US-UK FUNDERS AND RESEARCHERS WORKSHOP REPORT

United States Department of Agriculture
National Institute of Food and Agriculture

CONTENT

ANNEXES

1. EXECUTIVE SUMMARY

A US-UK Funders and Researchers Workshop was held in the US on 1-3 June 2015. It was co-funded and facilitated by the Biotechnology and Biological Sciences Research Council (BBSRC); the National Institute of Food and Agriculture (NIFA), United States Department of Agriculture (USDA); the Research Council UK (RCUK) Washington; and the UK Science and Innovation Network (SIN) - Houston. The University of Maryland-College Park also facilitated.

In general, there was great enthusiasm from both US and UK attendees for **joint partnership** and **an opportunity to bring together two large research entities** in the world with **complementary strengths** to address some of the major issues in animal health and welfare.

The workshop had two parts. During part one, 33 scientists (22 US; 11 UK) identified potential areas for cross-country collaborations in: vaccinology for animal health and food safety; antimicrobial resistance, including alternatives to current antimicrobials and antiparasitics; emerging & re-emerging animal pathogens, including zoonoses; and animal welfare. Six US Federal agencies (USDA-NIFA; USDA-Agricultural Research Service; National Science Foundation (NSF); National Institutes of Health (NIH); Department of Homeland Security (DHS); US Food and Drug Administration (FDA)) and 3 UK agencies (BBSRC; RCUK Washington; UK-SIN Houston) also attended and summarized their portfolios.

A SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis was done for the four workshop topics. Researchers highlighted that US-UK collaboration **builds on a history of successful collaboration in the topic area and provides a unique opportunity to exploit biodiversity and the unique agricultural and management models in both countries as a way to develop agri-system resilience in both countries**. Scientists in both countries noted insufficient resources to address the workshop topics; working cross-country could significantly leverage limited funding for mutual US-UK benefits.

Participants identified over 70 research topics for potential collaboration of which 26 {***Diagnostics, data modeling, antiparasitic resistance, immunology, disease (host and pathogen biology), vaccinology, welfare/wellbeing and microbiome linking to immunology***} were identified as high impact and high need for transatlantic collaboration. There were two research topics which were considered to be low impact but participants expressed high need for collaboration (Emerging pathogens of unknown clinical significance and tick-borne diseases). The group also identified two areas for joint US-UK networking activity: microbiome as marker for health, welfare and disease and animal behaviour as a predictor of disease outbreak. Following that classification, using the research topics as a starting point, **twenty-one short-, medium- and long-term deliverables** were identified that are ripe for impactful US-UK collaboration.

Scientists responding to a post workshop survey judged part one of the meeting to be excellent to very good.

Part 2 was a closed funders meeting (USDA-NIFA; NSF; NIH; DHS; FDA BBSRC; UK-SIN; RCUK). Next steps towards development of a strategic framework for multi-year collaborations around the workshop themes were confidentially discussed and will be continued outside of the workshop.

2. BACKGROUND

Building on the high quality science base in the US and UK, BBSRC and USDA-NIFA launched a joint pilot call (request for applications) in 2014 to support research of high strategic relevance to both countries in areas of Animal Health & Disease, including Veterinary Immune Reagents.

There was an overwhelming response from both US and UK communities to this call (including 51 letters of intent to submit proposals); some very strong US-UK research partnerships were developed and funded. BBSRC and NIFA jointly funded 5 US-UK collaborative projects through this call to control the spread of pathogens and minimize health risks and environmental impacts of food production worldwide. There was positive feedback from both communities.

BBSRC and NIFA agreed that there is a need to build a stronger and sustainable trans-Atlantic partnership between funders and researchers that will allow world-leading researchers in both countries to work together to address emerging and re-emerging threats in animal health and food safety while safeguarding food supplies, animal welfare and public health.

Subsequently, BBSRC and the UK-Science and Innovation Network (SIN) Houston Team developed a joint bid to secure UK funding to support a small, high-level workshop with government and research representatives from the US and UK. The focus would be to consider next generation vaccines, alternatives to antimicrobials in livestock, and other research challenges and areas of shared concern to address the global emergence and spread of antimicrobial resistance. NIFA provided USDA co-funding for the workshop and also partnered with the University of Maryland-College Park to support participation from the US research community, as well as oversee on-site workshop needs.

Through this joint researchers' and funders' workshop, BBSRC and NIFA are initiating the development of a strategic framework for working within Animal Health and Welfare, including Food Safety, Veterinary Vaccinology, and Antimicrobial Resistance. The aim is to develop a longer term US-UK partnership driven by scientific needs and priorities of mutual benefit. We welcome participation in the strategic framework's development from other federal partners whose mission areas complement one or more of the workshop themes.

3. AIMS AND OBJECTIVES

Part 1: RESEARCHERS AND FUNDERS WORKSHOP

Objective:
Bring together US & UK researchers to identify potential areas for joint collaboration in:

- Vaccinology (for animal health & food safety);
- Antimicrobial resistance: Alternatives to current antimicrobials & anthelmintics used for animal health;

- Emerging & re-emerging animal pathogens, including zoonoses; and
- Animal welfare/ well-being.

Specific Aims:

- Gain an understanding of current research landscapes, including research infrastructure in the US and the UK, as well as agency strategic plans relevant to workshop topics;
- Identify areas of particular strength in both countries; areas where research is complementary and synergistic; & key challenges that would benefit from being addressed by collaborative activities;
- Identify potential areas where additional research expertise from scientists in UK or US would add value to on-going research in the other country;
- Evaluate the timeliness and perceived benefits of future collaborative work between the US and the UK.

Part 2: FUNDERS MEETING

Objective:

Funders will discuss next steps to develop strategic framework for multi-year collaborations for veterinary vaccinology, antimicrobial resistance- including alternatives to antimicrobials & anthelmintics, emerging & re-emerging pathogens-including zoonoses, & animal welfare / well-being.

Specific Aims:

Based on Funders' current and future priorities, gap analyses of Funders' portfolios, & consideration of the suggested collaboration areas identified by the invited researchers:

1. Identify suitable mechanisms to address key gaps/areas such as: collaborative research programs, networking, exchange of scientists (mobility grants); partnering awards with money for research to establish proof of concept; supplemental funding to existing investments (e.g. glue/networking grants); innovative agency portfolio connections that do not require additional funding, etc.

2. Begin to identify key measures of success of new UK-US partnerships:
   - Outputs (e.g., One or more activities to support research or other collaborative activities that will strengthen joint working of US-UK animal health and disease-including food safety- research communities; joint publications & workshops);
   - Outcomes (e.g., Stronger collaborative projects and broader engagement); and,
   - Impacts (e.g., new vaccine technologies/candidates; new alternatives to antimicrobials/anthelmintics; improved readiness or understanding of emerging pathogens; identification of objective measurements of animal well-being, research feeding into evidence-based policy making etc.)

4. WORKSHOP

The workshop was held in the US and hosted by the University of Maryland on 1-3 June 2015. It was sponsored by the Biotechnology and Biological Sciences Research Council (BBSRC), the National Institute of Food and Agriculture (NIFA), United States Department of Agriculture (USDA), the Research Council UK Washington, and the UK Science and Innovation Network (SIN) - Houston. The workshop Programme is at **Annex 1**.

The workshop was attended by:

- 33 researchers: 22 from the US and 11 from the UK;
- 26 representatives from US Federal agencies:
  - USDA-NIFA – Institute of Food Production and Sustainability (8);
  - USDA-NIFA – Institute of Food Safety and Nutrition (5);
  - USDA-NIFA – Office of the Director (2);
  - USDA Research, Education and Economics-Office of the Chief Scientist (1);
  - USDA-Agricultural Research Service (2);
  - National Science Foundation (3);
  - National Institutes of Health-NIAID (2);
  - Department of Homeland Security (2);
  - US Food and Drug Administration (1).
- BBSRC (4);
- RCUK Washington (2); and,
- UK-SIN Houston (2).

A list of attendees is at **Annex 2**.

The workshop was opened jointly by the BBSRC's Chief Executive Professor Jackie Hunter and the Director of NIFA, Dr. Sonny Ramaswamy. Both stressed the importance of US-UK collaboration and joint working in Animal Health to address food security and emerging disease threats.

Over two and half days, attendees identified areas that would benefit and add value to the US-UK collaboration.

UK SIN-Houston conducted a survey following the workshop. Twenty responses were received from researchers; all rated the workshop as excellent, very good or good.

In general, there was great enthusiasm from both US and UK attendees for joint collaboration with a feeling that this is an opportunity to bring together two large research entities in the world with complementary strengths to address some of the major issues in animal health and welfare.

5. US-FEDERAL & UK-BBSRC PRIORITIES

There was representation from 6 US federal agencies and UK's BBSRC. Each funder presented a brief overview of their remit, which is summarized below:

NIH- National Institute of Allergy and Infectious Diseases (Cristina Cassetti)

The National Institutes of Health (NIH) is the largest source of funding for biomedical research in the US with the budget of $30.1 billion in the fiscal year 2014. Its mission is to support "science in pursuit of fundamental knowledge about the nature and behaviour of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability". It has 27 Institutes including the National Institute of Allergy and Infectious diseases (NIAID) and a number of centres.

NIAID maintains and grows a robust **basic and applied research portfolio in microbiology, infectious diseases, immunology and immune-mediated disease**. In addition, NIAID responds rapidly to **new and emerging disease threats**. NIAID's budget for the FY2014 was $4.3 billion.

NIAID supports research along the product development pathway by providing direct funding to investigators (grants and contracts), research tools & technologies, and preclinical and clinical services.

NIAID spent $921.5 million in 2014 on zoonotic diseases research focussing on pathogen, host and environmental factors, genetic basis for microbial/vector evolution, adaptation and pathogenicity, development of diagnostics, vaccines and therapies and new strategies to control diseases that are re-emerging due to drug and insecticide resistance. Examples of diseases: influenza, mycobacteria, flaviviruses, bat and rodent-borne infectious diseases.

Some of the NIAID's programmes described in detail include:

- Centers of Excellence for Influenza Research and Surveillance (CEIRS): Focus is on influenza surveillance and pathogenesis & host responses;
- Genomics: NIAID supports an extensive genomics and advanced technologies program. Projects include the NIAID-supported Influenza Genome Sequencing Project at the J. Craig Venter Institute (JCVI);
- Research on emerging paramyxoviruses Hendra and Nipah, including the development of a treatment currently in clinical trials;
- Antibacterial Resistance Programme: Budget of $227 million for basic and translational research. Some of the areas of interest includes:
    - new directions for drug discovery using systems biology,
    - harnessing the immune system to combat bacterial infections,
    - improving diagnostics, exploring anti-virulence strategies,
    - investigating synthetic microbiota – an eco-biological approach,
    - exploiting natural predators (phage therapy) and extending the clinical utility of antibacterial drugs.

As part of its Antibacterial Resistance Programme, NIAID supports the Antibacterial Resistance Leadership Group (ARLG). The mission of the ARLG is to prioritise, design and execute clinical studies that will reduce the public health threat of antibacterial resistance.

National Science Foundation (NSF) (William E. Zamer, Acting Division Director)

NSF's mission is to promote the progress of science; to advance the national health, prosperity and welfare; to ensure the national defense and for other purposes. NSF **supports basic research**; and accomplishes its mission through research **support made across the range of science, math, engineering, technology and education**.

NSF has 7 Directorates and relevant to this workshop is the Directorate for biological sciences (BIO).

BIO supports basic research that will yield **fundamental knowledge about animals, their biotic and abiotic environments, ecology and evolution**. It has three disciplinary divisions (Division of Environmental Biology (DEB), Division of Integrative Organismal Systems (IOS) and Division of Molecular and Cellular Bioscience (MCB)) and an Infrastructure division.

Division of Environmental Biology (DEB): supports fundamental research on the origins, **functions, relationships, interactions and evolutionary history of populations, species, communities and ecosystems**. One of the DEB's programmes, that is relevant to this workshop, is the **Ecology and Evolution of Infectious Diseases (EEID**) which is also supported by two other Directorates in NSF: Social Behavior and Economic Sciences and the GEO sciences. EEID is interdisciplinary program and its mission is to develop predictive principles to enable the prevention of infectious disease transmission. It is a highly collaborative program with other funding agencies, such as NIH, NIFA the UK Research Councils and the US-Israel Binational.

Division of Integrative Organismal Systems (IOS): supports research aimed at understanding the living organism including plant, animal and microbe and the four core programmes include: Behavioural, developmental, Neural and Physiological & Structural systems.

Other NSF's programmes are

- Innovation at the Nexus of Food, Energy and Water Systems (INFEWS) is a NSF-wide activity in the FY-16 aimed at advancing understanding of the complex interactions between food, energy and water systems.

United States Department of Agriculture (USDA)-Agricultural Research Service (ARS) (Eileen Thacker, National Program Leader – Food Safety and Animal Health)

ARS is one of the four agencies that come under the umbrella of Research, Education and Economics (REE), led by Dr Cathy Woteki – the Under-Secretary of REE. The research funds for ARS are appropriated by Congress; Research directions are derived from Congress, the USDA, other federal agencies, and other stakeholders/partners.

ARS is the in-house science research arm of USDA which **supports farm-to-table research**. There are 19 National Programmes comprising 800+ projects, implemented in 90+ laboratories throughout the United States (including four overseas labs) with a $1.1 billion annual budget.

Currently, the National Programme Staff has organized ARS research into 19 National Programmes aligned under four divisions: Animal Production and Protection; Nutrition, Food Safety, and Quality; Natural Resources and Sustainable Agricultural Systems; and Crop Production and Protection.

Animal Health is one of the 19 National Programmes with an annual budget of $65 million. There are 104 research projects at 11 US locations and 110 scientists. **Food Safety**, another ARS national programme, has a budget of $105 million.

US Food and Drug Administration (FDA) (Jeffrey Ward)

FDA's core responsibility is to protect consumers by applying the best possible science to its regulatory activities – from pre-market review of efficacy and safety to post-market product surveillance to review of product quality. It is responsible for the safety of 80% of all food consumed in the United States with exception of meat, poultry, frozen dried and liquid eggs, catfish and others that are regulated by USDA.

FDA provides regulatory support for Food Safety programs and **supports basic (foundational) and applied research (e.g. epidemiology and risk analytics, veterinary medical research, bioinformatics, IT infrastructure and Data Sharing Capabilities)**.

Future priorities include capacity building, develop methods that are rapid, sensitive, specific, easy to use, robust, portable platform, ability to test at the source, environment, and reduced product testing and preventive; data sharing and targeted statistically-significant surveillance.

FDA has a broad spectrum of partnerships to deliver advanced research and development for regulatory science to support the FDA Strategic Plan for Regulatory science. Some of their programmes include:

- Whole genome sequencing program – Genome Trakr: state and federal laboratory network collecting and sharing genomic data from foodborne pathogen.
- National Antimicrobial Resistance (AMR) Monitoring System is dedicated to the protection of human and animal health through integrated monitoring of foodborne AMR. It is a national collaborative network between the FDA, Centres for Disease Control (CDC), USDA, public health laboratories in all 50 states, and local health departments in three major cities. It was developed to monitor changes in susceptibility of select bacteria from animals, retail meats and humans to antimicrobial agents of human and veterinary importance. Future objectives for NARMS includes:
    - Monitor genomes in antimicrobial resistant foodborne bacteria;

    - Characterise the resistome in complex biological samples using culture-independent metagenomic analyses;
    - Disseminate timely information on precise changes in the resistome;
    - Conduct in vivo metagenomics research to better understand the emergence, persistence and spread of antimicrobial resistance under different conditions;
    - Provide comprehensive genetic data, along with detailed antibiotic use information.
- Consortium for Sequencing the Food Supply Chain: FDA is developing a new partnership with IBM and Mars Inc. to study the microbial ecology of foods and related processing environments, sequence all microorganisms and develop a more in-depth understanding of the microbiome.

Department of Homeland Security (DHS) (John Julias, Acting Branch Chief)

The Director of Homeland Security Advanced Research Project agency (HSARPA) sits within DHS Science and Technology Directorate. HSARPA **supports cutting edge research to produce revolutionary changes in technologies and capabilities for the homeland security enterprise**. There are number of division under HSARPA; the Agricultural Defense program is under the Chemical and Biological Defence Division.

The mission of Agricultural Defense is to enhance **current capabilities and develop state-of-the-art countermeasures for high priority foreign animal diseases**. This includes near- and long-term **research and development for vaccines and diagnostics**, in coordination with internal and external stakeholders. The Agricultural Defense Programs span the entire outbreak spectrum and supports development of:

- Enhanced passive surveillance;
- Tools to support planning and response, drive requirements for countermeasures development and inform post-outbreak response activities;
- High throughput diagnostics allow more rapid confirmation of disease status and increased sample processing capabilities;
- Vaccines to rapidly prevent disease;
- Agricultural screening tools to verify disease free status;
- Livestock decontamination, disposal and depopulation (3D);
- Diagnostics to distinguish vaccinated from infected animals.

National Institute of Food and Agriculture (NIFA) (Peter Johnson, National Program Leader)

NIFA is USDA's primary extramural agency to advance food and agricultural sciences and **supports research, education and extension in partnership with institutions across the US**. NIFA's annual budget is approximately $1.43 billion; the President's 2016 requested budget to Congress is $1.68 billion. NIFA provides: competitive grants to support basic and applied research, education and extension activities to solve national problems; capacity grants to US states to allow them to respond to local and regional problems while maintaining critical infrastructure; and Congressionally-directed line items to be used on specific targeted areas based on competitive peer review (e.g., aquaculture in 2014 and 2015). NIFA's funding for

its Food Safety portfolio is ~$40 million/year; Animal Health: ~$35 million /year; and Animal Welfare ~$4 million/year.

The Agriculture Food Research Initiative (AFRI) is USDA's largest grants programme with a budget of $325 million for 2015; the President's 2016 requested budget to Congress is $450 million. AFRI has several "Request for Applications" each year:

- Foundational Program: covers all aspects of food and agriculture. Relevant to this workshop are programs in: Animal Health and Disease; Tools and Resources: Animal Breeding, Genetics & Genomics; Tools and Resources: Immune Reagents for Agricultural Animals; Animal Well-being; and Food Safety;
- Challenge Programs: For 2015, 4 challenge programs are applicable to this workshop: Food Security (e.g., Animal management systems, breeding and genomics of livestock; Food Safety (e.g., mitigation strategies for AMR and enhancing food safety through improved processing technologies); Climate Variability and Change; and Water for Agriculture;
- Education & Literacy Initiative.

In summary, NIFA has several programs that support the themes of this workshop and has a history of partnerships with federal agencies. NIFA is growing its' engagement with BBSRC to link science communities and eager for innovative ways to enhance links around workshop themes with BBSRC & other federal agencies for mutual benefit.

Biotechnology and Biological Sciences Research Council (BBSRC) (Sadhana Sharma, Strategy and Policy Manager- Animal Health & Welfare)

BBSRC is the UK's leading funder of academic research and training in the non-clinical life sciences. One of 7 UK Research Councils that work together as Research Councils UK, BBSRC is funded by the UK Government Department of Business, Innovation and Skills, with an annual budget of around £484 million (2013-2014).

BBSRC has a unique and central place in supporting the UK's world-leading position in bioscience, investing in world-class bioscience research and training on behalf of the UK public. Our aim is to further scientific knowledge, to promote economic growth, wealth and job creation and to improve quality of life in the UK and beyond.

BBSRC's Strategic Plan: The Age of Bioscience which was refreshed in 2013 highlights three major strategic science priorities: Agriculture and Food Security; Industrial Biotechnology and Bioenergy, Bioscience for Health and three crucial enabling themes, which are critical to our vision for UK bioscience: Enabling innovation, exploiting new ways of working, partnership.

BBSRC operates flexible funding streams from small, pump-priming or proof of-concept studies through to strategic longer, larger programmes of research. Responsive mode funding, is the main funding mechanism that support excellent research in response to unsolicited ideas from research groups, consortia or individuals in any area relevant to BBSRC's remit.

BBSRC's responsive mode highlight number of priorities and those that are relevant to this workshop are: animal health; welfare of managed animals; the replacement, refinement and reduction (3Rs) in research using animals; combatting antimicrobial resistance; and sustainably enhancing agricultural production.

BBSRC has number of existing international collaboration in animal health and welfare with Brazil, Europe, India, USA (NSF and NIFA) and China.

6. US-UK PARTNERSHIP: SWOT (STRENGTHS, WEAKNESSES, OPPORTUNITIES AND THREATS) ANALYSIS

The participants performed a SWOT (STRENGTHS, WEAKNESSES, OPPORTUNITIES AND THREATS) analysis on all four workshop topics. The detailed analysis is at **Annex 3**. The group highlighted that US-UK collaboration provides a unique opportunity to exploit biodiversity, and unique agricultural and management models in both countries to develop agri-system resilience in both countries.

The top three opportunities and challenges identified by the participants are summarized below:

Vaccinology (for animal health and food safety)

Opportunities: Building on collaborative global networks (Veterinary Vaccinology Network, Global Foot and Mouth disease Research Alliance (GFRA), Global African Swine Fever Research Alliance (GARA)) between two countries, a joint US-UK collaboration could address **biogenomics** and **immunogenetics** that underpin vaccine research and address the gap in development of **immune reagents**.

Challenges: Participants highlighted developing vaccines to **large complex pathogens** and the **lack of immune reagents** as major challenges impeding vaccine research. In addition, there is a need to **develop better methods for discovery/predicting protective antigens**.

Antimicrobial Resistance - Alternatives to Current Antimicrobials & Antiparasitic

Opportunities: A joint collaboration between the UK and US, that between them have developed most of the world's antibiotics, could address the **dynamics of AMR** in populations, analyze gene flow, and strengthen research in developing **alternatives to current antibiotics**. Also, joint **training programmes,** including informatics, would help address a capacity gap.

Challenges: A key challenge is to identify **what alternatives should be pursued and influencing behavioural changes** (current versus adopted)**. Also, differences in regulatory frameworks in the US and UK** could restrict joint collaboration. Information on alternatives to antibiotics (ATA) that are currently in the research pipeline {see USDA ATA Resource Center: http://www.ars.usda.gov/alternativestoantibiotics/}

Emerging & Re-emerging Animal Pathogens, including Zoonoses

Opportunities: A joint UK-UK collaboration would be very beneficial to help address issues of emerging infections by developing **disease surveillance** systems and getting a **global perspective on disease emergence**. Collaboration would enable better **integration of data** e.g. genomics, location/movement of animals.

Challenges: Two most important drivers for disease emergence are: **climate change** and **global trade**.

Animal Welfare/ Well-Being

Opportunities: A joint collaboration would provide more **opportunities** in welfare research; coordinating research across countries would **reduce unnecessary duplication and the number of animals in research**. Working together, US-UK researchers would broaden a **multidisciplinary** approach; strengthen **collaborations between animal scientists and veterinarians;** and accelerate the **translation of basic research into applied research and outcome oriented results available for producer adoption.**

Challenges: There is **decreased funding** for animal welfare in both US and UK. There can be **competing interests** of funders, producers and consumers that make welfare research challenging. US-UK collaborations will need to consider **differences in regulation/legislation** between the two countries.

7. RESEARCH GAPS AND CHALLENGES

This session included a series of short presentations from the UK and US delegates to highlight key research challenges, current gaps and unmet needs.

Vaccinology (for animal health and food safety)

Vaccinology presents an ideal opportunity for collaboration as it builds on the UK's and USA's strengths in immunology and genomics and therefore, presents ideal opportunities for collaborative projects to apply novel technologies to vaccine studies for specific diseases. There are some existing US-UK links in development of underpinning technologies; expanding joint collaboration with funding would reduce duplication and accelerate progress. There are similar gaps and issues in vaccine research in both countries and a joint collaboration will enable them to be addressed effectively by accessing expertise and funding in both countries. Researchers agreed that collaboration between the US and UK historically has been difficult as little funding has been available from the US for this.

Gaps

- Diseases that have often proved refractory to vaccination
    - Frequently persistent infections
    - Antigenically complex pathogens (e.g. parasites)
    - Need to understanding immune mechanisms
- Difficulties in extrapolating from mice and humans: mouse models often do not translate to larger species
- Different requirements for animal and human vaccines (e.g. adjuvants and vectors)
- Limitations in immune reagents and genotyping tools

- Opportunities using high throughput technologies
  - New sequencing platforms
  - Decreasing cost
- Transcriptomic signatures of protective immunity
  - Technology is not new but has not yet fulfilled its full potential in field of vaccinology. To date, analyses have mostly been done of whole leukocyte populations but basic data on normal transcript profiles and pathways in farm animals improving rapidly
  - Opportunity for targeted analyses of defined cell populations following vaccination and challenge (difficult in human studies)
- High quality bioinformatics is critical for vaccine research

Challenges

Improving understanding of host pathogen interactions

- Markers for immune cell types
- Relationship between immune gene expression/ protein expression/function
  - indicators of protection against pathogens
  - impact of long /short term environmental changes on the virulence of pathogens and the efficacy of vaccines

Development of new vaccines, improvement of existing vaccines and vaccine delivery platforms

- Mechanism of adjuvant action, improving targeting and reducing side effects
- Use of DNA vaccines and live vaccines, including consideration of regulatory hurdles
- Development of oral vaccines based on better understanding of mucosal immunity
- Development of parasite vaccines
- Development of vaccine delivery platforms

Research areas that would benefit from joint US-UK collaboration include

- **Fundamental understanding of immune systems** in livestock species to underpin studies of immune responses:
  - Cell surface markers to identify cell types and their stages of maturation and activation
  - Molecular tools (MHC, NK receptors) to define host immunogenotypes and to dissect cellular immune responses (e.g. cloned MHC genes, MHC tetramers, transfected cell lines.
  - Reference reagents for analyses of antigen receptor repertoires (immunoglobulins and T cell receptor)
- **Working together to make 'applying next generation sequencing and bioinformatics for livestock' efficient and informative**
  - Discovery Platforms: High throughput sequencing to analyse transcriptomes, to define antigen receptor repertoires, to determine sequence diversity of targeted polymorphic genes and to analyse pathogen diversity.
  - Bioinformatics tools and expertise.
- **Application of reagents and omics technologies to**:
  - Evaluate immune responses to infectious agents in the target species
  - Discover potential vaccine antigens
  - Evaluate efficacy of existing vaccines – "correlates of immunity" in the target species

- Design new vaccines & reagents for 'strategic interventions'or 'countermeasures

Antimicrobial Resistance (AMR) - Alternatives to Current Antimicrobials & Antiparasitic

AMR is a global problem with huge efforts from both the US and UK to tackle this issue. US-UK collaborations will provide an opportunity for partnership of two of the best research entities in the world, which have developed most of the world's antibiotics. Both countries face similar problems and goals in this area. Both counties are trying to answer similar unanswered questions, such as:

- To what extent has clinically significant AMR been driven by antibiotic use in animals?
- What is the nature, direction & frequency of AMR transfer under selection & during infection?
- How rapidly does AMR decay on farm or food when selection is removed i.e. the effect of resistance on biological fitness?

Gaps

Group identified

- There are few drug classes and limited chemical space represented in current antibiotics
  - Few MoA (7) and few distinct chemical classes (11) (poor arsenal)
  - Contemporary drug screening is high throughput, but limited in "chemical space"
- Few drug mechanisms of actions (MoAs) have been exploited so far
- Recently developed drugs lack new MoAs

Challenges

- Resistance is an enormous challenge
- New chemical classes and MoAs have proven difficult to exploit
- Most novel ideas involve development of larger molecules, where delivery becomes a challenge
- Pathogen selective anti-bacterials are difficult to develop and market forces favour broad spectrum drugs
- Little or no progress with Gram-negative bacteria

Alternatives to Antibiotics

- Alternatives can take advantage of many unexploited essential genes to idemtify potential targets to screen for novel antimicrobials as well as drugs (e.g. there are 19 essential genes for DNA replication alone and only 3 targeted with current drugs).
- Alternatives could include
  - Nucleic acid targeting agents (e.g. DNA: bleomycin and RNA: aminoglycosides) or nucleic acid as drugs (antisense and repressor decoys)
  - Larger molecules that target proteins, such as antibacterial antibodies,
  - Nanoparticles, which could improve delivery or control release,
  - Resentace blocking strategies, which could rejuvenate current anti-bacterials as exemplified by clavulanic acid,

- Host defense peptides can be directly microbicidal & immunomodulatory
- Bacteriophages are licensed & partly effective as topical carcass treatments for foodborne pathogens
- Phytochemicals with antibacterial activity and/or enhancers of innate immunity
- Vaccines that could reduce the use antibiotics in animal production

Research areas that would benefit from joint US-UK collaboration include

- Target identification and prioritisation: which microbial genes are most essential for viability and virulence (i.e. most effectively targeted) and do not have close orthologues in the host, in order to exploit as antimicrobial targets?
- Developing better cell based high throughput screening assays
- Developing antimicrobials, including alternatives, that are unlikely to succumb to resistance
- Understanding the role of microbial communities (e.g. to what extent does the indigenous & unculturable microbiota receive & donate AMR elements) and rational manipulation of the microbiota
- Developing pathogen selective antimicrobials
- Identifying natural antimicrobial products and developing recombinant antimicrobial products
- Developing greater understanding of evolutionary biology of microbes
- Control of diseases that rely on antibiotics by selection and transgenesis.

Antiparasitic

Developing resistance to antiparasitic is an area of major concern that threatens the sustainability of livestock production. In poultry for example, incursion of ectoparasites (mites) into intensive layer industry is causing significant welfare and economic problems in Europe and North America, with very little effort invested into new/alternative methods of control. Lack of subunit/broad spectrum vaccines for coccidia is leaving the broiler industry reliant on a limited arsenal of drugs which poorly control parasite growth leading to suboptimal weight gains, poor welfare (pathological lesions even in the absence of external symptoms), and increasing risk of severe disease outbreaks. No drugs/vaccines at all for many protists including zoonotics such as Cryptosporidium (topical in the UK), toxoplasma. In addition, there are poor financial incentives for big pharma to develop new antiparasitics.

Gaps:

- **In vitro and HTS assays**
    - Culturing of most major veterinary parasites as they cannot be maintained outside of the animal host
    - Genetic manipulation remains intractable for the majority of parasites
- **Evolutionary biology of parasites** (and Hosts)
    - Microbial genetics and evolution as it is critical in driving resistance to drugs and vaccines
    - What parasites are out there? How diverse are they? How common is polyclonal infection? How likely is cross-fertilisation?
    - Need to combine genomics, genetics, epidemiology and modelling in order to predict longevity of targets in 'real' farm situations
- **Integrated management of agri-systems**

- Tackling parasitic diseases requires long-term investment (with public-private funding partnerships) and a co-ordinated interdisciplinary approach
- Solutions must consider sustainability, economic threats, potential financial returns, farm engineering, human behaviour and motivation, and societal opinions

Research areas that would benefit from joint US-UK collaboration include

- Generation of complete genome sequences of complex eukaryotic pathogens for which there are currently limited sequence data e.g. helminthes, ticks and mites including need for information on the genotypic structure and diversity of parasite populations {limited available information indicates that nematodes isolates are genotypically heterogeneous which has resulted in difficulties in assembling parasite genomes. Also implies frequent genetic crossing}
- Establishment of genetic markers for resistance to all antiparasitics
- Identification of novel drug targets
- Genetic identification of parasite-resistant breeding stock and understanding of the genetic and mechanistic basis
- Development of novel non-chemical approaches to decrease use of antiparasitics
- Working in collaboration to develop better high throughput screening assays
- Developing antimicrobials that are unlikely to succumb to resistance
- Understanding role of microbial communities including the effect of the microbiome on susceptibility to parasites or host responses

Emerging & Re-emerging Animal Pathogens, including Zoonoses

The US and UK bring complementary strengths in this area. A joint collaboration would increase the critical mass of researchers and enable sharing of reagents and facilities (e.g. high containment for large animals). Emerging and re-emerging pathogens of chicken (e.g. avian Influenza) and swine (e.g. porcine epidemic diarrhea virus**,** porcine reproductive and respiratory syndrome virus) were highlighted.

A recommended aim is **to develop knowledge-based integrated approaches that result in technological breakthroughs in animal production systems, disease management, detection, prevention and control (of pathogens).**

Challenges and Research areas that would benefit from joint US-UK collaboration

- Understanding and predicting cross-species transmission
  - Detailed understanding of pathogen biology to identify host and pathogen factors that enable/restrict replication
  - Ability of virus to adapt to new host
- Understanding the role of reservoir hosts and pathogen evolution and pathogenesis
- Studying multi-host pathogens at the epidemiological scale
- Uses of 'omics technologies for forensic epidemiology (in particular whole genome sequencing/phylodynamics, but also touching on transcriptomics)
- What are the drivers of emergence (climate change, global trade)
- Changing epidemiological paradigms with 'big data'

- Inadequate funding for emerging animal infectious agents especially those with unknown clinical implications in animals.
- Need strong international collaborations for emerging animal infectious agent surveillance and research

Animal Welfare/ Well-Being

Consumers in both the US and UK are very keen on wanting to be assured that the welfare of agricultural animals is not compromised in a negative way. A joint US-UK collaboration in this area would benefit from the diversity of animal management systems in both countries. The UK has a strong track record in underpinning research on behaviour, cognition, early experience, and welfare assessment; new technologies are being incorporated into welfare assessment approaches.

Gaps and Challenges:

- Welfare measures: that welfare / well-being are based on the assumption that animals can suffer and experience negative affective states – welfare measures should reflect these states and should be quick and practical.
- Animal behaviour: Understanding how animals view the world/others around them and understanding causes of abnormal and damaging behaviour, especially in the social context
- New metrics of well-being: Cognition and genomics based methods to objectively classify impacts of management practices on well-being
- Early life challenges: Understanding what types of prenatal and postnatal experience exert beneficial or detrimental effects on later behaviour, coping, productivity and welfare, and how they exert such effects
- Housing management and environment: managing animals in a way that provides for their behavioural wants and needs and systems that work for small and large operators
- Pain and nociception: Pain assessment is difficult. Recognising and managing animal pain and understanding the relevance of pain for animal welfare and welfare assessment. Lack of analgesic drugs in the USA compared to UK.
- Stress: Understanding the role of genetic variation in animal welfare / stress responses: Using that variation to improve animal welfare. Linking stress to AMR.
- Transportation: stress caused immunosuppression that lead to e.g. Bovine Respiratory Diseases. Understanding sources of transportation stress and research to optimize preconditioning.

Research areas that would benefit from joint US-UK collaboration include

- Comprehensive, multi-disciplinary approaches – improved links with other disciplines, with veterinary science and with social science
- New technologies to monitor animals – animal-mounted and environmental sensing platforms
- Stress biology, especially chronic stress, better tools for assessment
- Genetics and genomics – data-sharing or linked phenotyped populations
- Genetic selection for group housing
    - Epidemiological approaches to understanding welfare risks

- On farm assessment of welfare
    - Ability to identify outlier animals (highest welfare risks)
    - Standardized assessment tools/criteria?
- New metrics of well-being
- Translation and application of discoveries
- Ethical thinking and social acceptability of use of animals

8. SPECIFIC RESEARCH TOPICS IDENTIFIED FOR POTENTIAL US-UK COLLABORATION

The research participants identified over 70 research topics (**Annex 4**) for potential collaboration which fall within 12 broad headings as described below and depicted in Fig 1a and b:

1. **Antimicrobial Resistance** including best practices for minimizing antimicrobial resistance in animal production systems, anti-parasitic resistance, alternatives and markers for resistance.
2. **Data Modeling** including mathematical and epidemiological modeling and using modeling to predict emergence, outbreaks, control, climate change, demographic and environmental change, antimicrobial resistance.
3. **Diagnostics**: on farm diagnostics and identification of biomarkers for diagnosis of metabolic and infectious diseases.
4. **Disease** includes viral, bacterial, fungal, parasitic, vector-borne and prion pathogens with focus on pathogen and host biology and host-pathogen interactions.
5. **Genomics and bioinformatics** for animal health, welfare and anti-microbial resistance. Need for complete genomic sequence of pathogens and host. Also, highlighted is immunogenetics for highly polymorphic genes and resistance to parasitic infections in livestock.
6. **Immunology** with emphasis **on mucosal immunity** and developing and sharing immune reagents and developing high-throughput antigen discovery platforms.
7. **Management**: developing sustainable, smart and resilient agri-systems taking into account socio-economic considerations. Evaluating threats within small scale (organic) and intensive farming systems and defining biomarkers for resilience in animals.
8. **Microbiome** including microbial ecology as a marker for health, welfare and disease. The role of microbiome in AMR transfer.
9. **Vaccine**: need for vaccines for complex pathogens, multivalent vaccines, and those that do not drive resistance. Also, highlighted for joint collaboration were: structural vaccinology and tools to predict protective antigens; novel adjuvants and delivery systems; and immune-epidemiology for vaccine development.
10. **Welfare**: welfare indicators; welfare measures on farm; stress, pain and animal behavior as a predictor of disease outbreak; integration of husbandry practices in welfare research.
11. **Educational programs** for next generation of animal health, welfare, and food safety/AMR researchers.
12. **Miscellaneous** topic included: Prioritization of intervention strategies and disease targets; One Health approach.

Figure 1 a

Figure 1 b

9. PRIORITIZATION

The participants were divided into three groups and were asked to prioritize research topics into four categories:

- High impact and high need for trans-Atlantic collaboration
- High impact but can be addressed either by US or UK
- Low impact but high need for collaboration
- Not a priority at the moment

The details are in the **Annex 5.**

Some of the areas ranked as high impact and high collaboration include:

- Animal Welfare
- Anthelmintic/Antiparasitc Resistance
- Disease (Host and Pathogen Biology)
- Modeling (applied to AMR, disease emergence, transmission dynamics, genetic variation, population structure and dynamics
- Immunology
- Vaccine development

The scientists also identified two areas that may not have high impact but for which there is a high need for US-UK collaboration:

- Emerging pathogens of unknown clinical significance
- Tick-borne diseases

For two further areas where there are no significant advances yet and significant research collaboration initiatives would be premature, the group recommended US-UK networking activities (such as joint workshops):

- Microbiome: Microbiome as marker for health, welfare, disease, and emergence of antimicrobial resistance
- Welfare: Animal behaviour as a predictor of disease outbreak

Figure 2 below summarizes the raw data from discussions.

Figure 2: Prioritization of Research Topics

High impact and High need for trans-Atlantic collaboration

Diagnostics (all categories and includes topics related to AMR)
Data Modeling (all categories and includes topics related to AMR)
AMR6: Anthelmintic/Antiparasitc Resistance
Immunity (all categories)
Genomics (all categories including epigenetics)
Disease:

- D3 and D14: Prediction of pathogen emergence, virulence and host response
- D8: Cross species pathogen
- D10: Pathogen transmission dynamics
- D11: Genetics basis of pathogen evolution, host specificity and pathogenicity
- D12: Genetic basis of disease resistance in livestock
- D16 and D16: Effect of climate change on disease prevalence and transmission among food animals
- D17: Role of vaccines in emergence of disease

Education: Educational programs for next generation of animal health and welfare researchers
Vaccine

- V1 and V11: Understanding mucosal immunity and delivery technologies for eliciting mucosal immunity
- V2: Non-GMO methods to attenuate strains
- V3 (10, 14): Vaccines for complex pathogens
- V4 and V5: Novel antigen and adjuvant delivery systems and regulatory approval
- V6: Vaccines and therapeutics that do not drive resistance
- V8: Tools to predict protective antigens

Welfare

- W1: Impact of pain management on health immunity, AMR performance
- W3 (15): Integrated farm management systems and biological markers for animal welfare
- W4: Validation of indicators of pain/well being
- W13: Measure for welfare in the field

Microbiome

- Role of microbiome in development of immune competence

Low impact but high need for collaboration

D7: Emerging pathogens of unknown clinical significance
D9: Tick-borne disease

High Impact but can be addressed by either US or UK

AMR:

- AMR6: Alternatives to Antibiotics
- AMR 5 (1,4,7) Best practices for minimizing AMR in animal production systems

Disease

- D1: Mechanism of pathogenesis, resistance and persistence
- D2: Pathogen replication in cells and organisms
- D4: Culture systems for pathogen isolation and in vitro systems to predict pathogenesis
- D5: In vitro culture systems and high throughput screens
- D13: Disease complexes - mechanisms of pathogenesis

Microbiome

- MC1: Microbiome as marker for health, welfare and disease – Group recommended establishing a US-UK network

Welfare

- W11: Animal behaviour as a predictor of disease outbreak – Group recommended a US-UK network

Management

- M4: Developing sustainable and resilient agri-systems including socioeconomic considerations

10. DELIVERABLES SYNTHESIS

Twenty-one short-, medium- and long-term deliverables were identified. Completed synthesis forms for each deliverable is at **Annex 7**.

The main outputs from these deliverables will be improved production and management systems, food security and food safety, development of novel tools and platform technologies, policy advice, and developing resilient agri-systems in both US and UK.

Disease: Host and Pathogen Genetics and Biology

1. **Disease** (viral, bacterial, fungal, parasite, vector and prions): focus on those pathogens where there is low critical mass in both countries (for example, emerging diseases and parasitic diseases, trans-boundary and intractable diseases) to deliver complete understanding of host, pathogen and their interactions
    - *Outcomes: better risk assessment and disease control*

2. **Pathogen biology** including genetic basis of pathogen evolution, host specificity, and pathogenicity; prediction of pathogen emergence, virulence and host response; mechanisms of pathogenesis, resistance and persistence; pathogen transmission dynamics.
    - *Outcomes: ability to predict risk/assessment of disease; better understanding of disease/microbe/spread, new diagnostics, vaccines and trained work forces*

3. **Genetic improvement of animals**: a medium- to long-term deliverable focused on the animal host and building on shared expertise, on-going collaborations and maximizing the use of limited facilities. The deliverable focuses on **functional annotation of animal genomes**, genetic basis of disease resistance and production traits, and developing tools for genetic modification. The need for public engagement and education (social science and policy) is an important component of this deliverable.
    - *Outcomes: better validation of genomic and omics outputs, foot-print free animals, reagent KO models to investigate disease*

4. **Functional Genomics/Validation of QTL candidates**: Linked to the above deliverable, the focus here is on identifying genetics of disease resistance and developing tools for transgenesis tools.

    - *Outcomes: animal models and genetic tools for the community*

Modeling

5. **Modelling approaches to improving animal health and better understand AMR**: This deliverable builds on complementary skills in the US and UK including a mix of short- (modelling to inform AMR), medium- (modelling to inform control of endemic disease

and effect of climate change on disease) and long-term objectives (worldwide mapping of disease threats).

- *Outcomes: Preparedness for future disease outbreak, quantifying global burden of pathogen distribution and agro-systems resilience*

6. **Process-driven approaches to microbiome – mathematical models**: Building on the UK's strength in developing models and the US capacity to generate data, develop models of microbiome within host dynamics, microbial ecology of agricultural systems, and rumen microbiome as a modelling system for microbial community behaviour. In the short-term, use mechanistic approach (instead of data) to model microbiome ecology and evolution.
    - *Outcome: Will inform impact of microbiome on immunity (i.e. vaccines); enable development of in vitro and in vivo quantitative microbial ecology*

Animal Welfare/Well being

7. **Welfare as mediator of disease susceptibility** (Welfare as indicator of disease): Building on the UK's expertise with specific disease models and US genomic expertise, in the short-, medium- and long-term this deliverable will focus on improved disease detection and the value of disease intervention for better and earlier disease detection for targeted decision making. In addition, the deliverable will link welfare, stress and early life experience with immune function and disease susceptibility and epigenetics including how these factors influence individual 'resilience' to welfare challenges'
    - *Outcomes: Improved therapeutic outcomes; reduced antimicrobial use, more effective interventions; less ineffective interventions*

8. **Effective species-specific management to improve welfare**: this will build on the UK's field experience with alternative housing systems and focus on euthanasia, behavioural problems, and group housing strategies. In the long-term, understand impact of sustainable intensification.
    - *Outcomes: Less suffering, fewer damaging behaviours, better resource use*

9. **Validating measures of welfare/pain**: Building on complementary strengths in the US and UK, in the short-term, identify behavioural and physiological indicators; then from a short to long-term timeframe use trans-disciplinary approaches to validate measures of welfare including human-animal interactions and behavioural and physiological indicators and develop methods for automating the use of welfare indicators.
    - *Outcomes: welfare assessments tools validated on farms*

10. **Management practices to reduce pain**: In the short- to long-term, identify and validate markers of pain, understand why does pain matter to animals, identify alternatives to painful procedures and improved management of pain.
    - *Outcomes: Improved morale of farm workers, decreased pain; improved productivity, reduce disease*

Antimicrobial and Antiparasitic Resistance including Alternatives

11. **Improved antimicrobial stewardship**: Develop stewardship programmes for use of antibiotics for animal and aquaculture, including understanding motivation for antibiotics use.
    - *Outcome: reduced antimicrobial use*

12. **Effective alternative antibiotics (Therapeutics)**: This is a medium- to long-term deliverable combining social science (game theory models, and quantitative models of qualitative data) and linked to management and welfare. The aim would be to develop *in vitro* high throughputs systems, and new mechanisms.
    - *Outcomes: less need for therapeutic antibiotics and improved implementation*

13. **Understanding ecology (climate change)/transmission AMR across species**: Addressing the global problem of antimicrobial resistance this deliverable will characterize the resistome, model transmission dynamics, and understand effects of selection/infection and the withdrawal of antibiotics impact on immunity.
    - *Outcomes: improved management practices, and evidence based policy*

14. **Anthelmintics/Parasitics**: Both the US and UK have small research communities working on parasite; a joint collaboration would greatly enhance the critical mass of expertise. Recommended focus areas include: understand genome structure and evolution of parasites, identify genetic markers for resistance, improve culturing capability, identify novel targets and alternatives (including chemical alternatives) and novel delivery methods.
    - *Outcomes:* better management; monitoring of resistance, better/faster assays for novel drugs, reduce resistance development, intelligent design, therapeutics, vaccines

15. **Point of care/rapid/simple diagnostics for AMR/pathogens**: Using omics technologies identify host biomarkers, AMR markers and pathogen diagnostics for improved treatments and targeted therapy.
    - *Outcomes: improved treatment and targeted therapy*

16. **Alternative to antimicrobials** (Growth Promotion): There is a need to understand how antimicrobials work and the role of the microbiome and immune systems
    - *Outcomes: reduced used of antibiotics, improve productivity, energy retention, disease resistance*

Immunology and Vaccinology

17. **Defining immune systems in agricultural animals**: Different groups in the US and UK are working on different aspects of the immune system; they would benefit by coming together for the analysis of transcriptomics. Two main research projects were identified

under this deliverable: Reagent Development and Immunogenetics, including bioinformatics, tools to define host immunogenotypes and their exploitation to measure cellular responses etc.

- *Outcomes: community resources to enhance progress in vaccine development, information on protective immune responses, genetic diversity and the role of particular genes in protective immunity*

18. **Vaccines:** Building on US and UK expertise, develop technology platforms (antigen discovery and multivalent platforms) and delivery systems tools including vectors, adjuvants, nanoparticles, etc.
    - *Outcomes: enhanced control of disease to improve economic performance, welfare and reduce antimicrobial usage*

19. **Mucosal immunity**: The US and UK bring complementary expertise to address basic mechanisms of mucosal immunity in gut, skin, gills/lungs and immune-stimulants
    - *Outcomes: accelerated vaccine and immune-stimulant development, mitigated disease, increased animal productivity and prevent disease*

20. **Immunity to infectious disease** will build on strengths of both countries and with the added value of sharing expertise, reagents, methods and models it will increase efficiency and speed up outcomes. The research programmes identified under this deliverable include: identification of protective immunity, understanding of immune mediated pathogenesis, persistence and latency and prevention of transmission.
    - *Outcomes: national and informed basis for vaccine efficiency testing , advanced knowledge on host immunity*

Education and Extension

21. **Education and Extension**: Leveraging on the US Extension program the focus is on training of students and post docs, outreach and extension to producers and other stakeholders/partners.
    - *Outcomes: better trained workforce, behavioural change impacting practice and productivity*

WORKSHOP PROGRAMME AGENDA

PART 1: US-UK RESEARCHERS AND FUNDERS WORKSHOP

1 June 2015 Welcome Reception and Dinner at the hotel

18:00 – 21:00

- Welcome
- e-Introduction of participants

2 June 2015

07:30 **Continental Breakfast (Networking)**

08:00-8:30 Welcome and Opening Remarks: Sonny Ramaswamy, Director, USDA-NIFA and Jackie Hunter, CE, BBSRC

08:30-08:35 UK Science and Innovation Network: Lauren George, Head of Houston Team

08:35-08:45 Overview of the Workshop Programme

08:45-10:00 Presentations from US-Federal & UK-BBSRC priorities
08:45 – 08:55: NIH-NIAID (Cristina Cassetti)
08:55 – 09:05: NSF (Bill Zammer)
09:05 – 09:15: USDA-ARS (Eileen Thacker)
09:15 – 09:25: US Food and Drug Administration (FDA) (Jeffrey Ward)
09:25 – 09:35: Department of Homeland Security (John Julius)
09:35 – 09:45: NIFA (Peter Johnson)
09:45 – 09:55: BBSRC (Sadhana Sharma)

10:00-10:30 **BREAK**

10:30-12:00 US-UK Partnership: SWOT (Strengths, Weaknesses, Opportunities and Threats) Analysis

12:00-13:00 Research Gaps and Challenges Presentations: Session 1
Vaccinology (for animal health and food safety)
(Immunology for vaccinology, tools and technologies (e.g. Immune reagents), genetic/genomics tools for animal health research)
Bryan Charleston, Ivan Morrison, Sandra Adams
Paul Coussens, Cynthia Baldwin, Margie Lee

Antimicrobial Resistance - Alternatives to Current Antimicrobials & Anthelmintics
(Characterization of gut microbiome dynamics for immune development, health and diseases; Immune modulation approaches to enhance disease resistance & treat animal diseases; alternatives to antibiotics and current anthelmintics)

Liam Good, Mark Stevens, Fiona Tomley
Bill Sischo, Dave Donovan, William Witola

13:00-14:00 Working LUNCH

14:00-15:00 Research Gaps and Challenges Presentations: Session 2
Emerging & Re-emerging Animal Pathogens, including Zoonoses
(Ecology and evolution of pathogens, genetics/ genomic analysis of host-pathogen interactions, vector-borne diseases, surveillance and detection underpinned by omic technologies)
Matthew Baylis, Linda Dixon, Rowland Kao
Don Knowles, X.J. Meng, Daniel Perez

Animal Welfare/ Well-Being
(Objective Welfare indicators; Genetic components of animal stress and well-being)
Mike Mendl, Cathy Dwyer
Candace Croney, Johann Coetzee

15:00-15:30 General Discussion

15:30-16:00 BREAK

16:00-18:00 Scoping the Research Agenda

19:00 Working Dinner

3 June 2015
07:30 Continental Breakfast (Networking)

08:00-08:15 Welcome Back

08:15-09:30 Identifying Key Research Priorities

09:30-10:00 BREAK

10:00-13:00 Defining Deliverables

13:00-13:45 Wrap-up of Part 1 & Working Lunch
(Research delegates leave after lunch; Federal colleagues with competitive funding programs remain)

WORKSHOP PROGRAMME AGENDA

PART 2: FUNDERS MEETING

13:45-17:00

- Introduction and impression of the meeting
- US-UK Collaboration

  Mechanism for Future Engagement: Identify suitable mechanisms to address key gaps/areas such as: collaborative research programs, networking, exchange of scientists (mobility grants); partnering awards with money for research to establish proof of concept; supplemental funding to existing investments (e.g. glue/networking grants); innovative agency portfolio connections that do not require additional funding, etc.

- Defining measures of success

LIST OF ATTENDEES

Name	Affiliation
Abrahamsen, Mitch	Cobb-Vantress Inc.
Abrams, Desiree	NIFA- Institute of Food Production and Sustainability
Adams, Sandra	University of Stirling
Anandaraman, Neena	USDA – Office of the Chief Scientist
Austin, Suzanne	RCUK-Washington
Baldwin, Cynthia	University of Massachusetts-Amherst
Baylis, Matthew	University of Liverpool
Cassetti, Cristina	NIH-NIAID
Charleston, Bryan	The Pirbright Institute
Chitnis, Parag	NIFA- Institute of Food Production and Sustainability
Coetzee, Johann	Iowa State University
Collis, Amanda	BBSRC
Coussens, Paul	Michigan State University
Croney, Candace	Purdue University
Dixon, Linda	The Pirbright Institute
Donovan, David	USDA-Agricultural Research Service
Dwyer, Cathy	SRUC
Eblen, Denise	NIFA-Institute of Food Safety and Nutrition
Elsby, Stephen	RCUK-Washington
Funk, Julie	Michigan State University
Gay, Cyril	USDA-ARS National Program Staff
George, Lauren	UK SIN-Houston
Good, Liam	Royal Veterinary College
Green, Kim	USDA – Office of the Chief Scientist
Holland, Margo	NIFA- Institute of Food Production and Sustainability
Holland, Robert	NIFA-Office of the Director
Hunter, Jackie	BBSRC
Jaso-Friedman, Liliana	NSF
Johnson, Peter	NIFA- Institute of Food Production and Sustainability
Julias, John	Department of Homeland Security
Kao, Rowland	University of Glasgow
Kapur, Vivek	Pennsylvania State University
Knowles, Don	USDA-ARS-Pullman
Loneragan, Guy	Texas Tech University
Lunney, Joan	USDA-ARS-Beltsville
Margie Lee	University of Georgia
Matukumalli, Lakshmi	NIFA- Institute of Food Production and Sustainability
Mendl, Mike	University of Bristol

Name	Affiliation
Meng, XJ	Virginia Tech University
Morant, Mervalin	NIFA-Institute of Food Safety and Nutrition
Morrison, Ivan	Roslin Institute, University of Edinburgh
Motroni, Roxann	Department of Homeland Security
Mukhopadhyay, Suman	NIH-NIAID
Perez, Daniel	University of Georgia
Ramaswamy, Sonny	NIFA-Office of the Director
Reich, John	NIFA-Institute of Food Safety and Nutrition
Ruegg, Pam	University of Wisconsin
Saha, Dev	UK SIN-Houston
Samal, Siba	University of Maryland
Scheiner, Sam	National Science Foundation
Scott, Morgan	Texas A&M University
Sharma, Sadhana	BBSRC
Sherman, Gary	NIFA- Institute of Food Production and Sustainability
Sischo, Bill	Washington State University
Stevens, Mark	Roslin Institute, University of Edinburgh
Sunyer, Oriol	University of Pennsylvania
Tack, Danielle	NIFA- Institute of Food Production and Sustainability
Telugu, Bhanu	University of Maryland
Tengey, Davida Vanderpuye	NIFA- Institute of Food Production and Sustainability
Thacker, Eileen	USDA-ARS
Tomley, Fiona	Royal Veterinary College
Turzillo, Adele	NIFA- Institute of Food Production and Sustainability
Wagner, Bettina	Cornell University
Walls, Isabel	NIFA-Institute of Food Safety and Nutrition
Ward, Jeffrey L	U.S. Food and Drug Administration (FDA)
Welham, Melanie	BBSRC
Williams, Jodi	NIFA-Institute of Food Safety and Nutrition
Witola, William	Tuskegee University
Zamer, Bill	National Science Foundation

SWOT Analysis

Vaccinology (for animal health and food safety)

STRENGTHS

- Global Networks e.g. Veterinary Vaccinology Network, GFRA, GARA
- In developing polyvalent vaccines (fish/cattle US)
- BSL facilities in both countries
- There is a shared critical mass of scientists in vaccine research
- Mucosal immunity
- Genomics/bioinformatics
- Models (relevant host)
- Genome editing
- Delivery of vaccines (nano – other tech)
- Regulatory procedure
- Viral vectors

WEAKNESSES

- Polyvalent vaccines
- Mucosal immunity
- Adjuvants (specific/targeted)
- Bacterial vaccines
- Collaboration environment
- Discovery and prediction of protective antigens
- Immuno-genetics
- Mass vaccination
- Age-dependence
- Immune reagents
- Parasitic vaccines
- Large complex pathogens
- Antigenic variability
- Oral vaccine
- Cell lines
- Cross protection

OPPORTUNITIES

- Immuno-genetics (UK)
- Genomics and bioinformatics
- Vaccine vectors
- Immune reagents
- Translational pipeline
- Research and Collaborative Networks
- Develop protective antigen discovery platforms
- GAP analysis
- Industry partnerships
- Training opportunities

THREATS

- Decreasing workforce: Death/retirement of scientists
- Interminable training (pipeline blocked)
- DVM/PhDs
- Funding
- Regulatory
- Public awareness
- Emerging diseases
- Pathogen evolutionary emergence
- AMR ←→ withdrawal

Antimicrobial Resistance (AMR) – Alternatives to Current Antimicrobials & Anthelmintics

STRENGTHS

- Partnership of two of the best research entities in the world which have developed most of the world's antibiotics
- Similar problem and goals in this area
- There are enough similarities in the production systems for collaboration
- Both countries have existing funding programs (BBSRC, NSF, NIH) and pipeline for funding
- Pooling of bio resources/reagents
- Builds of pre-existing capacity and good surveillance system for US in food and UK food animals
- More models exist for the same problem (diversity of problem solving strategies)
- US through White House initiative pushing collaboration internationally and initiating global efforts
- Transatlantic taskforce on AMR (action plans, US, FDA< ARS)
- US Strength: High throughput assays
- No language barriers
- There are mechanisms exist for international collaboration

WEAKNESSES

- US animal AMR surveillance
- A global unregulated use of antibiotics still exists (this workshop) is only US-UK focused collaborations)
- Microbial evolution provides a challenge → needs investigation for movement between populations,
- Need to develop bioinformatics tool, epidemiologic techniques (quantitative)
- Understanding of microbiome
- Current focus is on animals - what are other drivers/factors for AMR?
- Prudent use, minimal clinical surveillance
- Analysis of surveillance (longitudinal data)
- Bacterial rather than microbial focused
- Lack of high throughput screens for testing new antimicrobials

OPPORTUNITIES

- Dynamics of AMR in populations – gene flow
- Develop joint training programs for informatics
- Develop training partnerships
- Rejig framework for drug regulations
- Expand capacity through international outreach
- A joint US-UK focus on specific aspects to limit duplication
- Regulatory differences to compare effects as a result
- Investigate role of microbiome in antibiotics
- Exploit growing microbes – develop new methods
- Trade barriers limiting animal movement and possibly other movement of disease- other world limitations can be capitalized
- Accept challenge to create new antimicrobials independently
- NGOs worldwide to disseminate US-UK best practices
- Develop hardware for storage of bioinformatics (having capacity for analysis)
- Generally Recognised as Safe (GRAS) –design perfect antibiotic

CHALLENGES AND THREATS

- Rejig framework for patents
- Lack of alternatives to replace growth promotion
- Behaviorial changes
- There is great biodiversity so need to focus
- There are regulatory limitations/differences
- Integrating climate change to microbe evolution

Threats

- Political will (economics, communication, behavioral change)
- Money
- Current strategies have narrow focus
- Low hanging solutions may lead to long term problems
- Biomed science & social science insufficient (need interdisciplinary approach)

Emerging & Re-emerging Animal Pathogens, including Zoonoses

STRENGTHS

US

- Technical expertise
- Infrastructure (high risk containment, high capacity for research populations)
- USDA: NIFA-Extension linkage/ ARS/Academia
- Stability of funding for graduate programs
- CDC: there is no equivalent in the UK
- Vector Biology (south and central America)
- Americas collaboration worldwide
- Business oriented
- Genomic approaches/technology
- Rewilding/Conservation biology

UK

- Historical strength (math models, evolutionary analysis)
- Data sets (large animals, extensive, inclusive, granular)
- Disease (pathogen biology, worldview Africa/Asia)
- Interface between wildlife/vet med
- Academic involvement international programs

WEAKNESSES

US

- Linkages between veterinarians and animal scientists
- Insufficient USDA funding for research on animal health, animal well-being, food safety and AMR

UK

- Vet/human health linkage
- Training vet students to impact/link to human health
- Disease surveillance (wildlife, economic impact, integration, communication)
- Shrinking budgets

US/UK

- Shrinking availability of pathologists
- Scientific basis for regulatory decisions/actions

OPPORTUNITIES

- US/UK leading worldwide holistic view of health
- Disease surveillance (technology, methodology, strategy – proactive vs. reactive)
- Shared agricultural production systems
- Increasing focus of One Health to animal side of problem
- Improve collaboration (interagency, human vet/interdisciplinary, international)
- Remove barriers
- More formal venues/meetings
- Expand US opportunity to contribute to and research foreign animal diseases
- Genomic approaches
- Systems approach to emerging disease
- Impact of human behaviour on emerging disease

THREATS/CHALLENGES

- Funding/responsibility seems to be moving from government → private, industry
- Global trade (restrictions, illegal activities)
- Climate change
- Organic markets (impact on disease/ health environment)

Animal Welfare/ Well-Being

Strengths

- Diversity of animal management systems
- Critical mass in UK
- Similar society values on welfare and need to protect well-being of animals

Weaknesses

- US
  - Small capacity of researchers
  - Drug approval and regulatory issues
  - Lacking diversity: trained by relatively few people
- Animal science vs. vet science silos
- Applied vs. basic limited
- Government funding very low; depends more on industry that has limited research funds

Opportunities

- Bring together UK critical mass to US
- Vet and animal science collaborations
- Industry engagement
- Blended applied and basic
- Integrate science, ethics, perceptions
- One health (mental health in animals and farmers)
- Companion animals
- Animals as models for human disease
- Stop reinventing research (avoid redundancy)
- Economic application of work across systems → adding disciplines
- Increase collaboration and coordination (thought process and expertise)
- Broaden multidisciplinary approach (scientists, ethicists, economics)
- Basic research -> translation→ applied extension

RESEARCH TOPICS

AMR	
AMR5 (1, 4, 7)	Best practices for minimizing AMR in animal production systems
AMR6	Markers for anthelminthic resistance
AMR8	Influence of pre and probiotics on microbiome and evolution of AMR
AMR2 and 3	Alternatives to antibiotics (including for growth promotion)
Data Modeling	
DM1	Epidemiologic methods for big data, omics, microbiome etc.
DM3 (2)	Mathematical models to predict emergence, outbreaks, control, climate change, demographic and environmental change, antimicrobial resistance
DM4	Quantitative methods for qualitative data (e.g. farmer behaviour, animal welfare, etc.)
DM5	Ecological modelling integrating genomics and transmission dynamics
Diagnostics	
DX1 and 2	On farm diagnostics and detection for emerging and re-emerging pathogens
DX3	Biomarkers for diagnosis of metabolic and infectious diseases
Disease (Viral, bacterial, fungal, parasitic, vector-borne, and prions)	
D1	Mechanisms of pathogenesis, resistance and persistence
D2	Pathogen replication in cells and organisms
D4	Culture systems for pathogen isolation and in vitro systems to predict pathogenesis
D5	In vitro culture systems and high throughput screens
D6	Genetics of eukaryotic pathogens
D7	Emerging pathogens of unknown clinical significance
D8	Cross-species pathogens
D9	Tick-borne disease
D10	Pathogen transmission dynamics
D11	Genetic basis of pathogen evolution, host specificity, and pathogenicity
D12	Genetic basis of disease resistance in livestock
D13	Disease complexes - mechanisms of pathogenesis
D14 and 3	Prediction of pathogen emergence, virulence and host response
D15 and 16	Effect of climate change on disease prevalence and transmission among food animals

RESEARCH TOPICS

D17	Role of vaccines in emergence of disease
Education	
ED1	Educational programs for next generation of animal health and welfare researchers
Genomics	
G1 and 4	Pathogen (including helminths) sequencing and databases
G2 and 6	Genomics and bioinformatics for animal health
G3 and 9	Transgenic including genome editing and Functional Genomics for health, welfare and resistance
G5	Studies of genetic and antigenic diversity of pathogens to understand virulence and vaccine coverage
G7	Refine genome assemblies of livestock species
G8 and 10	Immunogenetics for resistance to infections in livestock
Immunity	
IM1	Mucosal immune mechanisms and responses
IM2	Immune reagents - Shared resource for cell lines, hybridomas, MHC tetramers
IM3	Stimulating innate immunity
IM4	Systems immunology of livestock species
IM5	High-throughput antigen discovery platforms
IM6	Defining protective correlates of immune responses in livestock
IM7	Host immunology for vaccine development
Management	
M4 (1,3,5)	Developing sustainable and resilient agri-systems including socioeconomic considerations
M6	Evaluating threats combined with small scale (organic) and intensive farming systems
M2	Smart farming - biosensors, animal behaviour, air quality, organisms
M7	What will farms look like in the future
Microbiome	
MIC1	Microbiome as marker for health and disease

RESEARCH TOPICS

MIC2	Modulation of microbiome for health traits
MIC3	Microbiome role for AMR transfer
MIC4	Dynamics of microbial ecology
Vaccine	
V1 and 11	Understanding mucosal immunity and delivery technologies for eliciting mucosal immunity
V2	Non-GMO methods to attenuate strains
V3 (10, 14)	Vaccines for complex pathogens
V4 and 5	Novel antigen and adjuvant delivery systems and regulatory approval
V6	Vaccines and therapeutics that do not drive resistance
V7	Multivalent vaccines for multiple agents in multiple species
V8	Tools to predict protective antigens
V9	Structural vaccinology
V12	Vaccines for complex production related diseases to reduce antimicrobial use
V13	Immuno-epidemiology for vaccine development
Welfare	
W1	Impact of pain management on health immunity AMR performance
W2	Disease/immune effects of early life experience
W3 (15)	Integrated farm management systems and biological markers for animal welfare
W4	Validation of indicators of pain / well-being
W5	Aquaculture welfare and disease susceptibility
W8 (7, 9)	Develop methods and study effect of stress on disease susceptibility, vaccine efficacy and microbiome
W10	Integrate husbandry practices, stocking density on welfare and disease
W12	Integrate science ethics and perceptions related to animal welfare
W13	Measures for welfare in the field
W16	Biomarkers for "resilience" in animals
W11 (6, 14)	Animal behaviour as a predictor of disease outbreak
Miscellaneous	
Misc1	Prioritization of intervention strategies and disease targets (Gap Analysis)
Misc2	One health generating models of animal diseases
Misc3	Investigator initiated projects in topic areas

RESEARCH TOPICS

Clarification	
	Development of unbiased databases for factors driving disease emergence?
	Socio-ethical implications of judicious use of antimicrobial agents in intensive livestock production

PRIORITISATION

Group 1: AMR, Data Modelling, Diagnostics

High impact, High Need for Collaboration

Diagnostics

(DX1 and 2): On farm diagnostics and detection for emerging and re-emerging pathogens;
DX3: Biomarkers for diagnosis of metabolic and infectious diseases)

- Collaboration efforts can have strong impact
- D1 & D2 platform and discovery
- Should be AMR as well

Data Modelling

DM1: Epidemiologic methods for big data, omics, microbiome etc. and
DM3: Mathematical models to predict emergence, outbreaks, control, climate change, demographic and environmental

- Benefit of Big data you need to capture from different systems; synergy is required to get most efficient benefit

DM 5: Ecological modelling integrating genomics and transmission dynamics

- Transmission dynamics have strong correlation with DM 1 +3
- Once you have the data it can be leveraged better
- Investing into DM1 +3 the models have impact on transmission dynamics
- Skill sets in both countries are complimentary

AMR

AMR 6: Markers for anthelmintics resistance

- Only 4 classes of anthelmintics and the parasites are developing resistance to these drugs
- Critical mass in one country is not enough

High impact, Lower Need for Collaboration

AMR 2/3: Alternatives to Antibiotics (including for growth promotion)

- Production systems are different
- Finding best solution can use cross-Atlantic thinking
- Regulations are more restrictive - in UK they have less access to formulations
- How animals are managed is different
- Different practices of antibiotic use

AMR5: Best practices for minimizing AMR in animal production systems

- In order to minimize AMR, adopt new practices for targeted use of antibiotics or use alternatives to antimicrobials
- Shared best practices can be translated as appropriate.

Reasons

- Production systems are different
- Best practices are unique to a system

- It is a local problem ; requires regionalization solutions

Group 2: Disease, Education, Genomics and Immunity

High impact, High Need for Collaboration:

Immunity

- IM1: Mucosal immune mechanisms and responses
- IM3: Immune reagents – shared resource for cell lines, hybridomas, MHC tetramers
- IM4: Systems immunology of livestock species
- IM5: High-throughput antigen discovery platforms
- IM6: Defining protective correlates of immune responses in livestock
- IM7: Host immunology for vaccine development

Genomics

- All categories, including a new "G11" epigenetics

Education

- ED1: Educational programs for next generation of animal health and welfare researchers

Disease

- D3: Prediction of pathogen emergence, virulence and host response
- D8: Cross-species pathogens
- D10: Pathogen transmission dynamics
- D11: Genetic basis of pathogen evolution, host specificity, and pathogenicity
- D12: Genetic basis of disease resistance in livestock
- D14: Prediction of pathogen emergence, virulence and host response
- D15 and D16: Effect of climate change on disease prevalence and transmission among food animals
- D17: Role of vaccines in emergence of disease

High impact, Lower Need for Collaboration:

Disease

- D1: Mechanism of pathogenesis, resistance and persistence
- D2: Pathogen replication in cells and organisms
- D4: Culture systems for pathogen isolation and in vitro systems to predict pathogenesis
- D5: In vitro culture systems and high throughput screens
- D13: Disease complexes - mechanisms of pathogenesis

Lower impact, Higher Need for Collaboration:

Disease

- D7: Emerging pathogens of unknown clinical significance

- D9: Tick-borne disease

Group 3: Management, Microbiome, Vaccine, Welfare and Miscellaneous

High impact, High Need for Collaboration:
Vaccine: V1, V2, V3, V4, V5, V6, V8
Welfare: W1, W3, W4, W13

High impact, Lower Need for Collaboration:
Microbiome:

- MC1: Microbiome as marker for health and disease – Group recommended establishing a US-UK network

Welfare:

- W11: Animal behaviour as a predictor of disease outbreak – Group recommended establishing a US-UK network

Management:

- M4: Developing sustainable and resilient agri-systems including socioeconomic considerations

Additional information this group provided as important areas:

- Welfare and Disease;
- Role of microbiome in development of immune competence (high priority impact; medium need for collaboration)
- Microbiome is a high priority , but research perhaps premature for collaboration; networking is recommended;

DELIVERABLES

Disease: Host and Pathogen Genetics and Biology

DELIVERABLE 1	**DISEASE (VIRAL, BACTERIAL, FUNGAL, PARASITE, VECTOR AND PRIONS)**		
Names of US and UK representatives developing this deliverable	Siba Samal, Linda Dixon, Fiona Tomley, Vivek Kumar		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
For pathogens with low critical mass e.g. emerging diseases, parasitic diseases, trans-boundary and intractable disease to deliver; Genetic basis of pathogen evolution, host specificity, and pathogenicity; Pathogen transmission dynamics; Mechanisms of pathogenesis, resistance and persistence; Genetics of eukaryotic pathogens; Culture systems for pathogen isolation and in vitro systems to predict pathogenesis; In vitro culture systems and high throughput screens; Markers for anti-helminthic resistance;		Increased understanding of transmission/pathogenesis Global Research Networks Increased targets for vaccines/therapeutics Data on genetic polymorphisms	Better risk assessment Better disease control

Alternatives to antibiotics (including for growth promotion); Epidemiologic methods for big data, omics, microbiome etc. Mathematical models to predict emergence, outbreaks, control, climate change, demographic and environmental change, antimicrobial resistance On farm diagnostics and detection for emerging and re-emerging pathogens Biomarkers for diagnosis of metabolic and infectious diseases			
Targeted activities in vaccines/genomics/immunity etc. to these pathogens (esp. vaccines where none exists)	M→L		
Pathogenesis and virulence factors			
Research and Infrastructure Capability including needs to deliver (US and UK)			
Risks and potential barriers (feasibility)			
Added value of US-UK collaboration (why does this need joint working?)			
Define what success will look like			

DELIVERABLE 2	**PATHOGEN BIOLOGY: GENETIC BASIS OF PATHOGEN EVOLUTION, HOST SPECIFICITY, AND PATHOGENICITY; PREDICTION OF PATHOGEN EMERGENCE, VIRULENCE AND HOST RESPONSE; MECHANISMS OF PATHOGENESIS, RESISTANCE AND PERSISTENCE; PATHOGEN TRANSMISSION DYNAMICS**		
Names of US and UK representatives developing this deliverable	Siba Samal, Fiona, Linda, Vivek		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Prediction of pathogen emergence, virulence and host response (D14)	S (Basic Research)/M (Applied)/L (Policy)	Surveillance; Diagnostics; Tools; Databases; Models	Ability to predict Risk/Assessment for disease
Pathogen transmission dynamics	S (Basic Research)/M (Applied)/L (Policy)	Surveillance; Diagnostics; Tools; Databases; Models	Ability to predict Risk/Assessment for disease
Genetic basis of pathogen evolution, host specificity, and pathogenicity	L	Pathogen evolution (Gene Flow) Mechanism Diversity (protein structure)	Better understanding of disease/microbe evolution/spread
Mechanisms of pathogenesis, resistance and persistence (FAD, Emerging)	L	Markers Mechanisms of pathogenesis	Better understanding of disease/microbe evolution/spread
Genomics/diagnostics/Microbiome (beneficial microbes, symbiosis)/vaccines/DMS –data modeling)		Exchange people: One Health	Diagnostics, vaccines, models, trained workforces, public awareness
Research and Infrastructure Capability including needs to deliver (US and UK)	Facilities		

Risks and potential barriers (feasibility)	Funding Facilities (BSL3/4) Critical mass Limited surveillance in UK
Added value of US-UK collaboration (why does this need joint working?)	Facilities Critical mass/expertise
Define what success will look like	Multiple co-funded projects

DELIVERABLE 3	**GENETICS IMPROVEMENT OF ANIMALS**		
Names of US and UK representatives developing this deliverable	Bhanu, Dave D, Mark Stevens, Daniel P		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Functional annotation of animal genomes	M→L	Genetic validation of gene sequences	Better validation of genomic and omics output
Genetics Basis of disease resistance + production traits (incl health and welfare) Includes: Discovery, validation, mode of action and transfer/selection	M→L	More production animals to meeting emerging threats	Improved production; Food security and Food Safety
Tools for genetic modification (improved transgenesis, genome editing, animal models	M→L	Respond to novel challenges: Pandemics/climate change	Precise, faster, foot-print free animal Reagent KO models to investigate disease
Public engagement and education (social science and policy)	L	Improve policy making and public acceptance	Education of public and policy making is critical
Research and Infrastructure Capability including needs to deliver (US and UK)	Vital to do it in target species (NOT MICE!!)		
Risks and potential barriers (feasibility)			
Added value of US-UK collaboration (why does this need joint working?)	Shared expertise, limited facilities, ongoing collaboration		
Define what success will look like			

DELIVERABLE 4	**FUNCTIONAL GENOMICS/VALIDATION OF QTL CANDIDATES**		
Names of US and UK representatives developing this deliverable			
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Genetics of disease resistance: Discovery (mode of action); validation and transfer			
Transgenesis tools for genetic modification: genome editing; Genetic improvement (for disease/production/welfare)			
Animal Models for community			
Research and Infrastructure Capability including needs to deliver (US and UK)			
Risks and potential barriers (feasibility)			
Added value of US-UK collaboration (why does this need joint working?)			
Define what success will look like			

Modeling

DELIVERABLE 5	MODELING APPROACHES TO IMPROVING ANIMAL HEALTH		
Names of US and UK representatives developing this deliverable	Kao, Lee, Baylis, Funk, Sischo, Perez		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Use of modeling to inform AMR Strategy	S	AMR Strategy	AMR Strategy
Modeling to inform control of endemic disease	M	Research team focusing on endemic questions. Effect on welfare, vaccines, vector control and biosecurity etc.	Agri-system resilience
Effect of climate change on disease	M	Predictive model evidence for mitigation	Preparedness for future disease outbreak
Worldwide mapping of disease threats	L	Quantified uncertainty of prevalence, spatial distribution, emerging outbreaks	Quantifying global burden of pathogen distribution
Research and Infrastructure Capability including needs to deliver (US and UK)	• Existence of quantitative skill sets of appropriated hardware for analysis of data • Developing Industry/Research partnership for data acquisition and analysis		
Risks and potential barriers (feasibility)	• Generating network for global collaboration and data access • Managing datasets and storage		
Added value of US-UK collaboration (why does this need joint working?)	• UK has longer history of training in this area • US has more agricultural environment to model • Both have synergistic regional network of data lead to global perspective		
Define what success will look like	Tools for risk assessment and management assessment		

DELIVERABLE 6	**PROCESS-DRIVEN APPROACHES TO MICROBIOME – MATHEMATICAL MODELS**		
Names of US and UK representatives developing this deliverable	Sischo, Kao, Lee, Funk		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Modeling microbiome within host dynamic	M	Testable hypothesis for system stability at within host level	Recipes for intelligent data gathering
Modeling microbial ecology of agricultural systems	L	Testable hypothesis for system stability at agri-system level	Ecosystem stability
Mechanistic approach (instead of data) to modeling microbiome ecology and evolution	S	Testable hypothesis for system stability at within host level	Will inform impact of microbiome on immunity (i.e. vaccines)
Rumen microbiome as a modeling system for microbial community behaviour	M	Bring together microbial physiology animal sciatic modeler →community behavior assessment	Enable development of in vitro and in vivo quantitative microbial ecology
Research and Infrastructure Capability including needs to deliver (US and UK)	• Epidemiological and ecological models • Data generation from agricultural systems		
Risks and potential barriers (feasibility)	• Insufficient data: signal ratio (but better than in human systems) • Gap between theory and data still too large		
Added value of US-UK collaboration (why does this need joint working?)	• UK strength in models • US capacity to generate data		
Define what success will	New, process driven paradigms for microbiome ecology		

look like	

Animal Welfare/well being

DELIVERABLE 7	**WELFARE AS MEDIATOR OF DISEASE SUSCEPTIBILITY (WELFARE AS INDICATOR OF DISEASE)**		
Names of US and UK representatives developing this deliverable	Hans Coetzee, Cathy Dwyer, Candace Croney, Mike Mendl, Pam Ruegg		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Improved disease detection	S→L	Better, earlier disease detection, targeted decision making	Improved therapeutic outcomes; reduced antimicrobial use
Value of disease intervention	L		More effective intervention; less ineffective interventions
Impact of poor welfare on immune functions in disease susceptibility	S→L	Genetics, management changes, phenotype	Improved management
Stress: indicators, consequences to immunity			
Early life experience: epigenetics	M→L	Phenotype, epigenetics	Improved early life management, mitigation → disease resistance
Research and Infrastructure Capability including needs to deliver (US and UK)	UK: Expertise with specific disease models US: Genomics expertise		
Risks and potential barriers (feasibility)	Species specificity, benchmark: what ideal looks like; Age-related differences; environmental impacts on outcomes		
Added value of US-UK collaboration (why does this need joint working?)	• UK: epigenetics on farm, welfare on farms • US: large herd experience		
Define what success will look like	• Target decision making for groups versus individual • Improved management • Disease resistance: resilience		

DELIVERABLE 8	**EFFECTIVE SPECIES-SPECIFIC MANAGEMENT TO IMPROVE WELFARE**		
Names of US and UK representatives developing this deliverable	Hans Coetzee, Cathy Dwyer, Candace Croney, Mike Mendl, Pam Ruegg		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Euthanasia	S→L	Recommendations for timely euthanasia	Less suffering
Behavioral problems Stereotypic behavior	S→L	Recommendation for housing design	Fewer damaging behaviors
Group housing strategies (especially, swine; poultry; fish)	M→L		Practical, accommodating facilities
Sustainable intensification	L		Better resource use
Research and Infrastructure Capability including needs to deliver (US and UK)	UK: Experience with alternative housing in field testing US: Diverse management services		
Risks and potential barriers (feasibility)	Social acceptability; funding; resource availability; economic feasibility		
Added value of US-UK collaboration (why does this need joint working?)	UK has more field experience with alternative housing systems		
Define what success will look like	• Clarified definitions • Decision made on more complete dataset • Practices that are both feasible and supported by public • Understanding of economics • Policy Recommendation		

DELIVERABLE 9	**VALIDATING MEASURES OF WELFARE/PAIN**		
Names of US and UK representatives developing this deliverable	Hans Coetzee, Cathy Dwyer, Candace Croney, Mike Mendl, Pam Ruegg		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Validated measures of welfare: transdisciplinary approach – economics, practical social acceptance	S→L S: Lab identification M: Field validation L: Implementation, education and outreach		Assessments tools validated on farms
Human-animal interactions	S→L		
Physiological indicators includes BIOSENSORS	S: ID M: Validation L: Implementation		Assessment of biosensors Other measures
Behavior indicators	S→L		
Research and Infrastructure Capability including needs to deliver (US and UK)	UK: strength in behavior assessment, affective states, industrial contact US: Physiology, scales of farming, Extensions infrastructure		
Risks and potential barriers (feasibility)	Funding, diversity of management systems, diversity of species (specificity)		
Added value of US-UK collaboration (why does this need joint working?)	Complementary strengths		
Define what success will look like	• Welfare auditors will have tools consistent across farms • Research tools • Move away from cortisol as priority welfare measure • Policy recommendation		

DELIVERABLE 10	**MANAGEMENT PRACTICES TO REDUCE PAIN**		
Names of US and UK representatives developing this deliverable	Hans Coetzee, Cathy Dwyer, Candace Croney, Mike Mendl, Pam Ruegg		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Identify markers of pain versus nociception	S → L	S: Identification; M: validation; L: Implementation	Improved morale of farm workers, Decreased pain; improved productivity, reduce disease
Why does pain matter to the animal	M →L	Improved understanding	
Alternatives to painful procedures (3S's)	L	Genetics	
Management of pain especially chronic pain	S → L	Improved assessment	
Research and Infrastructure Capability including needs to deliver (US and UK)	UK: lab animal experience, access to drugs		
Risks and potential barriers (feasibility)	Species difference, stoicism, economics, practicality, social acceptability		
Added value of US-UK collaboration (why does this need joint working?)	UK: access to compounds		
Define what success will look like	I. New effective pain relief drugs; II. Strategy for reducing pain through selection (polled) III. Management changes IV. Public reassurance *V.* Policy recommendations		

Antimicrobial and Antiparasitic Resistance including Alternatives

DELIVERABLE 11	**IMPROVED ANTIMICROBIAL STEWARDSHIP**		
Names of US and UK representatives developing this deliverable	Liam/Guy		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Motivation for Antibiotic use (economic and social)		Understanding motivation	Reduce Antimicrobial use
Policy development		Policy	
Develop Stewardship Programme for animal/aquaculture		Program	
Human cognitive process interpretation of animal and environment			
Behavior and game theory math models			
Research and Infrastructure Capability including needs to deliver (US and UK)			
Risks and potential barriers (feasibility)			
Added value of US-UK collaboration (why does this need joint working?)			
Define what success will look like			

DELIVERABLE 12	**EFFECTIVE ALTERNATIVE ANTIBIOTICS/ANTIMICROBIALS (THERAPEUTICS)**		
Names of US and UK representatives developing this deliverable	Bhanu T/Mark Stevens		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Management/Welfare	L	New procedures	Less need for therapeutic Abx
In vitro systems high throughputs	M→L	New products/methods	One Health
New mechanisms (e.g., biologics, phage,)	M→L	New products/methods	
Antimicrobial peptides (AMPs): use as Antibiotics	M→L	New products/methods	
Social Science			
Game theory models	M→L	Optimal implementation	Improved implementations
Quantitative models of qualitative data	M→L	Optimal implementation	Improved implementations
Research and Infrastructure Capability including needs to deliver (US and UK)			
Risks and potential barriers (feasibility)			
Added value of US-UK collaboration (why does this need joint working?)			
Define what success will look like			

DELIVERABLE 13	**UNDERSTANDING ECOLOGY (CLIMATE CHANGE)/TRANSMISSION AMR ACROSS SPECIES**		
Names of US and UK representatives developing this deliverable	Guy and Mark Stevens		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Characterize resistome	L	Useful models, id reservoirs, determine biological relevance	Evidence based policy
Modeling transmission dynamics (to and from the farm)	L	Interventions and risk assessments	Management best practices
Effect of selection/infection/withdrawal	L		
Effects on immunity to the host			
Research and Infrastructure Capability including needs to deliver (US and UK)	Global problem		
Risks and potential barriers (feasibility)	Biodiversity/complexity		
Added value of US-UK collaboration (why does this need joint working?)			
Define what success will look like			

DELIVERABLE 14	**ANTHELMINTICS/PARASITICS**		
Names of US and UK representatives developing this deliverable	Witola, Fiona, Joan		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Genetic Markers for resistance (monitoring/management)	M/L	Novel marker	Better management; Monitoring of resistance
In vitro culturing (susceptibility testing)	L	• New methods • New models • High throughput screen	Better/faster assays for novel drugs
Novel targets for Anthelmintics	L	New targets	Effective treatments
Novel chemical alternative Anthelmintics	L	New treatments	Reduce resistance development
Novel delivery methods (e.g. Nano)	M/L	Improved formulation Low dosing	Improved efficacy of existing/new drugs
Genome Structure and evolution of parasites	L	Comparative info on diversity, evolution, pathogenesis, outcome	Intelligent design, therapeutics, vaccines
Research and Infrastructure Capability including needs to deliver (US and UK)	• Need both US/UK • Few in field		
Risks and potential barriers (feasibility)	• Low industry interest • Incentives		
Added value of US-UK collaboration (why does this need joint working?)	Critical mass of scientist		
Define what success will look like			

DELIVERABLE 15	POINT OF CARE/RAPID/SIMPLE DIAGNOSTICS FOR AMR/PATHOGENS		
Names of US and UK representatives developing this deliverable	Witola and Mark Stevens		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Omics			
Biomarkers (Host)	L	Rapid/simple kits	Better decision Antibiotic stewardship
Pathogen Diagnostics	L		• Improved treatments • Targeted therapy
AMR markers	M→L		
Research and Infrastructure Capability including needs to deliver (US and UK)	Input from surveillance		
Risks and potential barriers (feasibility)			
Added value of US-UK collaboration (why does this need joint working?)	Biodiversity; Global protection; trans boundary protection		
Define what success will look like			

DELIVERABLE 16	ALTERNATIVE ANTIMICROBIALS (GROWTH PROMOTION)		
Names of US and UK representatives developing this deliverable	Bill Sischo/Mark Stevens		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
How do they work	L	New targets treatments	Reduce Antibiotics, Improve productivity, Energy Retention, Disease Resistance
Role of microbiome	L	Prebiotics	
Non Antimicrobial role of ABK	M	Prebiotics	
Immune system regulation	M	Prebiotics	
Research and Infrastructure Capability including needs to deliver (US and UK)	In livestock		
Risks and potential barriers (feasibility)	Cost Large animal research target		
Added value of US-UK collaboration (why does this need joint working?)			
Define what success will look like			

Immunology and Vaccinology

DELIVERABLE 17	DEFINING IMMUNE SYSTEMS IN AGRICULTURAL ANIMALS		
Names of US and UK representatives developing this deliverable	Oriol, Joan, Sandra, Don, Bryan, XJ, Cynthia, Bettina, Ivan, Daniel		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Reagent development	M/L	Monoclonal antibodies; Functional proteins	Have community resources to enhance progress in vaccine development
Immunogenetics:			
I. Bioinformatics (analyze systems)	S/M	Computer programs	Have community resources to enhance progress in vaccine development
II. Define receptors and other immune response generic	M		Have community resources to enhance progress in vaccine development
III. Cellular responses (transcriptomics)	M		Inform on protective immune responses
IV. Fix genome	M	Perfect genome	Inform researchers of genetic diversity
V. Genetically manipulated animals	M	Animals with gene deletions	Will inform about the role of particular genes in protective immunity

HOST

VI. Immunogenetics determinants of infectious disease resistance and susceptibility in livestock			
Research and Infrastructure Capability including needs to deliver (US and UK)	Computer programmers to handle large datasets; Next gen sequencing capabilities		
Risks and potential barriers (feasibility)	Low as this is established for humans		
Added value of US-UK collaboration (why does this need joint working?)	Different groups in US and UK are working on different aspects of the immune system that needs to come together for the analysis of transcriptomics		
Define what success will look like	Easily accessible bioinformatics program that use the genomes of agricultural animals so researchers can analyze complex datasets; Sharing of large datasets among countries, i.e. transcriptome analysis in normal animals and in response to vaccines and infectious disease challenge studies and natural infections.		

DELIVERABLE 18	**VACCINES**		
Names of US and UK representatives developing this deliverable	Oriol, Joan, Sandra, Don, Bryan, XJ, Cynthia, Bettina, Ivan, Daniel, Fiona		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Antigen discovery • Proteomics • Reverse vaccinology • Cross protection • High throughput - omics	S/M/L	• Protidine antigens • Candidate vaccines • Advance platform technologies from livestock	Enhanced control of disease to improve economic performance, welfare and reduce antimicrobial usage
Multivalent platforms	S/M/L	Improved and more economical disease control programmes	
Delivery systems including vectors, adjuvant, nano particles, physical delivery, in ovo (poultry)	S/M/L	Enhanced protective immune response as a consequence of improved antigen delivery targeting	
Research and Infrastructure Capability including needs to deliver (US and UK)	Target species in vivo models, some pathogens limited capacity in individuals centers, linking centers working in vitro with in vivo facilities		
Risks and potential barriers (feasibility)	• Disease prioritization will be challenging for renew committees • Insufficient expertise – training required, • Regulatory framework - barrier to deployment		
Added value of US-UK collaboration (why does this need joint working?)	• Common high consequence pathogens – without sufficient critical mass in other country • Development of generic platforms for application to a wide range of pathogens • Improve translation pipeline by gaining US and UK different pharma models		

Define what success will look like	• Opportunity to target resources to endemic pathogens that impact on efficiency, welfare, and antimicrobial usage • Legacy of antigen discovery and vaccine delivery platforms for livestock species • Accelerate and expand the development of vaccines for high consequence diseases.

DELIVERABLE 19	**MUCOSAL IMMUNITY**		
Names of US and UK representatives developing this deliverable	Oriol, Joan, Sandra, Don, Bryan, XJ, Cynthia, Bettina, Ivan, Daniel,		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Basic mechanisms of mucosal immunity in • Gut (Tolerance) • Skin (Inductive Sites) • Gills/lungs (Effector sites)	S/M/L	• ID of key genes, molecules, targeting sites, • ID of immune pathways	Assist vaccine and immune-stimulant development
Models of mucosal immunity • Pathogen species • Vaccine • Cell lines	S/M/L	• Potential models for screening of vaccines/ immunostimulants • In vitro models to reduce use of animals	Assist vaccine and immune-stimulant development
Immunostimulants	S/M/L	Specific immunostimulant product	• Mitigate disease • Increase animal productivity • Prevent disease
Research and Infrastructure Capability including needs to deliver (US and UK)	• Specific research expertise in US and UK RE different species • Joining forces = increased capabilities		
Risks and potential barriers (feasibility)	Very feasible due to combined – unique UK-US expertise		
Added value of US-UK collaboration (why does this need joint working?)	Because we hold different areas of expertise that when combined increase the outcomes		
Define what success will look like	Ability to rationally design effective mucosal vaccines and immunostimulants		

DELIVERABLE 20	**IMMUNITY TO INFECTIOUS DISEASE**		
Names of US and UK representatives developing this deliverable	Oriol, Joan, Sandra, Don, Bryan, XJ, Cynthia, Bettina, Ivan, Daniel		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Identification of protective immunity + functional genomics + epigenetics	M/L (depending on pathogen)	Readout of protective immunity Pathogen target antigens	• National and informed basis for vaccine efficiency testing • Advanced knowledge on host immunity
Immune-mediated pathogenesis	M/L (depending in disease)	• Pathways and immune parameters involved • Comparative pathogenicity	• Development of improved vaccine and therapeutics • Advanced measure of protection (testing diagnostics) • Rationale for better treatment and interference
Persistence and Latency	M/L (depending in disease)	Pathogen based mechanisms	Interfere with key mechanism
Prevention of transmission	M/L (depending in disease)	Pathogen based mechanisms	
Research and Infrastructure Capability including needs to deliver (US and UK)	Can be done individually but would benefit from collaborative effort in all areas (see below for added value)		
Risks and potential barriers (feasibility)	May be barriers but need to be done to make progress and develop a better understanding		

Added value of US-UK collaboration (why does this need joint working?)	• Sharing expertise, reagent method, models • Increase efficiency and speed up outcomes • Prevent duplication/better use of resources
Define what success will look like	• Better control and preventive strategies for disease • Improved vaccines • Novel therapeutics • Cross-communication/better awareness

DELIVERABLE 21	**EDUCATION AND EXTENSION**		
Names of US and UK representatives developing this deliverable	Vivek, Pam, Cathy, Linda, Joan, Sandra, David		
Research programmes required (Basic, applied, policy evidence)	**Timeframe S/M/L**	**Outputs (activity, immediate product)**	**Outcomes (what difference will it make)**
Training • Students • Post-docs	S/M	• Online programs • Exchange programs • Conferences	Better trained workforce Next generation
Extension • Workers • Public	S/M	• Training programs • End user resources	Behavioral change impacting practice and productivity
Outreach	S/M/L	Training for policy makers	Behavioral change
Research and Infrastructure Capability including needs to deliver (US and UK)			
Risks and potential barriers (feasibility)	Funding		
Added value of US-UK collaboration (why does this need joint working?)	Leverage Extension (U.S.)		
Define what success will look like	• Multiple jointly trained students and post docs: sustainable high profile/competitive program • Pipeline of students/post docs for future workforce needs in animal health and welfare • Behavioral change in ender users resulting in better practices and productivity		

WORKSHOP HELD ON 1-3 JUNE 2015

GREENBELT MARRIOTT

WASHINGTON, DC METRO AREA