		
National Veterinary Institute	www.sva.se	Infectious disseases, zoonoses, animal health
Intervacc	http://intervacc.com/index.php?lang=en	Staphylococci, Strangles, Mastitis
United Kingdom		
The Pirbright Institute	http://www.pirbright.ac.uk/	Viral diseases
The Jenner Institute	www.jenner.ac.uk	human and veterinary vaccines against major global diseases, virus vectors, adjuvants
Moredun Research Institute	http://www.moredun.org.uk/	Bacterial and parasitic diseases, large animal vaccine development, immunology; animal models
Animal Health & Veterinary Laboratory Agency	http://www.defra.gov.uk/ahvla-en/	
Dstl Porton Down	https://www.dstl.gov.uk/	bacterial pathogen vaccinology especially germ warfare, Containment work, vaccine trials
Royal Veterinary College	http://www.rvc.ac.uk/	Diseases of pigs and poultry, Growing centre of vaccinology expertise
University College Dublin	http://www.ucd.ie/	Vaccines for TB in badgers
The Roslin Institute	http://www.roslin.ed.ac.uk/	Bacteriology, Immunology
United States of America		
USDA-ARS	www.ars.usda.gov	Vaccinology
Novavax	http://www.isconova.com/	Influenza
PIADC	http://www.orau.gov/piadc/	Foreign animal diseases
Department of Homeland	http://www.dhs.gov/	

Name	Web address	Expertise
Security		
APHIS	http://www.aphis.usda.gov/wps/portal/aphis/home/	
Global		
Zoetis	http://www.zoetis.com/	
GALVmed	www.galvmed.org	facilitation of vaccine development and distribution
Bavarian Nordic	http://www.bavarian-nordic.com/	developing and manufacturing novel cancer immunotherapies and vaccines for infectious diseases

National Funders

Some of the national funders identified through the survey are listed in Table 4.

TABLE 4: List of National Funders

Name	Website	Expertise	Comments
ACIAR	www.aciar.gov.au		Funded substantial research on I2 Newcastle disease vaccines, that are thermotolerant
Agencia Nacional de Promocion Cientifica y Tecnologica	http://www.agencia.mincyt.gob.ar/		
Animal Health Board			
BBSRC	http://www.bbsrc.ac.uk/home/home.aspx	Basic and fundament bioscience research	
Bill & Melinda Gates Foundation			
Bioproperties Australia	http://www.bioproperties.com.au/	leading Australian novel vaccine research company, GMP manufacturer and global supplier	
BMBF			
CONACYT	www.conacyt.mx	Main source for research grants	

Name	Website	Expertise	Comments
CONACYT	www.conacyt.go.mx	NATIONAL COUNCIL OF SCIENCE AND TECHNOLOGY	INCLUDE ZOONOSES, SSA
Defra	https://www.gov.uk/government/organisations/department-for-environment-food-rural-affairs		
Department of Biotechnology	www.dbtindia.nic.in		
Department of Biotechnology	http://dbtindia.nic.in/index.asp	Funds research projects in the field of biotechnology	
European Commission	http://ec.europa.eu/index_en.htm		
FOD Health	http://www.health.belgium.be/eportal/index.htm	Human Health related research projects	
IFAH	http://www.ifahsec.org/	Whilst located in Belgium, IFAH has a global focus	
Indian Council of Agricultural Research	http://www.icar.org.in/	Funds research projects in the areas Agriculture and Allied Sciences	
Italian Ministry of Health	http://www.salute.gov.it/		
IWT	http://www.iwt.be	Development of applications	
Ministry of Agriculture	www.deptan.go.id	-	
Ministry of Business, Innovation & Employment	www.mbie.govt.nz	multiple	Multiple funders but MBIE would be the best source to find out who all the funders and institutions are.
Ministry of Health	www.salute.gov.it	All animal diseases	
MOA	www.moa.gov.cn		
Ministry of Defence	https://www.gov.uk/government/organisations/ministry-of-defence		
MOST	www.most.gov.cn		

Name	Website	Expertise	Comments
Medical Research Council	www.mrc.ac.uk	funding clinical trials	
National Biosecurity Flagship	http://www.csiro.au/Organisation-Structure/Flagships.aspx	widespread and including both plants and animals	
National Institute of Food and Agriculture (NIFA)	http://www.csrees.usda.gov/		
National Institutes of Health	http://www.nih.gov/		
NZ Government			
Regional Councils, Italy			
RESAS	http://www.scotland.gov.uk/topics/research		
The Swedish Board of Agriculture	www.sjv.se	Agriculture, Laws and Regulations, Animal Welfare	
The Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning	www.forma.se	Reseach funding	
UFRGS	www.ufrgs.br	Vaccines against IBR and BVD	
UNAM	www.unam.mx	EDUCATION, RESEARCH AND CULTURE	LARGEST UNIVERSITY IN LATINAMERICA
USDA-ARS	www.ars.usda.gov	Intramural research	
USDA-REE-NIFA	http://www.csrees.usda.gov/	Extramural research	
Wellcome Trust	www.wellcome.ac.uk	Basic research into vaccinology	

Summary of the section II: Key players

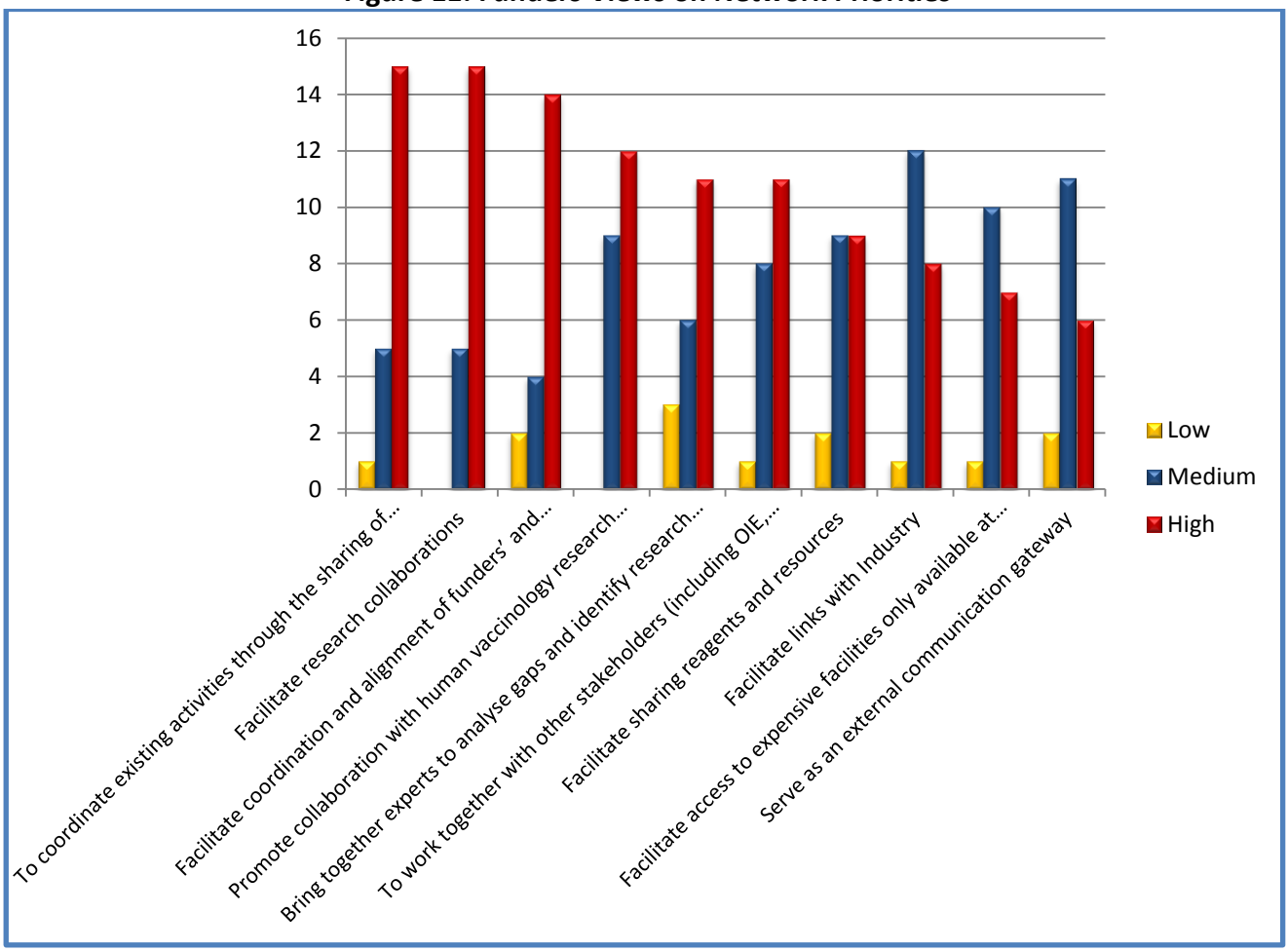
- There are a number of key vaccinology research institutes and funders in various countries

The survey included a set of 10 potential priorities for a Global Research Network for veterinary vaccinology which the respondent were asked to score 1-7 with 7 being essential and 1 not essential. Score of 1&2 was grouped as low priority; 3, 4 & 5 was grouped as medium and the score of 6&7 was combined to form the high priority.

Funders Views on Networking

Figure 11 below shows funders' views on the priorities for the Global Network.

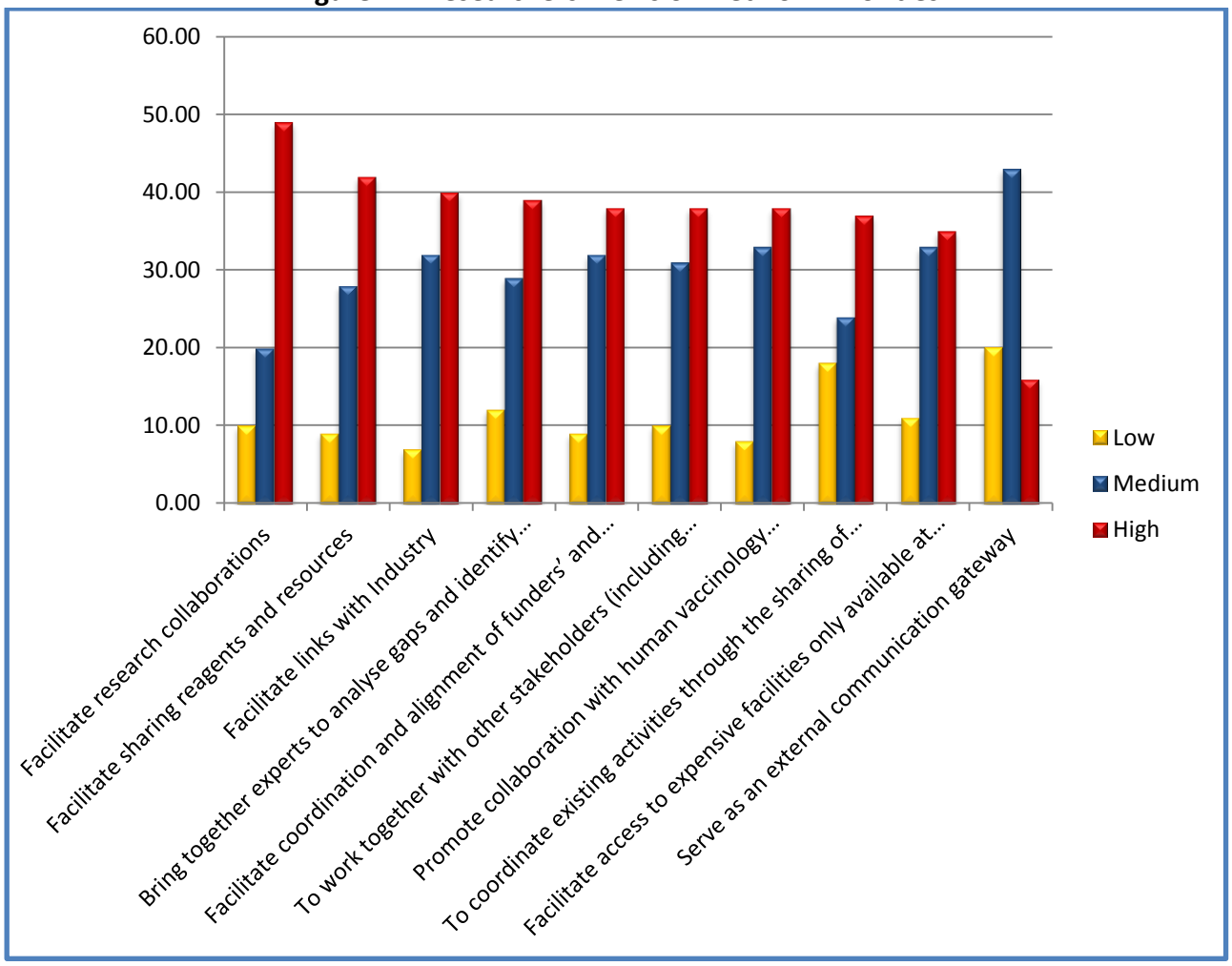
Figure 11: Funders Views on Network Priorities



Active Researchers' Views on Networking

Active Researchers' view on priorities of the Network is shown below in Figure 12.

Figure 12: Researchers Views on Network Priorities



In summary, respondents agreed that the 8 out of the 10 priorities listed were valid but the order of priorities is different for the two groups of respondents as shown in Table 5. The order of preference of the priorities for the Global Network is listed below:

Table 5: Priorities of a Veterinary Vaccinology Network

SCIENCE POLICY OR ADMINISTRATION PROFESSIONALS	ACTIVE RESEACHERS
To coordinate existing activities through the sharing of knowledge	Facilitate research collaborations
Facilitate research collaborations	Facilitate sharing reagents and resources
Facilitate coordination and alignment of funders' and researchers' priorities	Facilitate links with Industry
Promote collaboration with human vaccinology research community	Bring together experts to analyse gaps and identify research priorities
Bring together experts to analyse gaps and identify research priorities	Facilitate coordination and alignment of funders' and researchers' priorities
To work together with other stakeholders (including OIE, WHO) to ensure the effective coordination of national activities	To work together with other stakeholders (including OIE, WHO) to ensure the effective coordination of national activities
Facilitate sharing reagents and resources	Promote collaboration with human vaccinology research community
Facilitate links with Industry	To coordinate existing activities through the sharing of knowledge
Facilitate access to expensive facilities only available at selected locations	Facilitate access to expensive facilities only available at selected locations
Serve as an external communication gateway	Serve as an external communication gateway

SUMMARY OF THE SECTION III: PRIORITIES FOR GLOBAL VETERINARY VACCINOLOGY NETWORK

1. Facilitate research collaborations
2. To coordinate existing activities through the sharing of knowledge
3. Facilitate sharing reagents and resources
4. Facilitate coordination and alignment of funders' and researchers' priorities
5. Bring together experts to analyse gaps and identify research priorities
6. Facilitate links with Industry
7. Promote collaboration with human vaccinology research community
8. To work together with other stakeholders (including OIE, WHO) to ensure the effective coordination of national activities

CONCLUSIONS

There are generic vaccinology research gap/areas that would benefit from coordinated research effort

Current Research Landscape

- Vaccinology research currently covers most species of interest with the major focus on Ruminants
- Basic : Applied research - 62% :38% split
- African Swine Fever was the most common identified threat. Threat is global covering 4 continents
- There are a number of key vaccinology research institutes and funders in various countries.

Research Gaps

- Immunology of the protective immune response
- **Long term** research challenge: developing **new tools and technologies** (DIVA, Synthetic vaccines, Multivalent techniques)
- **Others**
    - Industry engagement
    - Facilities

Veterinary Vaccinology Network

- There is a need for a network in veterinary vaccinology with main aims to **facilitate collaborations**

Vaccinology in Animal Disease – DISCONTOOLS Database Analysis

Analysis of the animal diseases included in the DISCONTOOLs database shows three categories of disease: 1) those with no vaccine, 2) those with a vaccine but not well controlled, and 3) those with a vaccine and well controlled.

1 Diseases without a vaccine

- African Swine Fever
- BSE
- Campylobacter
- Congo Crimean Haemorrhagic Fever
- Cryptosporidiosis
- Liver fluke
- Nematodes
- Nipah Virus
- Swine Vesicular Disease
- Trypanosomiasis
- Varroa mite

In most cases the lack of vaccine is because classical methods of generation have failed and the immunological response is not sufficiently well understood to develop a vaccine using one of the new technologies available. Many are bacteria or parasites rather than viruses. New techniques may produce a vaccine but probably only when the immunology provides a target.

2) Diseases where the available vaccines are less than ideal in terms of the level of control provided

This is by far the largest group of diseases, there being several reasons for a disease to be poorly controlled despite the existence of a vaccine. At the vaccine level these can be simplified to:

1. Safety (particularly live vaccines), efficacy and longevity (particularly attenuated or subunit vaccines)
2. Licencing/production and development (if the market is small)
3. Delivery method and cost (particularly in developing countries)
4. DIVA- ability to distinguish vaccinated from infected animals for reportable diseases

Disease	Status
African Horse Sickness	Live vaccines for endemic situations. Safety issues. Do not protect against all strains. No commercial inactivated or recombinant vaccines

Disease	Status
Avian Influenza	H5, H7 and H9 available. Inactivated and Recombinant vaccines available. Can't vaccinate wildlife reservoir
BHV-1	Vaccines available. Variable efficacy, low duration requires regular boost. DIVA vaccine may show latency
Bovine TB	Vaccine available but not licenced for use, DIVA under development so may change. Efficacy unclear as not tested. Large wildlife reservoir
BRSV	Modified and killed vaccines available. Short term protection and not sterile.
Brucellosis	Live attenuated vaccines available, one of which does not interfere with diagnostic testing. Relatively well controlled in West through vaccination and testing and culling. Endemic in some areas. Increasing in Asia. Public health issue from infected milk
Contagious Bovine Pleuro Pneumonia	Not commercially available Attenuated T1/44 vaccines produced by various African institutions. Short term protection- 1 year , vaccine unstable at RT. Safety issue- Reactions occur requiring antibiotic treatment
Chlamydiosis	Killed and live vaccines available, not in all countries. Not completely protective and shedding still occurs
Cysticercosis A	Recombinant vaccine registered in New Zealand but not produced due to market changes. 2 vaccines effective in field trials. Duration of immunity unknown
E.Coli	Vaccine against type III secreted proteins in Canada. Another product has conditional approval in US. No global availability, may not protect against other types
Echinococcosis	Vaccine licenced for sheep in New Zealand. Testing required
Environmental/Streptmastitis	Inactivated vaccine available. Efficacy Questionable. Methods to evaluate efficiency in the field required
Foot and Mouth Disease	Inactivated vaccines available, Safety, and length of immunity are issues
hepatitis E	Vaccines available for humans not animals. One under development
Leishmaniasis	Available in Brazil but not EU. Too costly for endemic regions. Efficacy and DIVA testing required
Leptospirosis	Vaccines available for cattle, pigs and dogs. Large wildlife reservoir. Do not provide complete protection or prevent shedding, vaccines protection is short duration and lack broad specificity
Lumpy Skin Disease	Live attenuated vaccine available in Africa. Mechanism of attenuation is unknown, safety and potency issues

Disease	Status
Mycoplasma Bovis	Available in USA, chronic lesions can develop, research on immune response and disease development required.
Orthopox	Available in USA for humans
Peste des Petits ruminants	Live attenuated virus, good immunity but not Diva. Protection 3years.
Paratuberculosis	Live and attenuated vaccines available. Used only in young animals, not sterile, Issues with DIVA and TB testing. Large pool of non-symptomatic carriers
PRRS	Inactivated and attenuated vaccines available to both genotype 1 and 2. Reduced efficacy to different strains. Safety and Efficacy issues
Rift Valley Fever	One inactivated vaccine - low level protection ad requires booster. Live attenuated vaccine has some pathogenicity. Recently improved safety profile
Salmonellosis	Live and inactivated vaccines available. Genetically modified vaccines are available in certain countries but not universally. No marker vaccines are available currently. Gaps includes: Work to define efficacy of live-killed vaccine combination programmes; and Multi -serovar/serogroup protection and development and availability of Marker vaccines
Q- Fever	At the Global level, several vaccines have been developed against animal Q fever but only phase I vaccine has revealed to be protective against a virulent challenge, low production level and supply
Sheep and Goat Pox	Vaccines available. Mechanism of attenuation unknown. Efficacy of inactivated vaccines questionable
Small Ruminant Mastitis	Live vaccines are not permitted in Europe but formalin inactivated, adjuvanted vaccines are available. Globally live attenuated vaccines are available. In Europe formalin inactivated, adjuvanted vaccines are available. There appears to be little data available on the efficacy of these inactivated vaccines.
Staphylococcus mastitis	2 vaccines based on killed bacteria available. Efficacy needs testing. Apparently poor prevention.
Swine a. Pleuropneumonia	Some vaccines available. In EU autogenous bacterins or toxin based
Swine Mycoplasma	Effective reduction in Symptoms but transmission still occurs
Theileria	Cell culture vaccine. Risk of introducing new strains to tick population requires local production. Subunit vaccines in development- efficacy unknown
West Nile Virus	Several licenced in US. Good safety and efficacy but require boosts. No DIVA

Areas of research with potential general applicability:

- The immune response to understand why attenuated and sub unit vaccines are less effective than live viruses, including the use of adjuvants
- The immunological response to pests and parasites needs elucidation. Current successful vaccines are often based on whole parasite antigens which are expensive to produce.
- DIVA methods
- Improved Stability

3) Diseases with a vaccine where control has been achieved

These diseases have not been eradicated but current vaccines are effective and safe and have been used to control the effects of disease successfully when combined with proper management and testing.

Disease	Status
Anthrax	Requires annual treatment. Effectiveness in different species unknown
Bluetongue	Widely available live and inactivated vaccines. New serotypes may need vaccines. Some licencing issues. No DIVA
Classical Swine Fever	Excellent vaccines available, widely used in pigs and oral vaccines for wild boar. DIVA only tested in Romania.
Coccidiosis	Live vaccines available for Chickens. An effective anticoccidial vaccine is required to protect against clinical coccidiosis and minimise the economic and welfare impact of subclinical coccidiosis without compromising the efficiency of production. Sterile immune protection is not essential. New vaccines should be capable of inducing immune protection without a requirement for recycling of oocysts, indicating a need for improved immune stimulation.
PCVII	Vaccines available globally. Better delivery methods needed
Rabies	Wide range globally. Expensive for endemic areas
Swine Influenza	Variety of effective vaccines. Novel technologies also being tested.

ANNEX 2

STAR-IDAZ: VETERINARY VACCINOLOGY SURVEY QUESTIONNAIRE

The EU FP7-funded Global Network STAR-IDAZ (Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses) aims to coordinate research on the major infectious diseases of livestock and zoonoses. Details are available at http://www.star-idaz.net/. The Consortium has identified a number of priority diseases/issues for collaborative activities at a global level. Vaccinology is one of the areas where the need for global coordination was identified by the STAR-IDAZ members.

This questionnaire has two main aims:

- Identify current research activities, gaps and future needs in Veterinary Vaccinology
- Prioritise objectives for a Global Network in Veterinary Vaccinology and identify potential members and key stakeholders for such a Network

The information you provide will be used to inform the development of future collaborative activities within **STAR-IDAZ Work Package 4 - Networking of on-going research activities on major animal health issues**.

The collated survey results will be presented at the next STAR-IDAZ meeting and a written report will be published on the STAR-IDAZ website.
If you would like further clarification on any part of the survey, please contact either Dr Merewyn Loder (merewyn.loder@bbsrc.ac.uk) or Dr Sadhana Sharma (sadhana.sharma@bbsrc.ac.uk).

Please note: Individual information provided will only be used for the purpose of STAR-IDAZ and will only be available to STAR-IDAZ partners and the European Commission.

Deadline: 10 MAY 2013

1. Your name and contact details:

Name

Role

E-mail address

Telephone number

Country

Organisation

Web site

Please indicate whether you are completing the survey as an Active Researcher or as a Science Policy or Administration professional. If you are research active please respond as a researcher even if you also have policy or administration roles.

- Active Researcher
- Science Policy or Administration professional

SECTION I: CURRENT RESEARCH ACTIVITIES IN VETERINARY VACCINOLOGY

Q1. Where appropriate, please indicate the top diseases of various livestock sectors where you are providing funding for vaccinology research

Please leave blank any fields which you do not fund

Species	Diseases 1	Diseases 2	Diseases 3	Comments
Cattle				
Small Ruminants (Sheep and Goats)				

Pigs				
Poultry				
Equines				
Bees				
Aquatic				
Others				

Q2. Please indicate major diseases/threats in your country for which a vaccine is needed and why

Diseases/Threats	Species	Issues	Comments

Q3. Please indicate whether there are any legal, intellectual property, regulatory or safety issues you are aware of which inhibit specific vaccines becoming available for use.

Q4. What are the long-term research challenges in veterinary vaccinology which need to be addressed (please list up to 3 major challenges which could include scientific, technical, or logistical issues)?

SECTION II: KEY PLAYERS

Q5. Please provide the names and any contact information for key vaccinology players in your country:

Institutions	Web address

Researchers	Expertise

Funders	Web address

Q6. Please provide names (and any contact information) of key veterinary vaccinology industries/companies in your country. (Key companies might include large pharmaceutical companies with a vaccinology component or small specialist companies).

Name	Contact Information (Website address)

Q7. Please provide names of any other national or regional veterinary vaccinology networks/organisations (e.g. learned societies, industrial platforms).

SECTION III: GLOBAL VETERINARY VACCINOLOGY NETWORK

Q8. What should be the priorities of a Global Research Network for veterinary vaccinology? Score 1-7 with 7 being essential and 1 not essential

Priorities	1	2	3	4	5	6	7	Comments
To coordinate existing activities through the sharing of knowledge								
Facilitate research collaborations								
Serve as an external communication gateway								
Bring together experts to analyse gaps and identify research priorities								
Facilitate sharing reagents and resources								
Facilitate links with Industry								

Facilitate coordination and alignment of funders' and researchers' priorities								
To work together with other stakeholders (including OIE, WHO) to ensure the effective coordination of national activities								
Facilitate access to expensive facilities only available at selected locations								
Promote collaboration with human vaccinology research community								
Other (please specify)								

Thank you for taking the time to complete the survey.

ANNEX 3

STAR-IDAZ: VETERINARY VACCINOLOGY SURVEY QUESTIONNAIRE

The EU FP7-funded Global Network STAR-IDAZ (Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses) aims to coordinate research on the major infectious diseases of livestock and zoonoses. Details are available at http://www.star-idaz.net/. The Consortium has identified a number of priority diseases/issues for collaborative activities at a global level. Vaccinology is one of the areas where the need for global coordination was identified by the STAR-IDAZ members.

This questionnaire has two main aims:

- Identify current research activities, gaps and future needs in Veterinary Vaccinology
- Prioritise objectives for a Global Network in Veterinary Vaccinology and identify potential members and key stakeholders for such a Network

The information you provide will be used to inform the development of future collaborative activities within **STAR-IDAZ Work Package 4 - Networking of on-going research activities on major animal health issues**.

The collated survey results will be presented at the next STAR-IDAZ meeting and a written report will be published on the STAR-IDAZ website.
If you would like further clarification on any part of the survey, please contact either Dr Merewyn Loder (merewyn.loder@bbsrc.ac.uk) or Dr Sadhana Sharma (sadhana.sharma@bbsrc.ac.uk).

Please note: Individual information provided will only be used for the purpose of STAR-IDAZ and will only be available to STAR-IDAZ partners and the European Commission.

Deadline: 10 MAY 2013

ANNEX 3

Your name and contact details:

Name

Role

E-mail address

Telephone number

Country

Organisation

Web site

Please indicate whether you are completing the survey as an Active Researcher or as a Science Policy or Administration professional. If you are research active please respond as a researcher even if you also have policy or administration roles.

- Active Researcher
- Science Policy or Administration professional

SECTION I: CURRENT RESEARCH ACTIVITIES IN VETERINARY VACCINOLOGY

Q1. Where appropriate, please indicate the top (up to five) diseases of various livestock sectors in which you are undertaking research in vaccinology. Please indicate if the research is applied or basic and a major or minor research area. (Applied research includes: vaccine development, production, or testing etc. Basic research includes: underpinning immune responses, host-pathogen interaction, pathogen biology etc.).

Please leave blank any fields where you do not work.

Species	Diseases (up to 5)	Basic Vaccinology	Applied Vaccinology	Major Area	Minor Area
Cattle					

ANNEX 3

Species	Diseases (up to 5)	Basic Vaccinology	Applied Vaccinology	Major Area	Minor Area
Small Ruminants (sheep and goats)					
Pigs					
Poultry					

ANNEX 3

Species	Diseases (up to 5)	Basic Vaccinology	Applied Vaccinology	Major Area	Minor Area
Equine					
Bees					
Aquatic					

ANNEX 3

Species	Diseases (up to 5)	Basic Vaccinology	Applied Vaccinology	Major Area	Minor Area
Any other					

Q2. Where possible, please describe the research challenges which are currently limiting progress of veterinary vaccine research in diseases that are your major focus of research.

Diseases and Species	Immunology (e.g. understanding the protective immune response, immunological reagents)	Vaccinology tools (e.g. safe adjuvants, vectors that are able to express multivalent antigens)	Technologies (e.g. vaccine delivery system, thermostablization technologies, challenge models)	Epidemiology Data	Novel Approaches (Systems, Synthetic and Structural Biology)	Understanding Host, pathogen and their interactions	Other (please specify)	Any other comments

ANNEX 3

Q3. Please list any potential vaccine candidates where there are scientific and technical factors that are currently preventing them from practical field use.

Vaccine and Disease	Vector used	Safety	Does not provide rapid protection	Does not provide sterile immunity	Insufficient duration of immunity	Multiple doses required	Not DIVA Compatible	Difficult to administer

Q4. Please list any potential vaccine candidates in your field where scientific and technical factors mean that they are not ideal for use (giving the reasons why?)

Q5. What specific gaps are there in our understanding of the protective immune response which impact on vaccine research? (Please list up to 3 gaps)

Q6. What are the long-term research challenges in veterinary vaccinology? Please list up to 3 major challenges (<50 words each) which could include technical, logistical or scientific issues.

Q7. Please describe any post-discovery issues that have prevented specific vaccines becoming available for use (e.g. legal, intellectual property, regulatory or safety issues, industrial uptake, scale-up facilities, production, cost and others).

Disease	Species	Issues	Comments

Q8. Within you country, is access to any of the following facilities directly impacting your research?

	Containment Level 3	Containment Level 4	Structural Analysis (e.g. Synchrotron)	Livestock Research Facilities	Scale-up Facilities	Others (please specify)	Comments
Access to							

SECTION II: KEY PLAYERS

Q8. Please provide the names and any contact information for key vaccinology players in your country:

Institutions	Web address

Researchers	Expertise

ANNEX 3

Funders	Web address

Q9. Please provide names (and any contact information) of key veterinary vaccinology industries/companies in your country. (Key companies might include large pharmaceutical companies with a vaccinology component or small specialist companies).

Q10. Please provide names of any other national or regional veterinary vaccinology n
e
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SECTION III: GLOBAL VETERINARY VACCINOLOGY NETWORK

works/organisations (e.g. learned societies, industrial platforms) you are aware of.

Q11. What should be the priorities of a Global Research Network for veterinary vaccinology? Score 1-7 with 7 being essential and 1 not essential

Priorities	1	2	3	4	5	6	7	Comments
To coordinate existing activities through the sharing of knowledge								
Facilitate research collaborations								
Serve as an external communication gateway								
Bring together experts to analyse gaps and identify research priorities								
Facilitate sharing reagents and resources								
Facilitate links with Industry								
Facilitate coordination and alignment of funders' and researchers' priorities								

To work together with other stakeholders (including OIE, WHO) to ensure the effective coordination of national activities								
Facilitate access to expensive facilities only available at selected locations								
Promote collaboration with human vaccinology research community								
Other (please specify)								

Thank you for taking the time to complete the survey. It will really help.

ANNEX 4

Diseases of livestock Species for which there is on-going vaccine research

Large Ruminants	Small Ruminants	Pigs	Poultry	Equine	Aquatic
Anaplasmosis	Abortion (Toxoplasma gondii)	Actinobacillus pleuropneumoniae	Avian metapneumovirus	African horse sickness	A. veronii
Anthrax	Anaplasmosis	African swine fever	Adenoviruses	Anthrax	Aeromonas salmonicida
Arcanobacterium pyogenes	Anthrax	Atrophic rhinitis	Avian Influenza	Equine babesiosis	Bacterial infections
Babesiosis	Arcanobacterium pyogenes	Brachyspira hyodysenteriae	Avian Paramyxoviruses	Equine Herpes Virus Infection	Betanodavirus
Bovine Herpes Virus (Bovine Herpes mammillitis)	Babesiosis	Chlamydia suis	Campylobacter	Equine herpesviruses	Candida albicans
Bluetongue	BDV	Clostridium enterotoxiemia	Chicken anaemia virus	Equine Influenza	Herpesvirus
Bovine piroplsamosis	Blackleg	Classical Swine Fever	Chlamydia psittaci	Equine rhinitis viruses	Infectious Pancreatic Necrosis
Bovine respiratory syncytical virus (BRSV)	Bluetongue (BT)	E. coli	Coccidiosis	Equine Rotavirus gastroenteritis	Lactococcosis
Bovine TB	Campylobacter abortion	Enterotoxigenic E. coli (ETEC)	E. coli	Equine theleiriosis	Mycobacterium marinum
Bovine Viral Diarrhoea	CCPP	Foot Mouth Disease	Escherichia coli (APEC)	Glanders	Parvovirus
BPV	Chlamydial abortion (OEA) (Chlamydial infections)	Ileitis (Lawsonia intracellularis)	Inclusion body hepatitis (FAdV)	Hendra virus	Proliferative kidney disease
Contagious bovine pleuropneumonia	Clostridiosis	Influenza	Avian infectious laryngotracheitis (ILT) herpesvirus	Japanese Encephalitis	Saprolegnia
Chlamydia abortus	Colibacillosis	Leptospirosis	Infectious bronchitis	Rhodococcus equi	Staphylococcus aureus
Clostridium enterotoxiemia	Contagious agalactia	Oedema disease	Mareks Disease	Strangles	Streptococcus
E. coli O157 & other STEC	Corynebacterium pseudotuberculosis	Parasitic diseases	Mycoplasma	Streptococcus equi	Viral infections
Foot and mouth disease	Foot and Mouth Disease	Pleuropneumoniae	Necrotic enteritis	West Nile virus	Yersinia ruckeri
Heartwater	Fasciola hepatica	Porcine circovirus type 2 (PCV2)	Newcastle Disease		

ANNEX 4

Large Ruminants	Small Ruminants	Pigs	Poultry	Equine	Aquatic
Helminth infection: D. viviparus	Haemonchus contortus	Porcine reproductive and respiratory syndrome (PRRS)	RAI		
Helminth infection: Fasciola hepatica	Johnes Disease	porcine respiratory disease complex (PRDC)	Red mite		
Infectious bovine rhinotracheitis	Mastitis including Staphylococcal mastitis	Mycoplasma hyopneumoniae	Salmonella		
Intestinal nematodes	Mycoplasma agalactiae	Respiratory tract bacterial disease			
Johne's Disease	Nairobi sheep disease/Ganjam	S. suis infection			
Leptospirosis	Pasteurellaceae	Salmonella			
Lumpy skin disease	Peste des petits ruminants (PPR)	Swine dysentery			
Malignant Catarrhal Fever	Q fever	Toxoplasma gondii			
Mastitis - E. coli, Streptococcus uberis	Rift Valley Fever	Tuberculosis			
Mecistocirrus digitatus	Salmonellosis abortion	Verotoxigenic E. coli (VTEC)			
Metritis	Schmallenberh	Weaning diarrhoea			
Mycoplasma bovis	Sheepox and goat pox				
Neospora caninum	Teladorsagia circumcincta				
Papillomatosis	Tuberculosis				
Parasitology - Flies	Zoonosis, EHEC				
Parasitology - ticks borne Diseases					
PPCB					
Q fever					
Rabies					
Rift Valley Fever					
Salmonella					

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
The interaction of the pathogen with the host immune system, especially during early infection	Discriminating between immunogenicity, immunodominance and immunoprotection	Lack of immunological tools	Poor understanding of epitopes	The virus components contributing to pathogenesis
Impact of different types of immune responses on the disease process	Poor understanding of disease associated immune profiles	Few reagents available to describe the nature and consequences of immune responses in food-producing animals.	Understanding the structures of immunogenic glycans and glycan-receptor interactions . Glycan-based vaccine formulation	Lack of understanding of in vivo pathogenesis
Onset of immunity and duration of immunity	Essential protective response, correlates of protection	Lack of availability of reagents for testing protective immunity	Knowledge of protective antigen / epitope within an antigen	Basic virus replication and pathogenesis
Lack of understanding of basic mucosal immunity	Needs of marker/indicator of protection	Lack of reagents for determining the cellular immunity for some target species	identity of protective antigens	Need to apply vaccines in a therapeutic setting post infection
Lack of understanding of immune regulation	Correlates of immunity and pathology	There are no reactives for determining the cellular immunity for some target species	Contribution of antigen folding and post-translational modification to protective immunity	Understanding virulence and pathogenicitity of the pathogen

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
Sequence information on innate immunity genes in livestock	Lack of understanding of fundamental aspects of protection	Lack of antibodies to leucocyte markers, and secreted products.	Better understanding of epitopes/structures/modifications important for inducing protective immune responses	
Interaction of innate and adaptive immunity	Failure to understand the basic immunology of protection	Relevant practical livestock models	How immune responses are driven by particular antigens	
Role of innate immunity mechanisms of persistence	How to initiate protective immune response	Experimental model systems and reagents for adequately monitoring pathogen-host interactions and immunity in target species	What antigens stimulate a protective immune response	
Understanding of Basic Immunology of various species	Immune correlates of protection against primary infection and transmission	Species specific Adjuvants/delivery systems	Ideal antigen candidates	
Uncertain importance of mucosal versus systemic immunity	IgG response detected in blood has been never	Lack of safe, effective delivery systems suitable for bait or	Consequences of vaccine-induced immunity on antigenic variation	

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
	related to clinical protection	aerosol delivery		
Innate and adaptive response interplay	Poor understanding of disease associated immune profiles	Adjuvants cheap and effective ones	high variability and antigenic variants of many viiruses	
Understanding activation of innate immunity to improve vaccine delivery systems	Innate immune signatures to improve protective immunity.	Adjuvancy required to stimulate the correct response	The specific antigens that are protective have not been fully characterised	
How can we efficiently activate the intestinal mucosal immune system via the parenteral route	Precise identification of immune mechanism really involved in long-term protection/rapid protection	Adjuvants cheaps and effective ones -In fishes, delivery systems and appropiate diagnostic tests	Understanding of pathogen determinants that prevent or evoke protective immune responses and prohibit or promote protection against infection	In some vaccines (e.g. MDV), we have no understanding of how vaccine works
Role of small ruminant peripheral immune system (udder and mammary lymph-nodes) in establishment of protection against the disease	Defining precisely which immune responses are crucial for protection	immunogenicity and adjuvants		

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
Interaction host-bacteria	Lack of knowledge of the role of antibodies in protection	Safe adjuvants for specific improvement of immune mechanism involved in protection.		
how best to elicit effective and prolonged immunity at both mucosal and systemic immune effector sites	Lack of knowledge of protective antigens including those recognised by CD8 T cells	DIVA vaccines		
unknown immune response against BTV and AHSV in ruminants and horses.	Basis for cross-protective immune responses	Effective detection method		
Signals received by a naive B or T cell in the priming phase to develop into memory cell	Basis of protective responses in different organ systems (e.g. udder)	Methods for routine mucosal delivery to stimulate an appropriate local response in the gastrointestinal mucosa		
More attention should be given to cell mediated immunity	Unknown correlates and mediators of protection	Challange for wildlife vaccines is lack of safe, effective delivery systems suitable for bait or aerosol delivery		

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
Role of innate response on protection.	Understanding how to induce immunoprotective responses that will protect against infection by different parasite species	Difficulties in laboratory maintaining of Babesia strains in culture due to the need of fresh bovine blood as culture medium.		
How can we efficiently target the mucosa with subunit vaccines (circumvent tolerance and reach mucosa-associated lymphoid tissues)	Understanding the protective immunity mechanism against parasitic diseases			
Insufficient understanding of udder immunity	Innate immune signatures to improve protective immunity			
Cellular immune response along with antibody-responses are not well defined for diseases like EHV, JEV, Equine Influenza.	Contribution of cellular immunity to protection from infection of (facultative) intracellular bacterial pathogens in			

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
	animal hosts			
Mechanisms of immunity to most fish pathogens are unknown.	How to initiate protective immune response			
It is important to improve the use of the flow cytometry to better understand the interaction host-pathogen in the immunity contest	Contribution of cellular immunity to protection from infection			
The antigenic variation of M. agalactiae surface antigen could reasonably be one of the causes of the loss of efficacy of host immune response but there is still lack of information regarding host immune response induced by mycoplasma	Understanding the protective immunity mechanism against parasitic diseases			

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
Role of small ruminant peripheral immune system (udder and mammary lymph-nodes) in establishment of protection against the disease	Innate immune signatures to improve protective immunity			
Interaction host-bacteria	What is the precise protective immune response? Helminth parasites stimulate Th2 responses - are these protective or does this bias prolong parasite survival			
Understanding how best to elicit effective and prolonged immunity at both mucosal and systemic immune effector sites	Correlates of protection for different types of vaccines			
unknown immune response against BTV and AHSV in ruminants and horses.	Early identification of protective immune response			

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
Mechanisms that drives long-term antibody responses	Understanding of differences in response of different pigs to vaccination with live attenuated strains.			
Signals received by a naive B or T cell in the priming phase to develop into memory cell	Nature and scope of immune response at vaccination			
Significant gaps in our understanding of avian immune system.	How the vaccine works			
More attention should be given to cell mediated immunity	How can a vaccine circumvent maternal immunity			
Role of immune system in persistence / latency	Why certain vaccines can not generate long term immunity			
How can we efficiently activate the intestinal mucosal immune system via the parenteral route	Why certain vaccines can not generate long term immunity (CTL response?)			

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
How can a vaccine circumvent maternal immunity	Mechanisms that drives long-term antibody responses			
Insufficient understanding of udder immunity	We need more information on immune responses to different vaccines and pathogens			
Cellular immune response along with antibody-responses are not well defined for diseases like EHV, JEV, Equine Influenza.	In some vaccines (e.g. MDV), we have no understanding of how vaccine works			
	Role of innate response on protection			
	Precise identification of immune mechanism really involved in long-term protection/rapid proteccion			

Gaps in Understanding of Protective Immune Response

ANNEX 5

Basic Immunology	Markers of Protective Immunity	Immune Reagents	Biology of Immunogen	Pathogenesis
	How can we efficiently target the mucosa with subunit vaccines (circumvent tolerance and reach mucosa-asscociated lymphoid tissues)			
	Understanding how to induce immunoprotective responses that will protect against infection by different parasite species			
	Consequences of vaccine-induced immunity on antigenic variation and how this may affect vaccine efficacy, cross-protection/immune enhancement			

LONG-TERM CHALLENGES

IMMUNOLOGY

Basic Immunology

- A basic understanding of the host immune system
- Probing the microbiome and its development in new-borns
- Cellular immunology and driving a cellular mediated immune response instead of the focus on antibody response
- How to elicit effective and prolonged immunity at both mucosal and systemic immune effector sites
- Role of the immune-inflammatory response

Protective Immunology

- Understanding protective immune phenotype and correlates of protection
- Basic scientific studies in natural host about immune responses against pathogen and vaccines
- Identifying effective modifications to enhance disease resistance and regenerate it after major disease challenge
- New immune modulators to increase protective immunity

Immunogenetics

- Large animal immunogenetics and proteomics
- Immune gene function

HOST-PATHOGEN INTERACTIONS

Pathogen diversity, emergence and re-emergence of pathogens will remain a challenge for effective vaccination. There is need for better understanding host response for a more rational design of vaccine strategies

TECHNOLOGIES

Veterinary vaccinology research has to be focused in adopting new developments in technology and there is insufficient use of new technologies to design vaccines for the purpose intended; e.g., prevent transmission, DIVA

OMICS

- Genomics tools to study host-pathogen interactions

Vaccine Development Technologies

Future research should be aimed at developing vaccines that approach the ideal as closely as possible and which are directed against diseases not yet controlled by vaccination and against newly emerging diseases. There is a need for technologies for generating

- Multivalent vaccines
- Carbohydrate vaccines
- DNA vaccines
- Recombinant vaccines that are cheap, safe and effective
- Mutant vaccines
- DIVA (markers vaccine): safe and effective
- Vaccines against intracellular infections
- Vaccines that provide long duration immunity, cross-protection & sterile immunity
- Single dose vaccines
- One-shot vaccination in presence of maternal immunity and targeting all serotype
- Vaccines that induce strong and long-term immunity
- Safe vaccines that meet regulatory and consumer needs
- Efficient vaccine in the filed
- Cheap, effective, practical and cost-effective vaccines

<u>Production/Scale up</u>

- Affordable production platform technologies to grow large-scale vaccines and recombinant vaccines
- Effective pathogen-free vaccines with yields suitable for industrial production
- Improvement of cold chain system

<u>Generic Technologies</u>

- Thermostabilisation technologies
- Reverse Genetic Technology
- Novel recombinant expression systems for production of viral, bacterial and parasitic recombinant vaccines
- Strategies to broaden heterologous protection
- New technologies for studying viral diversity

<u>Delivery systems</u>

- Better knowledge of the responses in different hosts following immunisation with various delivery systems and effective delivery systems to stimulate appropriate immune response
- Easy and cost effective delivery system with broad coverage
- Effective and safe oral (aersol) and nasal delivery systems

- Effective delivery systems for mass administration
- Non-invasive delivery

BIOLOGY OF IMMUNOGENS

- Identification/selection approaches to rapidly identify & define new, effective, protective and cross-reactive antigenic epitopes and important targets at the host level. This would then feed into different areas of research on exploitation and mechanistic description on relevant (meaningful) host pathogen interactions.
- Development of thermo-stable immunogens for vaccine programs in developing countries
- Understand virulence determinants for recombinant vaccines
- Identification of "universal" immunogens that are able to protect against different serotypes, subtypes, etc.

TOOLS

Immunological Tools

- Tools/assays/reagents to measure and follow immune response and host immune systems
- Immunological reagents to decipher mechanisms of immune evasion and protective immunity
- Availability of suitable species-specific reagents for use in livestock studies, gene sequences, antibodies, cytokines

Adjuvants

- Appropriate, effective and approved adjuvant and biotherapeutics for each host species
- Safe and non-toxic adjuvants able to stimulate cellular (Th1) immunity
- Adjuvants suitable for use with mucosally-delivered vaccines, DNA vaccines
- Assays to evaluate adjuvants (cocktails) for their potency to induce adverse effects on a longer term

Vectors

- Vectors to express protective antigens of several pathogens simultaneously

Animal Models

- Appropriate animal model

- Refinement of animal tests by replacing experimental techniques with alternative methods

FACILITIES

- Lack of critical mass and facilities for in vivo challenge work particularly at high containment
- Access to field trial sites

REGULATION AND LISCENSING

- Licensing for genetically modified viral vector or capsid vaccines
- Cost-effective registration for wildlife vaccines
- Finding financial support/partners for the jump from the lab to the license.
- Increasing regulatory requirements have become major impediment in marketing of the new vaccine candidates arise from research

WORKING WITH INDUSTRY

- Major challenge is gaining investment at an early stage of research as most major vaccine companies will not invest until proof of concept shown
- Less expensive stream-lined procedures for manufacturing small run specialised vaccines.

GENERAL

<u>Funding</u>

- Governments are not likely to sponsor large-scale vaccine developments unless the diseases have major impact (mortality, morbidity, zoonotic) and are getting out of endemic diseases control. If "big" animal pharma does not pick up that gap and funds more the development costs, nothing will happen

PUBLIC ACCEPTANCE

GM: The challenge is not only science based but also demonstrating the safety of such Genetically Modified Organisms (thoroughly and convincingly) to the extent that public has clear perception about the safety and utility of such products.

ECONOMICS OF VACCINE PRODUCTION

- Cost (to farmer) and value of benefit to society
- The economics of livestock keeping make rational development of veterinary vaccines a low priority for industry, who are looking for low-cost solutions

- Implementation of clever new tech vaccines will not happen because pharma companies will not take on the development of a vaccine that will make them very little money due to the fact that farmers are making no money and the industry can therefore only afford a very small cost per dose

DISEASE/SPECIES SPECIFIC VACCINES

- African Swine Fever
- Pan reactive vaccines for Avian Inflenza and Foot and Mouth Disease
- Avian Influenza: Improved influenza vaccines for domestic avian species and porcine species, and administration strategies
- Live attenuated vaccines for fish
- Parasitic diseases
- TB and para TB (DIVA compatible)
- TB vaccines for wildlife
- EHV-1, EIV and JEV
- Anthrax, Contagious agalactia, Clostridiosis
- Bluetongue, African Horse Sickness
- Rift Valley Fever to develop a recombinant vaccine.
- PPCB to understand disease pathogenesis and develop a safe and effective vaccine
- The development of a vaccine directed versus the vector of a number of pathogens so that it should be protective versus all the pathogens transmitted by this vector

OTHERS

- Understanding of many pathogens that are significant causes of animal disease lags far behind that of pathogens causing human diseases.
- Understanding of microbiota of livestock is also negligible and is particularly significant for pathogens that cause enzootic diseases in particular and which may transition from "commensal" to pathogenic status.
- The means to induce an effective, protective immune response in animals for which primary purpose is conversion of feedstuff to high grade protein for human consumption.
- Operational research
- Interdisciplinary collaboration
- Inter-Institutional studies - one health