Non-technical summary: African swine fever virus control

Project duration
5 years 0 months

Project purpose
(a) Basic research
(b) Translational or applied research with one of the following aims:
(i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants
(iii) Improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes

Key words
African swine fever virus, Vaccines, Antiviral therapy, Transmission, Immunology

Animal types	**Life stages**
Pigs	adult, juvenile

Retrospective assessment
The Secretary of State has determined that a retrospective assessment of this licence is required, and should be submitted within 6 months of the licence's revocation date.

Reason for retrospective assessment
This may include reasons from previous versions of this licence.
Contains severe procedures

Objectives and benefits
Description of the projects objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.
What's the aim of this project?
African swine fever is a lethal haemorrhagic viral disease of pigs for which there is no vaccine or treatment. Through basic and applied research into the disease this project aims to develop tools to protect animals, farmers and global food security from this devastating disease.

A retrospective assessment of these aims will be due by 2 September 2026
The PPL holder will be required to disclose: Is there a plan for this work to continue under another licence? Did the project achieve its aims and if not, why not?

Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.
Why is it important to undertake this work?
African swine fever is an invariably fatal disease of domestic pigs and wild boar that can cause the death of infected animals in as little as a week. There is no vaccine or treatment for African swine fever and therefore control is only possible through rapid diagnosis, movement restrictions and slaughter of affected herds. Good farm biosecurity can prevent disease transmission, however a single mistake can lead to disaster and this approach cannot be applied to free-ranging wild boar. Due to the severity of the disease, trade

restrictions are applied to countries that are suffering from outbreaks, therefore an African swine fever outbreak within the United Kingdom would inevitably lead to the loss of the export market for pig products, valued at around £500 million in 2018, as well as having a significant impact on the domestic market. African swine fever is now present on four continents and the recent outbreaks in East and Southeast Asia have led to the deaths of millions of animals through disease and culling and has led to a shortage of meat and knock-on effects on food prices. African swine fever has restricted the development of pig farming in sub-Saharan Africa for decades which particularly impacts the rural poor and subsistence farmers. African swine fever is therefore a risk to both the United Kingdom and to global food security.

This project is designed to improve our understanding of the host immune responses that are important for protection against the virus, as well as the mechanisms by which African swine fever virus manipulates host defence pathways. Virus proteins important for inducing protection will be identified, characterised and tested for their ability to induce immune responses in pigs. This data will be used to advance development of vaccines against African swine fever. Antivirals will be tested for their ability to control virus replication in pigs and parameters relating to the transmission of the virus by biting insects will be explored. Taken together this will improve the tools we have available to control African swine fever. This would contribute to the welfare of pigs and wild boar and would limit economic losses for pig farmers and the pork industry. It would also help secure global supplies of pork and pigs.

What outputs do you think you will see at the end of this project?
The project will progress work leading to more effective control of African swine fever virus outbreaks. It will lead to increased knowledge of the basic biology of African swine fever virus as well as applied knowledge that may lead to effective vaccines or treatments. The availability of such vaccines or treatments would provide an alternative policy for African swine fever control, avoiding mass slaughter of pigs in the case of an outbreak of the disease. Successful vaccine development is essential to ensure global food security which is threatened by the devastating effects of this fatal pig disease. Pigs provide a stable and cheap supply of high protein food and financial security for many back yard farmers in developing countries and are a main source of protein in many developed countries. A vaccine may even lead to the first steps of African swine fever eradication. Data generated during this project will lead to publications in high impact journals in the field and potentially vaccine or antiviral candidates suitable for commercial development. This will be achieved by:
1) Further development and safety testing of weakened strains of African swine fever virus that could be used as vaccines. This will include comparison of effects of deleting different combinations of viral genes to improve safety and efficacy of these weakened viruses.
2) Identification of viral proteins involved in protection and defining a minimal number of African swine fever virus proteins that can induce protection against infection with a normally lethal dose of African swine fever virus. Use of compounds that can boost the immune response and different combinations of viral proteins will be tested to improve protection.
3) Improved understanding of virus host interactions. This will help to define the role of different African swine fever virus genes in manipulating host responses and the host responses that lead to disease. Further benefits will come from a greater understanding of the protective immune response allowing identification of immune correlates of protection, which may allow subsequent development of African swine fever vaccines to be carried out without the need to infect pigs with the virus itself.

4) The project will generate tools which are applicable for diagnosis of African swine fever, for studies on other porcine diseases, and other basic studies such as pig immunology.
5) Identification of antivirals that can control African swine fever virus replication in pigs could produce new tools to control disease outbreaks. These could be used either alone to reduce transmission of African swine fever virus and hence limit spread of epidemics, or in combination with vaccines when these become available.

Who or what will benefit from these outputs, and how?
African swine fever is a lethal disease and therefore the welfare of pigs would benefit from methods to effectively control the virus. The general public would benefit from new methods to control African swine fever due to increased global food security. Farmers and associated food production and distribution industries would directly benefit, as would governmental organisations responsible for managing these supply chains. Commercial companies would be able to exploit vaccine and antiviral candidates, and suppliers of diagnostic tools could benefit from validation data.

How will you look to maximise the outputs of this work?
Many of the objectives outlined in this project involve collaborative work, either with other research institutes or commercial companies. Results from the studies will be published in high impact open access journals and will be discussed at international conferences. Due to the topical nature of African swine fever it is likely that negative data will be publishable, however in the unlikely event that it is not then draft manuscripts will be uploaded to an online repository such as bioRxiv to ensure the data is made available to all.

Species and numbers of animals expected to be used
Pigs: 480

Predicted harms
Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.
Explain why you are using these types of animals and your choice of life stages.
Only domestic pigs, wild boars, feral pigs and four species of African suid - warthogs, bushpigs, red river hogs and giant forest hogs are susceptible to African swine fever virus. The virus only causes disease in pigs and wild boar and the disease in these two animals is practically indistinguishable, therefore pigs are the most appropriate animal to use. There is no small animal model for African swine fever and therefore pigs cannot be replaced. The protective immune response to African swine fever virus cannot yet be studied using tissue culture, isolated organs, non-vertebrate systems or computer modelling.

Typically, what will be done to an animal used in your project?
An animal could be immunised with a vaccine and blood samples and nasal swabs taken to see if the vaccine has induced an immune response. The animal could be given one or two more immunisations to act as boosters and blood samples will be taken before and after these immunisations to measure changes in the immune response. In some experiments parts of the immune system may be blocked using specific treatments. These procedures will take place over the course of three to eight weeks. After this animals are likely to be infected with Africa swine fever virus. Pigs will then be monitored closely for signs of disease and blood samples or swabs taken to study virus replication. Following infection with African swine fever virus, pigs may develop fever, which will consist of high temperatures, lack of interest in food and lethargy, in some cases pigs will suffer increased respiratory rates. Some experiments will involve treatment of African swine fever infected pigs with antivirals.

In some cases animals will suffer moderate disease, which would likely include high temperatures, reduced interest in food and lethargy for several days, before going onto recover.

What are the expected impacts and/or adverse effects for the animals during your project? Immunisations, blood collections, swabbing and insect feeding will only cause mild and transient distress that the pigs will quickly recover from and will have no lasting impact.

In a natural situation infection with African swine fever virus would lead to the death of the animal. Through careful monitoring of the animals in our care we will ensure that individual animals suffer at most five days of fever before we intervene and stop the study. However, in a typical study we will intervene after two or three days of fever.

Expected severity categories and the proportion of animals in each category, per species.
What are the expected severities and the proportion of animals in each category (per animal type)?
All the animals will suffer mild severity due to immunisations and/or blood collection.

Animals infected with African swine fever virus may suffer, no adverse effects, mild, moderate or severe clinical signs of disease depending on the study. The proportion of animals affected will depend on the type of study. For example in a successful vaccination trial most of the animals may suffer no or only mild adverse effects, however if such a trial was not successful then animals may suffer moderate or severe clinical disease.

Naïve, control pigs will develop clinical signs of disease following ASFV infection, which will be limited to moderate severity in the majority of studies. In some experiments animals will suffer moderate disease and then go onto to recover.

What will happen to animals at the end of this project?
Killed

A retrospective assessment of these predicted harms will be due by 2 September 2026
The PPL holder will be required to disclose: What harms were caused to the animals, how severe were those harms and how many animals were affected?

Replacement
State what non-animal alternatives are available in this field, which alternatives you have considered and why they cannot be used for this purpose.
Why do you need to use animals to achieve the aim of your project?
The aim of the project is to develop tools to help control African swine fever, a disease of domestic pigs and wild boar. There is no vaccine to help control the disease because classic approaches to vaccine development have not worked for African swine fever. Inactivated virus does not protect pigs and weakened viruses prepared by repeated cycles through tissue culture cause a chronic form of disease. Therefore to develop safe and effective African swine fever vaccines we need to better understand the mechanisms by which the virus causes disease and how the pig's immune response can be stimulated to fight off the virus.

Because African swine fever virus only causes diseases in pigs and virus pathogenesis and protective immunity cannot be studied in the test tube or with computer modelling we need to use animals for this research.

Which non-animal alternatives did you consider for use in this project?
We considered cell culture systems, analysis of historic samples and the use of membrane feeding systems for biting flies.

Why were they not suitable?
Cell culture and analysis of previous samples will enable us to make reasonable, but not certain, predictions based on previous knowledge and experience about which vaccines or antivirals might be effective. Therefore, we need to test vaccines and antivirals in pigs to prove they are effective. We also need to study the immune response in pigs so that we can improve our predictions about vaccine efficacy.

Cell culture systems cannot replicate the course of disease caused by African swine fever virus in pigs.

A retrospective assessment of replacement will be due by 2 September 2026
The PPL holder will be required to disclose: What, if any, non-animal alternatives were used or explored after the project started, and is there anything others can learn from your experience?

Reduction
Explain how the numbers of animals for this project were determined. Describe steps that have been taken to reduce animal numbers, and principles used to design studies. Describe practices that are used throughout the project to minimise numbers consistent with scientific objectives, if any. These may include e.g. pilot studies, computer modelling, sharing of tissue and reuse.
How have you estimated the numbers of animals you will use?
The number of animals used in each experiment is determined with the help of statisticians to ensure the data generated is scientifically robust, reproducible and uses the fewest animals possible.

What steps did you take during the experimental design phase to reduce the number of animals being used in this project?
Statistical analysis is an essential requirement from our external funding bodies and the project involves professional statisticians who help calculate group sizes required to distinguish between treatment groups based on our previous observations. These observations have established that severity of disease is correlated with maximum levels of virus detected in blood and established the variation of virus titres observed within groups of pigs infected with the same virus by the same route and titre. In some experiments different vaccine formulations will be compared with each other saving the need for a naive control group. Power calculations will be carried out to calculate group sizes required to detect differences with at least 80% power and 95% confidence. In these calculations we will incorporate data from new and previous experiments using either inbred or outbred pigs as appropriate.

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project? Extensive use of in vitro and ex vivo assays will ensure that statistically sound results are obtained and will be used to identify

correlates of protection that may be used in future to predict pathogenesis of an isolate and/or induction of protective immunity. The calculations will be refined as new data on host responses that correlate with protection and data on levels of virus in protected compared to unprotected or control pigs is collected during experiments. Animal numbers will also be reduced by using samples that will be collected during vaccination trials which will then be used to complete other objectives within the project.

A retrospective assessment of reduction will be due by 2 September 2026
The PPL holder will be required to disclose: How did you minimise the numbers of animals used on your project and is there anything others can learn from your experience?

Refinement
Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.
Which animal models and methods will you use during this project? Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.
We will use pigs because they are natural host of African swine fever. Animals infected with African swine fever will be carefully monitored for clinical signs of disease by staff who are trained in animal handling, husbandry and the recognition of signs of pain, distress, disease as well as the ethics of using animals in research. Clinical signs will be recorded daily on score sheets designed to clearly and unambiguously indicate when humane endpoints have been reached. Pigs can be monitored remotely 24/7 if required. Experienced staff will also be responsible for all procedures and so ensure that pain and distress is minimised while procedures are being carried out.

Why can’t you use animals that are less sentient?
There is no less sentient model available for African swine fever virus, therefore we have to use pigs for this research. Small animal models have been tried in the past and were not successful. It would not be possible to follow disease progression in a terminally anaesthetised animal.

How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?
We will measure immune responses throughout the project. As our knowledge of the protective immune response increases we will be able to make more informed decisions about whether pigs are likely to be protected after infection with African swine fever virus. This will allow us to minimise welfare costs by removing animals earlier from studies.

Animals will be regularly monitored by trained staff and the frequency of this will be increased if the pigs get sick.

All pigs housed within the unit are given positive reinforcement after a procedure to associate a potentially negative experience with a positive one i.e. grapes are given after procedures. The pigs are also given an acclimatisation period to familiarise them with the staff and routines within the unit. This helps the technicians to also get them used to touch which is needed for taking temperatures without restraint. This is a refinement in animal handling methods to improve animal welfare and the value of animals in research.

Analgesics and non-steroidal anti-inflammatory drugs will be given to animals under supervision of a veterinarian if required.

We will continue to trial the use of pig slings to restrain animals during sampling in order to minimise suffering.

What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?
We will follow guidelines from the NC3Rs and the Code of Practice for the Housing and Care of Animals Bred, Supplied or Used for Scientific Purposes.

How will you stay informed about advances in the 3Rs, and implement these advances effectively, during the project?
By regularly consulting resources available from national and international organisations such as the NC3Rs and from the local Named Information Officer. Discussions on the 3Rs is agenda item of meetings that are scheduled with PILHs after every study.

A retrospective assessment of refinement will be due by 2 September 2026
The PPL holder will be required to disclose: With the knowledge you have now, could the choice of animals or model(s) used be improved for future work of this kind? During the project, how did you minimise harm to the animals?