STAR-IDAZ
International Research
Consortium on Animal Health

1. Roadmaps for the development of diagnostic tests and therapeutics for helminths

2. Roadmaps for the development of candidate vaccines and control strategies for liver fluke and nematodes

3. Roadmaps for the development of candidate vaccines, diagnostic tests and control strategies for FMD

4. Roadmap for research to underpin the development of control strategies for ASF

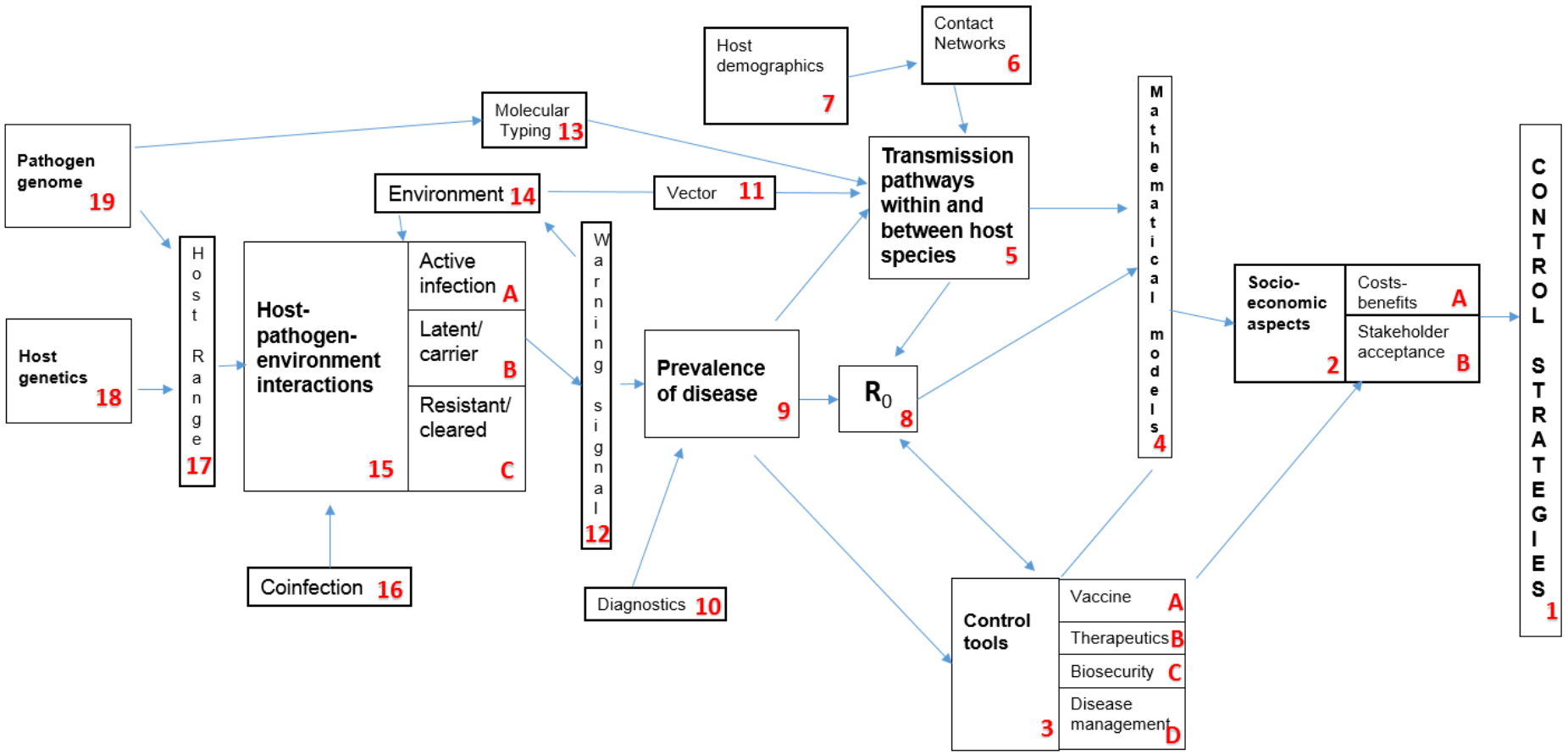
SIRCAH Deliverable 3.4

30/09/2019

Interactive versions of the roadmaps in this report can be found at https://roadmap.star-idaz.net

The Secretariat for the STAR-IDAZ IRC (SIRCAH) is funded from the European Union's Horizon 2020 research and innovation programme under grant agreement No 727494

4) Roadmap for the research to underpin the development of control strategies for ASF



The ASF roadmap lead summaries for the development of control strategies are in draft form until validated by the Global ASF Research Alliance (GARA)

ASF Epidemiology - Lead Summary 1

Title:	Develop strategies to prevent the introduction of African swine fever (ASF) in free countries, eradicate it from countries having epidemics and to control it in endemic ones

Research Question

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

To validate outbreak surveillance measures, epidemiological investigations need to be performed on the implementation of emergency control measures and the use of 'diagnostic tests to detect infected pigs in exposed populations. Investment in the implementation of research priorities to support preparedness plans and ensure the effective use of countermeasures to prevent, control, and eradicate ASF are needed.

Challenge(s)

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

Perform epidemiological investigations on the implementation of emergency control measures and the use of diagnostic tests to detect infected pigs in exposed populations.
Support preparedness plans and ensure the effective use of countermeasures to prevent, control, and eradicate ASF.
Establish global ASF surveillance system that provides high quality, accurate, and real-time information on ASF risk to cover critical gaps of information of the ASF situation worldwide and to support ASF control and eradication on a global scale.

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?

Developing an ASF vaccine.
Improving biosecurity.
Investigating the transmission pathways within and between host species.

State of the Art

Existing knowledge including successes and failures

African swine fever (ASF) is a transboundary animal disease that currently threatens swine production worldwide. Even though ASF is an African disease, it is now well entrenched in the Caucasus, Russia, Europe, and Asia. The most significant cause of this recent geographical spread is most likely due to the illegal movement of animals, trade, and contaminated products. This places other countries that trade in pig and pig products in danger, including Europe, South America, and North America. Furthermore, the epidemiological implications of ASF outbreaks in new geographical and ecologically unique environments are unknown, complicating control measures. Surveillance programs will be the first line of defence against ASF. Diagnostic tests are available and need to be incorporated in diagnostic laboratories. A key control measure would be vaccines, but they are currently unavailable, a major gap in the availability of countermeasures to control ASF outbreaks.
ASF may show unique regional patterns of presentation, associated with unique set of risk factors that should be assessed to establish proper surveillance and control strategies.

Projects

What activities are planned or underway?

Lead Summary 2

Title:	To investigate socio-economic aspects of ASF

Research Question

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

To better understand the socioeconomics of the disease and pig and pork value chains, particularly those related to low biosecurity settings.

Challenge(s)

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

To investigate the socioeconomics of the disease and pig and pork value chains, particularly those related to low biosecurity settings.

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 introduction of ASF into countries outside Africa has had important economic consequences for swine industries. A significant consequence of the introduction of ASF is the loss of status for international trade and the implementation of drastic and costly control strategies to eradicate the disease. In endemic countries, such as in Africa, the impact is also considerable, particularly on numerous poor households that depend on pigs to pay for many of the necessities of life. The acceptance of stakeholders of the current stamping out policy is weak, either for ethical and economic reasons.

Projects

What activities are planned or underway?

Lead Summary 2A

Title:	To investigate the costs-benefits of ASF control strategies

Research Question

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

Good understanding of the real cost, both direct and indirect, of ASF is fundamental to be able to perform a cost benefit analysis of implementing ASF control strategies.

Challenge(s)

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

To better understand the costs (direct and indirect) of ASF, both in epidemic and endemic situations.

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 introduction of ASF into countries outside Africa has had important economic consequences for swine industries. A significant consequence of the introduction of ASF is the loss of status for international trade and the implementation of drastic and costly control strategies to eradicate the disease. In Cuba, the introduction of the disease in 1980s led to a total cost of U.S $9.4 million. In Spain, the final 5 years of the eradication programme alone were estimated to have cost $92 million. Given the effect on pork production and trade as well as the costs of eradication, it was estimated in 1994 that the net benefit of preventing ASF introduction in the United States would amount to almost $450 million, nearly 5 per cent of the value of total sales of pork products. In endemic countries, ASF has huge economic implications both for the individual farmers, especially the smallholder producers and at national scales.

Projects

What activities are planned or underway?

Lead Summary 2B

Title:	Investigating strategies to improve stakeholder acceptance of ASF control strategies

Research Question

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

There is a need to come up with sustainable and effective alternatives to stamping out for countries that cannot afford compensation, as well as to improve stakeholder acceptance and participation in ASF control strategies.

Challenge(s)

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

Develop strategies to improve the effectiveness of passive surveillance.
Develop sustainable and effective alternatives to stamping out for countries that cannot afford compensation.

Solution Routes

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

Passive surveillance is often the only economically viable solution for many countries but has weaknesses due to the difficulty of differentiating ASF from many common endemic infectious diseases. Passive surveillance can be greatly improved by awareness campaigns targeting all stakeholder along the pig value chain, as well as the establishment of fair compensation plans to incentivise reporting.

Dependencies

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

State of the Art

Existing knowledge including successes and failures

The acceptance of stakeholders of the current stamping out policy is weak, either for ethical and economic reasons.
The effectiveness of stamping out in the absence of a fair and timely compensation scheme is highly dubious; *i.e.*, in the absence of compensation there is no incentive for pig owners to report, who will instead sell or slaughter their pigs further spreading the disease. Lack of funds to compensate owners, particularly for culling of healthy pigs on neighbouring premises, also constitutes a challenge in less wealthy countries.

Projects

What activities are planned or underway?

Lead Summary 3

Title:	Development of appropriate ASF control tools

Research Question

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

Develop appropriate ASF control tools

Challenge(s)

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

Develop a safe and effective ASF vaccine.
Improve biosecurity.
Develop disease management tools.

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

As no vaccine is available yet, the only control strategy would be based in the early detection of infected animals and their elimination, and strict control of the movement of pigs. Minimum control measures will include depopulation of infected herds, surveillance and movement restriction within established control zones together with surveillance in herds that have been in contact with infected herds. Depopulation of contact herds and neighbouring herds might be established. This entails high costs, and might not be sustainable in some contexts. This control measure is effective in countries or geographic areas where pigs are housed in well-defined premises or pig farms. In areas where domestic pigs are kept on free-ranging scavenging systems, depopulation might be difficult

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:	Developing therapeutics for ASF

Research Question

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

To develop therapeutics for ASF.

Challenge(s)

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

Testing Ad5-IFN distribution and expression in swine for rapid onset of protection against ASFV 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

There are no licensed anti-viral drugs available to treat pigs against ASF.

Projects

What activities are planned or underway?

Lead Summary 3C

Title:	Implement improved biosecurity measures

Research Question

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

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Challenge(s)

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

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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

Implementing biosecurity measures on the farm is one of the most important countermeasures to prevent and protect commercial swine operations, but specific measures need also to be included and integrated in an eradication campaign to prevent further transmission and geographical spread through transport and person-to-person contacts. Personal protective equipment (PPE) should be suitable to prevent farm-to-farm virus spread by animal health officials involved in eradication. The main goal of a biosecurity plan is to decrease the probability of infection and significantly reduce the cost associated with losses. A set of zoo-sanitary measures should be put in place to accomplish the goals set by the biosecurity plan. The more measures are implemented, the higher the cost, but warranted in a disease outbreak situation. The OIE Terrestrial Animal Health Code (Chapter 15.1. and Chapters 4.3. and 4.4.) provides guidelines for the establishment of compartments free of ASF.

Projects

What activities are planned or underway?

Lead Summary 3D

Title:	Development of better ASF management

Research Question

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

To develop better tools for the management of ASF.

Challenge(s)

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

Identify better management tools to control the disease in wild boars

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

Explore the use of disinfectants to reduce the risk of ASFV infections from ASFV-infected carcasses.

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

Acaricides for controlling the soft tick may not be useful as the tick lives off the host and burrows underground as well as crevices in buildings. The best ASF method is to remove the pigs from infected premises.

Projects

What activities are planned or underway?

Lead Summary 4

Title:	Improving ASF modelling

Research Question

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

To improve the modelling of ASF control or spread in different scenarios.

Challenge(s)

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

Assess and model the epidemiology of ASF in emergency control programmes on the level of the individual pig, the herd, and the demographics of the region (low versus high density pig populations).
Perform risk assessments with regards to control or spread of ASFV.

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?

Investigating the transmission pathways within and between host species.
Improving knowledge on ASF host demographics (including wildlife).
Assessing the R_0 for the different strains of ASFV.

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 5

Title:	Investigating the transmission pathways within and between host species

Research Question

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

To investigate the transmission pathways within and between host species, including domestic and wild swine.

Challenge(s)

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

Investigate basic parameters governing host to host infection, including domestic and wild swine as well as the ticks.
Investigate the role of swill feeding in ASF transmission.
To assess ASF time survival in dry cured meat.

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?

Defining ASF host range.
Assessing the relevance of ticks in ASF epidemiology.

State of the Art

Existing knowledge including successes and failures

Two types of transmission cycles have been defined for ASF based mainly on the mode of transmission of the virus among different pig populations: a domestic pig cycle and sylvatic-wild pig cycle. To this, an additional cycle has been added, the environmental cycle, which includes the issue of wild boar and persistence in the environment as observed in the Baltics and Central Europe. The presence/absence of arthropod vectors (*i.e.*, tick species) in the affected area will impact the spread and maintenance of the virus in the environment. In sub-Saharan Africa, ASFV is maintained in a sylvatic cycle between wild suids (warthogs) and argasid ticks of the genus *Ornithodoros*. However, other wild pigs such as bush pigs do not inhabit burrows, and therefore would most likely spread ASFV via direct transmission, although evidence for such occurrences is limited. In endemic areas of Africa, infected ticks and warthogs are the source of virus responsible for disease outbreaks in domestic swine. Once established, virus is efficiently contact-transmitted between domestic swine. Infection through direct contact between domestic pigs and warthogs has not been observed. The initial expression of ASF in a previously ASF-free country could be variable and unpredictable due to the myriad of host factors and the broad diversity of virulence among strains of ASF viruses. Thus, ASF may show unique regional patterns of presentation, associated with unique set of risk factors that should be assessed to establish proper surveillance and control strategies

Projects

What activities are planned or underway?

Lead Summary 6

Title:	Contact networks

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

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

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 7

Title:	Improving knowledge on ASF host demographics (including wildlife)

Research Question

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

The monitoring og both captive and wild suid populations distribution is essential to effectively address the ASFV problem in endemic area

Challenge(s)

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

Continuate molecular epidemiology studies to monitor both captive and wild suid populations distribution, especially in 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?

Defining ASF host range.

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 8

Title:	Assessing the R_0 for the different strains of ASFV

Research Question

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

Improve knowledge of the basic reproduction number (R_0) of different strain of ASFV in the different host species.

Challenge(s)

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

Assess the rate of transmission of strains of ASFV of different virulence in infected-contact animal experiments.

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

Several studies were conducted to estimate the R_0 for ASF across the years. For the Malta'78 isolate, a first approximation of the basic R_0 resulted in an estimate of 18.0 (6.90–46.9). For the Georgia 2007/1 ASFV strain, models showed that R_0 is 2·8 [95% confidence interval (CI) 1·3–4·8] within a pen and 1·4 (95% CI 0·6–2·4) between pens

Projects

What activities are planned or underway?

Lead Summary 9

Title:	Investigating the prevalence of ASF

Research Question

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

Prevalence of ASF should d be investigated.

Challenge(s)

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

Continuate molecular epidemiology studies to monitor prevalence in both captive and wild suid populations.

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?

Implementation of ASF surveillance programmes.

State of the Art

Existing knowledge including successes and failures

At the herd or population level, infections may result in 50-100% of the pigs seroconverting, but showing no signs of disease, with variable proportion of the pigs dying of acute ASF.

Projects

What activities are planned or underway?

Lead Summary 10

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 11

Title:	Assessing the relevance of ticks in ASF epidemiology

Research Question

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

There is an important need to identify if the ticks in an affected region (where ASF outbreak occurred) could become biological vectors or not.

Challenge(s)

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

Continuate molecular epidemiology studies to monitor soft tick distribution.
Identify if the ticks in new geographical areas where ASF outbreak occur could become biological vectors or not.
Determine whether new ASFV isolates can productively infect local ticks and whether they become persistently infected.
Research is needed to further understand the distribution of soft ticks.
Investigated basic parameters governing host to host infection, including ticks.
Develop tests for detecting ASFV in ticks.

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?

Implementation of tick surveillance programmes.

State of the Art

Existing knowledge including successes and failures

The presence/absence of arthropod vectors (i.e., tick species) in the affected area will impact the spread and maintenance of the virus in the environment. In sub-Saharan Africa, ASFV is maintained in a sylvatic cycle between warthogs and ticks of the genus *Ornithodoros*. In endemic areas of Africa, infected ticks and warthogs are the source of virus responsible for disease outbreaks in domestic swine.
Acaricides for controlling the soft tick may not be useful as the tick lives off the host and burrows underground as well as crevices in buildings. The best ASF method is to remove the pigs from infected premises.

Projects

What activities are planned or underway?

Lead Summary 12

Title:	Warning signal

Research Question

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

Based on the complexity of the epidemiology of ASF and multiple clinical manifestation of the disease it is necessary to develop surveillance activities based on diagnostic testing.

Challenge(s)

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

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 resemblance of ASF clinical manifestation to other diseases in swine such as Erysipelas and Classical Swine Fever hamper syndromic surveillance in domestic swine based exclusively on clinical signs.

Projects

What activities are planned or underway?

Lead Summary 13

Title:	Molecular typing of circulating ASF viruses

Research Question

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

There is a continuing need for knowledge on the molecular epidemiology of ASFV isolates mainly in relation to wild populations and ticks.

Challenge(s)

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

Ongoing molecular characterisation of currently circulating isolates in Africa, Europe and Asia.

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?

Ongoing surveillance and sample collection in the different regions.

State of the Art

Existing knowledge including successes and failures

Although there is only a single virus species, currently 24 genotypes have been described, with Genotype 23 and 24 just described in 2017 and 2018 respectively. Nevertheless, this designation is based on the sequencing of a single gene. Full genome sequence of the p54-gene has been confirmed as a valuable additional genotyping method for molecular epidemiological studies. Enhanced discrimination is obtained by analysis of the central variable region (CVR) within the B602L-gene, described as the most variable locus to distinguish between closely related isolates and identify virus subgroups within several of the 24 genotypes. Clearly, there are significant differences in genome size, virulence and immunogenicity (no cross-protection), but little is known about the genes responsible for virulence, host range, and viral-vector-host interactions.

The PCR based genotyping might be a tool in endemic areas like sub-Saharan Africa; however, in the event of an outbreaks in new geographical areas, the single most important task is to complete the sequencing of the viral genome. This will provide essential information not only about the potential origin of the virus but possible homologies to other strains.

Projects

What activities are planned or underway?

Lead Summary 14

Title:	The role played by the environmental contamination in the ASF cycle

Research Question

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

To better understand the role played by the environmental contamination in the ASF cycle.

Challenge(s)

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

To assess ASFV inactivation in buried carcasses and soil.
To assess the role played by the environmental contamination in the ASF cycle.

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 survivability of ASFV in faeces and urine of experimentally infected animals was recently investigated: based on the calculated half-lives it can be assumed that ASFV remains infectious at 37°C for almost four (urine) or three (faeces) days. In a study from 1999, it was shown that at 40°C, the inactivation of ASFV in pig manure is realised after 4 hours, and within 5 minutes at 65°C.
Studies to assess ASFV inactivation in buried carcasses and soil are on-going but not yet completed. For soil, the pH found in forest seems to be a limiting factor for virus survival.

Projects

What activities are planned or underway?

Lead Summary 15

Title:	Investigation of ASF host-pathogen environmental interactions

Research Question

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

ASF virus cause acute – chronic infection reflecting the virulence of the virus strain or the host (genetics). Understanding the different responses could shed light on the protective mechanisms and virulence factors.

Challenge(s)

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

Investigate host and virus mechanisms causing virus attenuation.
Determine patterns of activation of immunologically relevant host genes, particularly at early stages after infection.
Study the pathogenesis of ASFV isolates with different virulence in diverse susceptible host in order to identify, and ultimately subvert the early events of infection.
Investigate the role of specific genomic determinant(s) in disease outcome
Determine global expression profiles of host cells infected with ASFV.
Once the host cell response is understood at a cellular level, this information could also be gathered and applied to the response in the host.
Implement Viral Transcriptomic Studies.

Solution Routes

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

The use of attenuated strains obtained by genetic manipulation or by adaptation to different cell substrates provides a valuable tool to study mechanisms of attenuation. Comparative analysis of host and virus behaviour using parental virulent versus their derived attenuated strains, particularly focusing the early stages of the infection, would provide critical data regarding the host and virus mechanisms causing virus attenuation.
Genomic wide either on the RNA or Protein level data for ASFV gene expression would be relatively easy with current technologies and could provide data to determine differences in ASFV gene expression in vitro and in vivo in different hosts

Dependencies

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

State of the Art

Existing knowledge including successes and failures

African swine fever virus infection of domestic swine results in several forms of the disease, ranging from highly lethal acute manifestations to subclinical depending on contributing viral and host factors. In Africa, highly virulent viruses produce a broad range of responses in populations of pigs in endemic areas. At the herd or population level, infections may result in 50-100% of the pigs seroconverting, but showing no signs of disease, with variable proportion of the pigs dying of acute ASF. Unlike domestic swine, wild African suids infected with ASFV are generally asymptomatic with low viremia titres.

Projects

What activities are planned or underway?

Lead Summary 15A

Title:	Active infection

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

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

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

Infection usually occurs through the oronasal route with primary virus replication in tonsils followed by a viremia with further secondary replication of all organs of the haemolymphatic system. In the acute form of the disease, the incubation period ranges from 5 to 15 days. Survival times for animals infected with African ASFV strains range from 2 to 9 days. Subacute cases last 3–4 weeks.

Projects
What activities are planned or underway?

Lead Summary 15B

Title:	Investigation of the mechanisms of ASFV persistence and the role of survivor pigs in disease epidemiology

Research Question

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

The mechanisms of virus (or experimental vaccine) persistence is unknown.

Challenge(s)

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

Establish how viruses result in persistent infection.
Improve knowledge of the role of the survivor pigs as potential shedders by the use of appropriated diagnostic serological and virological tests for identification/detection of these animals.
Investigate the mechanisms involved in the protective immune response responsible for the appearance of carrier animals.

Solution Routes

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

Perform studies on natural survivors.

Dependencies

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

State of the Art

Existing knowledge including successes and failures

Long term persistence following infection of pigs with genotype I isolates of reduced virulence has been demonstrated. These persistent infections have been demonstrated to be transmissible from pigs persistently infected with the low virulence genotype I NH/P68 isolate to contact pigs. Low virulence isolates can cause chronic forms of the disease. Pigs that survive infection have been shown to carry virus in tissues or blood for long periods of time, which may contribute to virus transmission, disease persistence, sporadic outbreaks and sudden reactivation of the disease. There is limited experimental evidence for transmission from persistently infected to naïve animals, and the relevance of persistently infected animals as carriers of ASF in the field is not clear, but data on healthy infected animals keeps accumulating, suggesting that the virulent virus could survive for long periods of time in the recovered pigs and a recrudescence of virulence may occur at later times. Recent data using a moderately virulent isolate of different genotype during a shorter period of time, do not support the establishment of a carrier status in animals surviving infection, though long term detection of viral genome in blood (for at least 90 pi) is consistent with many other reports. Persistent infection with ASFV is reported to occur in warthogs and in domestic pigs surviving acute viral infection.

Projects

What activities are planned or underway?

Lead Summary 15C

Title:	Investigate the mechanisms of animal survival and resistance to ASF infection

Research Question

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

The mechanisms responsible for animal survival to infection are not well understood.

Challenge(s)

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

Investigate the mechanisms responsible for animal survival to 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

Homologous protective immunity develops in pigs surviving acute infection with moderately virulent or experimentally attenuated variants of ASFV. These animals develop long-term resistance to homologous, but rarely to heterologous, virus challenge.

Projects

What activities are planned or underway?

Lead Summary 16

Title:	Coinfection

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

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

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 17

Title:	Defining ASF host range

Research Question

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

Feral swine and wild suidae may have an important role in the spread and maintenance of ASF. The potential role of these species as a reservoir for ASF should be further investigated.

Challenge(s)

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

Identify ASFV genes and genetic determinants (group of genes like multigene families) involved in host range, virulence and pathogenicity.
Study the pathogenesis of ASFV isolates with different virulence in diverse susceptible host.

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

ASF is a contagious viral disease of domestic pigs In Africa, ASF virus (ASFV) produces unapparent infections in wild suids: wart hog (*Phacochoerus africanus*), bush pigs (*Potamochoerus larvatus, P. porcus*) and the giant forest hog (*Hylochoerus meinertzhageni*) (a single report). The reservoir of ASFV is considered the soft tick *Ornithodoros moubata*.
The virus Georgia 2007 affects both domestic pigs and European wild boar, with the latter proving to be as susceptible as domestic pigs and the disease established self-sustaining cycles within the wild boar population. This was unprecedented as so far, any previous introduction into the European wild boar population had been self-limiting, unless sustained by co-infection and spillover from domestic pigs.
It is increasingly apparent that the terminal genomic regions and Multigene Family (MGF) genes play a significant role in ASFV host range.

Projects

What activities are planned or underway?

Lead Summary 18

Title:	Study of host genomes for identifying factors contributing to resistance

Research Question

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

There is a lack of available sequences for host genomes of ASFV susceptible species, including the species and subspecies of both domestic and wild pigs in endemic or outbreak areas, and the genomic sequences of animals that are able to survive an outbreak.
In order to conduct genomic studies as to what factors contribute to resistance of some of these breeds, a large-scale sequencing effort should be conducted.

Challenge(s)

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

Obtaining genomic sequences of the wild and domestic pigs, boar and warthogs in outbreak areas.
Development of CRISPR/Cas9 or siRNA libraries targeting swine genomes.

Solution Routes

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

Development of a swine specific knockout libraries are critical for in vitro genomic screens for ASFV. Libraries targeting the swine genome would be highly valuable to perform host genomic screens for ASFV for a wide range of experimental avenues that could lead to the discovery of potential receptors, pathways modulated to avoid immune detection or for increased virus virulence.

Dependencies

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

State of the Art

Existing knowledge including successes and failures

The course of ASF infection varies depending not only on the particular virus strain but also on host characteristics. Fourteen individual genomes are available from breeds of *Sus scrofa* on NCBI, but the genome sequences of the wild and domestic pigs, boar and warthogs in outbreak areas of Africa and Europe remains largely unknown.

Projects

What activities are planned or underway?

Lead Summary 19

Title:	Genome sequencing of ASF strains

Research Question

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

There are a range of viruses' strains which differ in terms of virulence. Having virus genome sequences is essential for identifying the host-pathogen interactions and how this can be manipulated. Establishing the genomic differences of the various strains will assist in the identification of virulence mechanisms. The annotation and analysis of genomes in the size range of ASFV is difficult and requires specialised tools.

Challenge(s)

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

ASF virus complete genomic sequences from each genotype/ different virulence/ and viruses that have replicated exclusively in domestic pigs, wild pigs and ticks.
Generation of reference sequences that have been confirmed by different techniques in different laboratories to account of sequencing errors in repeat regions and other difficult stretches.
Harmonisation of sequencing workflows and validation of different enrichment techniques and host exclusion.
Automation and standardisation of viral genome sequencing for subtyping ASFV strains.

Solution Routes

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

Using current, very robust technologies would be highly valuable to establish a comprehensive database, which would include full length genome sequence of large number of isolates to replace the current less meaningful genotype-based classification.
Next-generation sequencing could be aided by enrichment through targeted sequence capture technology.

Dependencies

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

Collect isolates from different origins and hosts including domestic pigs, wild boar, warthog and ticks.
Collect field strains from current outbreaks in Africa.

State of the Art

Existing knowledge including successes and failures

ASFV virion is comprised of more than 50 polypeptides. External to the inner membrane is the capsid, composed of the structural protein p72, ASFV genome include homologs of cellular ubiquitin conjugating enzyme, trans-prenyltransferase, NifSlike protein, and components of a base-excision repair pathway.
Several of the putative virulence/host range proteins, along with certain multigene family (MGF) proteins, the central variable region protein 9-RL (pB602L as annotated in BA71V), and the variable tandem repeat-containing structural protein p54 (pE183L) are among the most variable among multiple field isolates.
Currently 22 genotypes have been described, based on the sequencing of a single gene (*p72*). Full genome sequence of the *p54*-gene has been confirmed as a valuable additional genotyping method for molecular epidemiological studies. Enhanced discrimination is obtained by analysis of the central variable region (CVR) within the B602L-gene.

Projects

What activities are planned or underway?