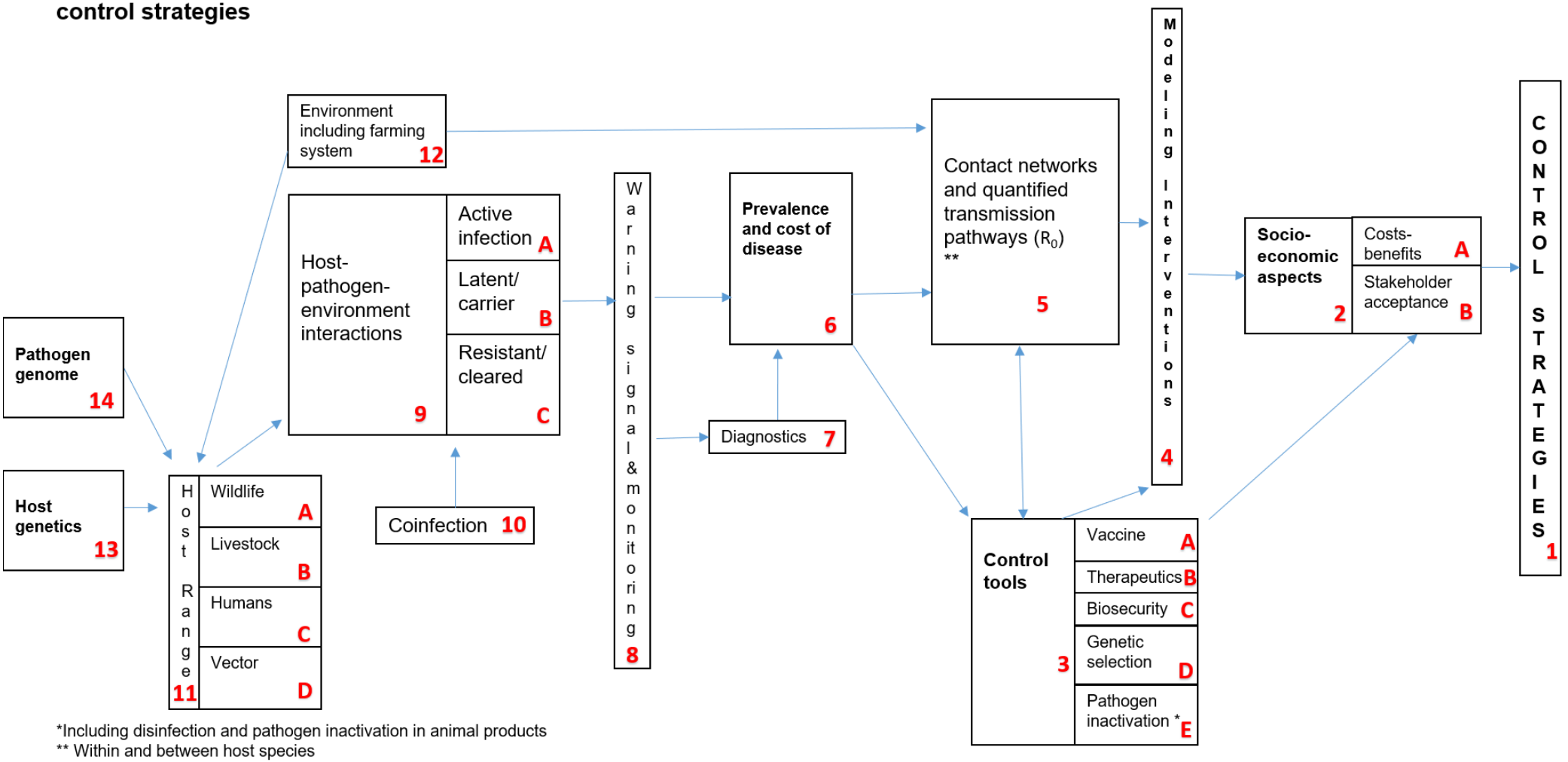
STAR-IDAZ
International Research
Consortium on Animal Health

Roadmap Lead Summaries

Disease/pathogen	Foot and mouth disease (FMD)					
Roadmap type	Development of Disease Control Strategies					
Version: Date	V1	17/10/2019				
	V2	21/10/19				
	V3	31/10/2019				
	V4	31/10/2019				
	V5	25/11/2019				
	V6	23/02/2024				

Research roadmap for development of disease control strategies



*Including disinfection and pathogen inactivation in animal products
** Within and between host species

Lead Summary 1

Title:	Development of effective and sustainable control strategies for FMD

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To develop a next generation of control measures and strategies for their application, in free and endemic countries.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Development of better analytical tools to support decisions for FMD control.
Provision of evidence to inform development of policies for safe trade of animals and animal products in FMD-endemic areas.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

A global FMD surveillance system that provides high quality, accurate, and real-time information on FMD risk is needed to cover critical gaps of information of the FMD situation worldwide and to support FMD control and eradication on a global scale
Consideration of socio-economic aspects.
Development of adequate control tools and diagnostic.
Improve modelling of interventions.
Improved knowledge on FMD epidemiology.
Cost: benefit model for different FMD control strategies.
Identification of hot spots for FMD strain emergence, which can be targeted for interventions.
Develop models that measure field control strategy success rates.

Projects

What activities are planned or underway?

State of the Art

Existing knowledge including successes and failures

Countries or zones can be divided into three categories depending on their FMD status: FMD-free without vaccination, FMD-free with ongoing vaccination, and endemic. As each category will feel the threat and impact of FMD differently, they would have different priorities in terms of research, prevention and disease control. Depopulation is the first line of defence against an FMD outbreak in a free country, but entails high costs and is not widely accepted by society. Countries FMD-free with ongoing vaccination have similar interests to free countries that do not routinely vaccinate, but may have different priorities in terms of vaccination, with long-term immunity deemed necessary to reduce the impact of future virus incursions. In endemic countries, there is a need for potent, quality assured vaccines inducing a quick and long-lasting immunity and that can be produced in vast quantities at low cost. Control programmes in endemic regions often lack clear evidence-based guidance and evaluation, resulting in limited or unknown programme impact.

Lead Summary 2

Title:	Social and economic impacts of the new generation of improved FMD control strategies

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To assess the social and economic impacts of the new generation of improved FMD control strategies.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Assessment of social and economic factors related with the burden FMD, including animal movement data, to improve the understanding of data.
Integration of data collected between research area and social area.
Linking epidemiologic and economic models in endemic and free regions to support policy and management, including strategies for disease mitigation other than, or complimentary to, vaccination.
Keep up and expand the tracking of long-distance movements, migration, geographical devastation, market development, and other socio-economic indicators that link epi and economic models to support policy/management and decision making.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Develop LMIC local control approaches with enhanced quarantine and testing.
Develop LMIC animal identification programmes.

State of the Art

Existing knowledge including successes and failures

The implementation of a choice of a control strategy against FMD epizootics should take into account several criteria in the decision-making process: the direct economic impact (e.g. public costs), the indirect economic impact (e.g. the export losses for agri-food industries), and the social impacts that may induce a distrust of public control of animal disease.

Projects

What activities are planned or underway?

Lead Summary 2A

Title:	Costs-benefits of FMD control strategies

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To assess the costs and benefits of new generation of improved FMD control strategies.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Assess and disseminate information on the real impact of the disease on the people or the real impact of control strategies (both in endemic and free countries).
Design models able to evaluate in real-time the cost-effectiveness of various control, surveillance, and sampling strategies.
Better consider the level of expenditure appropriate for contingency planning in order to advise governments.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Knowing the prevalence and cost of FMD.
Develop cost: benefit models to advocate for routine vaccination in endemic areas.

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 2B

Title:	Stakeholder acceptance of new generation of improved FMD control strategies

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To assess the acceptance of new generation of improved FMD control strategies by stakeholders, including the general public, in endemic and free countries.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Investigate social constraints and motivation associated with FMD surveillance and control strategies, at multiple level.
Define methods for improving the level of stakeholder involvement in FMD control (including exploring new methods for improving cross-stakeholder communication).
Design and implement surveillance strategies for collecting, storing, and sharing data to inform policy and decisions (epidemiological data, economics, social data, sequences).
In endemic regions (e.g. Africa), FMD might not be a priority and as resources are scarce, vaccination is only implemented during outbreaks. Awareness on the disease burden should be raised as to improve the involvement of society in the implementation of disease control.
Improve understanding of farmer participation in disease reporting and control, including how best to use compensation in control programmes.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

Studies on the 2001 UK epizootic underlined the importance of public opinion on the implementation of massive slaughter to control the disease.

Projects

What activities are planned or underway?

Lead Summary 3

Title:	Improved control tools against FMD

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To develop improved vaccines, therapeutics, biosecurity measures and disinfectants for controlling FMD.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Develop improved vaccines.
Develop effective bio-therapeutics.
Develop effective disinfectants.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

Currently available control tools have enabled FMD eradication in much of the developed world; however, in many developing countries, FMD remains uncontrolled. In these settings, the biosecurity measures that have been fundamental to successful FMD control in the developed world can seldom be implemented effectively.
Vaccines play a vital role in FMD control, used both to limit the spread of the virus during epidemics in FMD-free countries and as the mainstay of disease management in endemic regions, particularly where sanitary controls are difficult to apply. As it takes a few days for the immune system to respond to vaccination, in an outbreak situation, protection could potentially be provided in this period by the application of rapid, short-acting biotherapeutics, aiming either to stimulate a non-specific antiviral state in the animal or to specifically inhibit a part of the viral life cycle. Effective disinfectants for FMDV have long been available, but research is being conducted to further develop methods for quantitatively evaluating their performance under field, or near-field, conditions.
Effective disinfectants for FMDV have long been available, but research is being conducted to further develop methods for quantitatively evaluating their performance under field, or near-field, conditions.

Projects

What activities are planned or underway?

Lead Summary 3A

Title:	Vaccine

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

See dedicated roadmap

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

See dedicated roadmap

Solution Routes

What approaches could/should be taken to address the research question?

See dedicated roadmap

Dependencies

What else needs to be done before we can solve this need?

See dedicated roadmap

State of the Art

Existing knowledge including successes and failures

See dedicated roadmap

Projects

What activities are planned or underway?

See dedicated roadmap

Lead Summary 3B

Title:	Effective bio-therapeutics

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To develop effective and practical bio-therapeutics against FMD.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Test Ad5-IFN distribution and expression in cattle after aerosol exposure.
Evaluate the ability of Ad5-type I IFN platform to confer rapid onset of protection (18 hr) against several FMD serotypes and subtypes
Develop efficient delivery system for mass treatment of livestock.
Continue basic research on the molecular mechanisms of IFN-induced protection, FMDV pathogenesis and disease resistance in cattle, as to identify lead biotherapeutics or immunomodulators, which can induce very rapid and sustained protection and provide rapid protection in cattle.
Make the use of lower doses possible (to date, high doses are required).
Solve issues related to short half-life.
Solve species specificity issues.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

The development of bio-therapeutics such as characterisation of cell transcription factors that induce IFN, antiviral ISG biology, siRNA and miRNAs, Morpholino antisense oligonucleotides, IFN inducers, and 3D pol inhibitors is ongoing. Proof-of-concept efficacy studies using Ad5-pIFN-α in swine have demonstrated its potential as a FMDV biotherapeutic. Efficacy studies with Ad5-pIFN-α in a swine contact challenge model, its efficacy against additional FMDV serotypes, and its enhanced potency have increased the development product potential for this platform in swine.

Projects

What activities are planned or underway?

Lead Summary 3C

Title:	Biosafety risk

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To assess the biosafety risk of shipping penside tests containing inactivated FMD virus.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Assess biosafety and biosecurity of transportation of inactivated virus in penside test.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Suitably validated pen-side diagnostics available in LMICs.

State of the Art

Existing knowledge including successes and failures

Currently available control tools have enabled FMD eradication in much of the developed world; however, in many developing countries, FMD remains uncontrolled. In these settings, the biosecurity measures that have been fundamental to successful FMD control in the developed world can seldom be implemented effectively.

Projects

What activities are planned or underway?

Lead Summary 3E

Title:	Pathogen inactivation

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To develop low cost commercially available disinfectants for use in the inactivation of FMDV on contaminated surfaces found in farm settings and other susceptible environments.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Development of low cost commercially available disinfectants for use in the inactivation of FMDV on contaminated surfaces found in farm settings and other susceptible environments.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Develop agree disinfection protocols.

State of the Art

Existing knowledge including successes and failures

Sodium hydroxide (2%), sodium carbonate (4%), and citric acid (1 to 2%, depending on the surface to be treated) have been reported to be effective disinfectants for FMDV.
Less ideal disinfectants include iodophors, quaternary ammonium compounds, hypochlorite, and phenols, because they rapidly lose the ability to disinfect in the presence of organic matter.
Surfactants alone have little efficacy against FMDV due to the non-enveloped structure of the virus. There are newer disinfectants that are not as corrosive, including Virkon-S®, a chlorinated compound.

Projects

What activities are planned or underway?

Lead Summary 4

Title:	Modelling interventions

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To develop mathematical models and analytical tools to identify the most appropriate, cost-effective surveillance and control strategies, supporting the decision-making process and planning of FMD control interventions. Additionally, optimising the use of resources and efforts.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Develop analytical tools to support the decision-making process, including, a) anomaly detection methods to identify outlier events; b) prediction models for identification of genetic variants of viruses, to predict severity, duration, and likelihood of transmission of disease, and to evaluate the degree of success of control and prevention interventions; c) epidemiological models that project spread of disease in a defined region under various control strategies and that can be used in developing disease control programmes and for active surveillance sampling.
Apply epidemiological models to identify key areas of the world to be targeted for active collection of samples and information, and for monitoring the evolution of the disease as part of the global FMD surveillance system in critical regions of the world.
Develop models to predict the spread of FMDV lineages and highlighting risk.

Solution Routes

What approaches could/should be taken to address the

Develop an epidemiological model that can reduce the sampling to determine the sanitary status.
Develop intervention models to improve understanding of endemic circulation of FMDV, to estimate critical community sizes and identify appropriate control points.
Improve interpretation of trees, detect rapid evolutionary changes, and understand the effects of under-reporting cases which help to develop predictive models in case of intervention policies (vaccinate to live or sanitary killing, for instance).

Dependencies

What else needs to be done before we can solve this need?

Prevalence of FMD.
Improved knowledge on FMD epidemiology.

State of the Art

Existing knowledge including successes and failures

Over the past years, there has been significant research in mathematical modelling for FMD, mostly on transmission models to predict the consequences of outbreaks in FMD-free countries, estimate resource requirements and compare different control options, particularly the impact of vaccination.

Projects

What activities are planned or underway?

Lead Summary 5

Title:	Quantification of FMD transmission pathways (R_0)

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To define and quantify the spread, emergence, and transmission of FMDV lineages in different epidemiological contexts.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Integrate molecular data with complimentary datasets (meta data) for field epidemiology to facilitate conversion of phylogenetic tree into transmission trees for use of genetic data during ongoing epidemics and to understanding endemic circulation of strains at a fine scale.
Use seroprevalence studies ins several species allowing comparison among cases.
Assess the role of goats in different epidemiological situation.
Formulate models predicting the spread (and emergence) of FMDV lineages (e.g. accommodating sequences, immune status, trading patterns) and highlighting risk.
Define the meaning of the genetic variants (topotypes) and new lineages, like for instance, identify genetic determinants of phenotypical treats (virulence, host range, adaptation, neutralisation).

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Adequate surveillance.
Improved knowledge on FMD epidemiology.
Models that relate strain variation to likely virulence and transmission risk (R0).
Better understanding of the role of small ruminants in FMDV transmission/outbreaks.

State of the Art

Existing knowledge including successes and failures

During the recent years there have been advances identifying low scale genetic tracking of outbreaks, application of NGS to epidemiological studies, estimation of unbiased prevalence for better control FMD, include recombination in the equation of phylogenetic analysis, managing meta-data to facilitate understanding of endemic settings, and integrating molecular epidemiology with vaccine matching and serology.

Projects

What activities are planned or underway?

Lead Summary 6

Title:	Evaluation of FMD burden

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To assess the prevalence and cost of FMD at the country and at the global level.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Assess the direct and indirect cost, and control cost of FMD outbreaks in different contexts.
Measure whether efforts to control FMD are having a positive impact upon burden of disease in the different regional roadmaps.
Use a standardised design and analysis to allow clearer estimation of the burden of disease and accurate comparison of that burden between different serosurveys.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Adequate surveillance.

State of the Art

Existing knowledge including successes and failures

Although a disease of low overall mortality, FMD places a huge burden on both individual livestock keepers and national economies. As a collective body of work, FMD seroprevalence studies are undermined by a lack of consistent and rigorous sampling methods, and the outcome, seropositivity, has an uncertain period at risk. In a given setting, animals that have a longer period at risk are more likely to have been infected at some point, and unless this is adjusted for, estimates of incidence will be confounded

Projects

What activities are planned or underway?

Lead Summary 7

Title:	Diagnostics

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

See dedicated roadmap

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

See dedicated roadmap

Solution Routes

What approaches could/should be taken to address the research question?

See dedicated roadmap

Dependencies

What else needs to be done before we can solve this need?

See dedicated roadmap

State of the Art

Existing knowledge including successes and failures

See dedicated roadmap

Projects

What activities are planned or underway?

See dedicated roadmap

Lead Summary 8

Title:	Warning signal and monitoring

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To develop reliable and comprehensive FMD surveillance systems to collect and analyse information

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Apply a sequence-based approach to estimate the true prevalence of different lineages.
Develop and implement surveillance systems, including the implementation of quick, simple, cost-effective pipelines for collection and submission of good quality samples for early recognition of signs, or to find evidence using antigen detection, antibody, or virus detection.
Monitor populations of susceptible wildlife species.
Define sampling density that is required to “accurately” describe endemic FMD circulation (genomic data).
Investigate the mechanisms of emergence of viruses, such as the India 2001, which became very successful replacing all other serotype O strains.

Solution Routes

What approaches could/should be taken to address the research question?

For what concerns the spread of India 2001, it is possible that this lineage is very good at causing subclinical infections and perhaps that is the key to its success.

Dependencies

What else needs to be done before we can solve this need?

Reliable comprehensive international surveillance systems to collect and analyse information.
Quality of veterinary services.
Collaboration with endemic countries.
Funding availability to ensure sustainability.
I&R.
Training of veterinarians/stock keepers in the identification of FMD.
Serological assay to differentiate infection from vaccination.

State of the Art

Existing knowledge including successes and failures

Good surveillance is needed for early detection of outbreaks and to provide knowledge of the distribution of disease in order to direct control measures. Several studies assessed surveillance data and its use in disease management

Projects

What activities are planned or underway?

Lead Summary 9

Title:	Host-pathogen-microbiome-environment interactions

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To elucidate FMD host-pathogen-environment interactions

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identify virus-host protein-protein interactions (systematic and comprehensive).
Increase knowledge of the functions of FMDV proteins including interaction with host factors.
Investigate the role of microbiome on FMDV response and impact.
Define strain specificity of virulence including SATs.
Identify of factors defining cellular tropism.
Define the role of RNA structure (coding and non-coding regions).
Determine the role of cellular innate immune responses in FMDV infection of cattle and swine.
Develop a reproducible FMDV challenge method in swine.
Study virus life-cycle at animal population´s level (e.g. how can virus genomic diversity influence pathogenesis).
Investigate serotype-host preferences
Assess establishment and longevity of memory responses, importance of CMI.
Integrate environmental variables- host species.
Determine FMDV immune evasion mechanisms (is diversity a virulence factor?).
Big data integration (i.e. for interactions with the environment).
Multi-disciplinary data analysis (i.e. for interactions with the environment).

Solution Routes

What approaches could/should be taken to address the

Dependencies

What else needs to be done before we can solve this need?

Check in vitro results in animal models: it is important to make a correlation between the cell cultures and animal models.
Collaboration with endemic countries.

State of the Art

Existing knowledge including successes and failures

Though many aspects of the pathogenesis of FMD remain incompletely elucidated, it is clear that rapid systemic dissemination with high titre viral replication and dysregulated host immune responses are central to the observed pathological processes. In contrast to the well-defined role of humoral immune responses, the contribution of T-cell-mediated responses to immunity and their role in the induction of protective B-cell responses to FMDV in the natural host species are poorly understood. Virulence is a phenotype influenced by a highly complex virus-host interaction, and produces different results during infection with very close isolates (same serotype, topotype, and even same isolate).

Projects

What activities are planned or underway?

Lead Summary 9A

Title:	Understanding virus host interactions during early phases of FMD infection

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To understand virus host interactions during early phases of FMD infection in susceptible species.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identify critical aspects of bovine nasopharynx and porcine oropharynx which define tropism.
Investigate virus-host interactions at the primary sites of infection in ruminants, their role in determining infection, and the mechanisms that lead to the formation of vesicles and how the infection carry on.
Investigate how to prevent replication in primary sites.
Achieve holistic and unified understanding of: viral processes, functional genomics, deep sequence analysis of diversity, host response to infection: transcriptomic and/or predictive proteinomics.

Solution Routes

What approaches could/should be taken to address the research question?

Enhancement of mucosal immunity has high probability of improving protection.

Dependencies

What else needs to be done before we can solve this need?

Understand the bases for functional and predictive genomics.
Improve knowledge of innate immunity.

State of the Art

Existing knowledge including successes and failures

Major gaps in our understanding of the molecular events of early pathogenesis limit the design and development of completely effective countermeasures. Yet, it is becoming increasingly apparent that the early stages of disease are characterised by pan-respiratory tract infection. Continued efforts to improve the understanding of virus host interactions during early phases of infection will greatly contribute to the development of effective tools to block viral infection. New molecules involved in the FMDV life cycle have been published, some may have a role in virulence such as: RHA, Sam68, JMJD6, Gemin5, Beclin 1, Vimentin, DCTN3 and LYPLA/ATP1. However, it is still not clear which host factors are critical for virulence, an important issue to help in controlling the disease.

Projects

What activities are planned or underway?

Lead Summary 9B

Title:	Latent/Carrier

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To determine mechanisms of FMDV persistence in livestock and their role in disease transmission.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Determine viral and host determinants of establishment and maintenance of persistence.
Define persistence, sites of persistence, and meaning of persistent infection in nature.
Understand the difference between carriers and not carriers.
Identification of animals during transitional phase.
Study mucosal responses to acute and persistent infections in cattle.
Support research on the immunological mechanisms of cross protection in susceptible species
Determine the role of persistent animals in FMD transmission.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

In domestic and wild ruminants, FMDV may persist (i.e. carrier state) with intermittent viral shedding in the oral-pharyngeal fluid for extended periods of time. Persistence may result from symptomatic or asymptomatic infection of naïve, convalescent or vaccinated animals. Evidence suggests that the sites of viral persistence are in the pharyngeal region, specifically the dorsal soft palate, dorsal pharyngeal area, and associated lymph nodes. The mechanisms mediating the establishment and maintenance of persistent infections in ruminants remain unclear, but it is noteworthy that both primary and persistent infections with FMDV have been associated with pharyngeal tissue in ruminants. The role of persistence in the transmission of FMDV is poorly understood, although some evidence indicates that persistently infected African buffaloes (Syncerus caffer) can serve as a source of infection to cattle. Despite the uncertainty surrounding the true threat posed by FMDV carriers, it is clear that the perception of threat from these animals is one of the main driving forces dictating FMD-associated trade issues. Thus, one of the long-term goals of novel FMD countermeasures must be prevention or cure of the carrier state.
Experimental studies evaluating persistent infections have demonstrated that only some ruminant species exposed to FMDV become carriers, irrespective of whether they are fully susceptible or immune; i.e., protected from disease as a result of vaccination or recovery from infection.

Lead Summary 9C

Title:	Resistant/Cleared

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To establish the immune mechanisms underlying protection to FMDV during the time-course of infection.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Establish the immune mechanisms underlying protection to FMDV during the time-course of infection.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 10

Title:	Coinfection and viral competition

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To study multiple infection and viral competition.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Study field situations such as competition during multiple infections in wild species and persistence.

Study multiple infection and viral competition (e.g. it is not known if shedding can be triggered by other infectious diseases, such as Bovine Viral Diarrhea).

Identifying issues related with co-circulation of different virus lineages.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Surveillance data.

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 11

Title:	Host range

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To determine the host-range and role of the different species on long-term maintenance of FMDV.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Define host range determinants at molecular level (e.g. buffalo vs. cattle, SAT1 vs. SAT2 vs. other).
Investigate key events that define permissiveness.
Define role of different species on long-term maintenance of FMDV.
Define role of different species on virus evolution.
Perform multi-disciplinary data analysis.

Solution Routes

What approaches could/should be taken to address the research question?

Further elucidate 3A mutation as best-defined host range determinant.

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

FMDV has been found in more than 70 species, including cattle, buffalo, sheep, goats, pigs, and deer.

Projects

What activities are planned or underway?

Lead Summary 11A

Title:	wildlife

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To define the role of wildlife and persistent infection in FMD endemic settings.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Define role of wildlife in FMD endemic settings.
Study viruses circulating in wildlife (e.g. are they ancestors of those isolated from domesticated animal viruses? What do we know about their reproduction cycle in wild species?).
Assess the role of different species on long-term maintenance of FMDV in nature.
Investigate pathogenesis in African buffalos (immunological data is lacking).
Develop strategies to deal with wild species during outbreaks.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Surveillance data.
Collaboration with endemic countries.

State of the Art

Existing knowledge including successes and failures

There is evidence of infection in several wildlife animal species, including buffaloes, impalas, warthogs, wildebeest, giraffe, and pachyderms. However, the overwhelming evidence from countries eradicating FMD, is that vaccinating cattle is enough to eradicate the disease in presence of wildlife, suggesting that the importance of wildlife in controlling the disease in some endemic scenarios might be neglected.
FMDV can be detected in African buffalo isolated herd for 24 years, and in an individual for up to 5 years (peak between 1-3 years). However, the frequency and titre of virus recovered decreases over time, and a significant number of animals fail to maintain persistent infection for prolonged periods, with and the proportion of persistently infected animals decreasing with age (peak in 1-3-year age-group). Studies of antibody levels in adult and sub-adult buffalo over time is variable and may be the reason of having “waves” of new infection and/or recrudescence of symptoms.

Projects

What activities are planned or underway?

Lead Summary 11B

Title:	Livestock

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To identify determinants of viral virulence for different serotypes of FMDV in cattle, sheep, and swine.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Investigate variability of virulence across cattle breeds.
Identify determinants of viral virulence for different serotypes of FMDV in cattle, sheep, and swine.

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

There are differences in FMDV pathogenesis among animal species: ruminants, in contrast to pigs, are highly susceptible to infection by the respiratory route. They may be infected experimentally by airborne exposure with doses over 103 times lower than pigs. This coincides with differences in the primary sites of viral replication and primary responses to infection between these two animal species.

Projects

What activities are planned or underway?

Lead Summary 12

Title:	Environment including farming system

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To improve the knowledge of transhumance and dynamic of FMD virus.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Transhumance involves the seasonal movement of livestock between fixed points to access different climatic zones at different times of the year. Gathering comprehensive data on these movements and associated livestock health status can be challenging
Complexity of FMD Virus Dynamics
Climate Change and Environmental Impact

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

Surveillance data.
Evaluate impact of intensifying livestock production in LMIC settings.

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 14

Title:	Pathogen genome

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To understand the bases for functional genomic and predictive genomics for FMD.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identify and deal with recombination in full genome sequencing, including phylogenetic models.
Achieve holistic and unified understanding of functional genomics and deep sequence analysis of diversity.
Develop methods allowing rapid FMDV strain typing.
Apply NGS full genome to better understand the ecology and microenvironment of the virus.

Solution Routes

What approaches could/should be taken to address the research question?

There is a range of FMD viruses' strains which differ in terms of virulence and there are continuous changes in FMDV RNA sequences. Establishing the genomic differences of the various strains will assist in the identification of virulence mechanisms. Continuous monitoring of FMD sequences will be necessary to ensure the diagnostic are adequate.

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

Next-generation sequencing technologies that allow sequencing of not only the predominant sequence but also minority variants present within a single sample have emerged. This technology has been used to explore within host virus evolution and selection in a way not previously possible, substantially advancing knowledge of FMDV dynamics within the host. A protocol, suitable for usage in a high-throughput laboratory, has been published for whole FMDV genome consensus sequencing.

Projects

What activities are planned or underway?