Combating Infectious Diseases of Livestock for International Development

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Scientific push to beat animal diseases and tackle poverty

Poverty, hunger and food security are three of the biggest challenges facing the world and most acutely developing countries. For the 900 million people in the developing world who live in rural areas and have less than \$1 a day, agriculture is vital for their livelihood and survival. The World Bank estimates that, for the world's poorest people, GDP growth originating in agriculture is about four times more effective in reducing poverty than any other sector growth.¹

Cattle, sheep, goats, pigs, chickens and other livestock represent a lifeline for people in developing countries who live below the poverty line. This is especially true for women, who make up over 60 per cent of agricultural labour in Sub-Saharan Africa and South Asia, employed on subsistence smallholdings, commercial farms and in food production.²

Just one animal can meet a whole family's needs for food and milk and more than this, they can be used for ploughing, manure, transport and trade, offering individuals a way out of poverty. But deadly and debilitating livestock diseases jeopardise this and can also accelerate the rise in food prices.

To support farmers and families in the developing world the Biotechnology and Biological Sciences Research Council (BBSRC) and the Department for International Development (DFID) have joined forces to announce over £13 million of new research to harness the UK's world-class bioscience base to address the challenges posed by livestock diseases and work with developing countries to provide practical and sustainable solutions.

Combating Infectious Diseases of Livestock for International Development (CIDLID)

The initiative is made up of 16 projects which will look at some of the most prevalent, damaging and costly diseases of livestock in developing countries. Over the next four years, UK researchers will work with more than 20 overseas institutes to not only control or prevent these diseases but also to build scientific capacity at a local and national level within these countries to enable them to manage these diseases and apply new findings and technologies to other disease areas, in both livestock and humans.

The projects will also offer significant benefits to farmers and consumers in the UK - animal diseases do not respect national boundaries and are estimated to have cost the UK economy over £15 billion over the past 15 years. Several of the diseases being tackled by the initiative are spreading across countries and continents and some are already a direct threat to UK livestock such as foot and mouth disease and bluetongue virus. New technologies developed as part of this research could also be transferable for use to combat other animal diseases and possibly human ones too.

By bringing together the best science and the brightest minds from around the globe, the initiative aims to generate workable solutions on the ground to improve animal welfare, productivity and ultimately enhance the lives of millions of people.

- ¹ World Bank (2008) Agriculture for Development
- ² International Labour Organization (2009) Global employment trends for women

Facts

- £13M+ investment from BBSRC and DFID with contributions from the Scottish Government
- 16 projects, 15 UK institutions and 8 other countries
- Agriculture is vital for the livelihoods of 75 per cent of the world's poor
- Food demand is predicted to increase by 50 per cent by 2030

Development of vaccines against multiple diseases to save sheep and goats

Across the developing world, viral diseases such as peste des petits ruminants virus (PPRV), bluetongue virus (BTV) and Rift Valley fever virus (RVFV) place a huge disease burden on agriculture. These viruses affect sheep and goat production, the agricultural mainstay of some of the poorest people on the planet.

A live attenuated 'one-shot' vaccine preparation is available for PPRV that is safe and highly effective. However, for BTV and RVFV multi-dose vaccine regimes hamper vaccination strategies in areas where the economic capabilities to drive such programmes are poor.

The current PPRV vaccine is used to combat the disease in several regions of the world including Africa, India and the Middle East. Researchers from the UK, India and South Africa aim to increase the effectiveness of the PPRV vaccine by using it as a carrier to deliver proteins from BTV and RVFV to protect sheep and goats from these diseases too.

As well as developing a multi-disease vaccine, the researchers plan to genetically tag the vaccine to enable vaccinated animals to be differentiated from naturally infected animals. This will make it possible to assess the circulation of wild-type virus within the herd in the absence of disease.

The application of such a vaccine would greatly help alleviate poverty in the less developed regions of the world enabling the development of sustainable agriculture in areas where livelihoods are frequently devastated by these viral plagues.

Collaborations

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African goats being herded in Mali





A goat displaying classic symptoms of peste des petits ruminants virus

Dip-stick test for 'Goat Plague'

Sheep and goats are the main source of income for herders and livestock keepers in the developing world. peste des petits ruminants virus (PPRV), also known as 'Goat Plague', causes a serious disease in these animals leading to major losses; the Indian Council for Agricultural Research recently estimated losses in their country at about £24 million per annum.

PPR is a painful condition causing mouth ulcers, diarrhoea and ultimately death in sheep and goats. While PPR has never occurred in the UK, it is a growing problem, spreading through large parts of Africa, the Middle East, the Indian subcontinent and other countries in South-East Asia, with the United Nations Food and Agriculture Organisation estimating that 1.1 billion animals are at risk worldwide.

Vaccines against PPRV exist, but they don't allow people to distinguish vaccinated animals from animals which have had the disease and recovered. This is a problem for trade, as farmers cannot prove that an animal has only been vaccinated and not had the disease.

Researchers from the UK and Uganda have joined forces to make an improved vaccine against PPRV by using a bird virus called fowlpox virus (FPV). FPV is already the basis of a number of useful animal vaccines. The researchers will modify FPV so that it expresses two PPRV proteins. The immune response to these proteins will protect the animals against PPRV; however, because animals that have had the disease will have antibodies to all the viral proteins, and vaccinated animals antibodies to only two, it will be possible to tell the two groups apart.

Alongside developing this new vaccine, the researchers will also design new diagnostic tests, including a 'pregnancy test' style device to enable the diagnosis of PPRV in the field, without the need for a laboratory.

Collaborations

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Looking at midge control to tackle bluetongue virus

The bluetongue virus is a major challenge for farmers across the world including the tropics, sub-tropics and, in recent years, Europe. The virus can infect all ruminants, having a major impact on productivity, and is a particular threat to sheep, killing up to 30 per cent of a flock during epidemics.

Subsistence farming communities in southern India are all too aware of the danger posed by bluetongue. The virus is spread by biting midges, so flocks in this part of the world are particularly at risk following monsoons, due to the increase of midges emerging from breeding sites.

Researchers from the UK and India will spend the next three years looking at how, when and where these epidemics arise and what can be done to reduce the overall impact of the virus.

By defining which species of midge can transmit the virus and using expert local knowledge of bluetongue epidemiology in India the researchers will explore how and when transmission occurs at a farm level and provide an insight into what drives bluetongue epidemics. Then, using mathematical modelling to examine what determines midge abundance, the researchers will investigate whether the occurrence and severity of outbreaks can be predicted using these factors and used as an early warning system to farmers.

The researchers will also examine new means of midge control that may reduce the current reliance upon synthetic insecticides in this region. This will be carried out in parallel to studies that will assess the ability of these and more traditional control methods to impact on transmission of the virus in the field.

Collaborations

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Blood-feeding Culicoides biting midges that are responsible for transmission of bluetongue virus





Women often own and manage chickens

Reducing chicken disease in Ethiopian villages

Poultry play an important economic, nutritional and socio-cultural role in the livelihoods of poor rural households in many developing countries, including Ethiopia, where they are an integrated part of the smallholder production systems and play a significant role in poverty alleviation. Purchase and rearing of poultry is often seen as the first step out of poverty. Women tend to own and manage chickens which often provides them with their only independent source of cash income.

Indigenous chicken varieties are well adapted to local environments but tend to grow slowly and produce fewer and smaller eggs compared to commercial stocks. Breeding programmes using local varieties of chicken suggest that low cost and relatively low input improvement in productivity might be possible while keeping the local adaptive traits such as heat tolerance and disease resistance.

Researchers from the UK and Ethiopia will look at identifying the causes of infectious diseases which have a major impact on poultry production in Ethiopia and will link this with an ongoing poultry breeding programme in the country to improve resistance to these priority infectious diseases whilst enhancing productivity and production. Knowledge from this study will also enable more precise disease control planning by Ethiopian policy makers and animal health professionals and will also provide a legacy of improved scientific capacity within Ethiopia, including training of local scientists and enhanced laboratory facilities for poultry testing.

Collaborations

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Comparing foot and mouth disease in wildlife and livestock

Foot and mouth disease (FMD) is one of the most devastating animal diseases worldwide, affecting all cloven-hooved animals including cows, sheep, pigs, goats and deer. The 2001 outbreak in the UK cost the economy over £8 billion and more than six million animals were slaughtered.

Outbreaks aside, the disease has been largely eradicated in most developed countries through a combination of containment and vaccination. However, FMD is common in livestock and wildlife in Sub-Saharan Africa, impacting on the livelihoods of some of the world's poorest farmers and affecting wildlife management policies. Despite this, very little is known about the disease in most parts of Africa.

Researchers from the UK and Tanzania will spend the next four years looking at developing effective strategies for controlling FMD in Africa. A major problem is the genetic variation in the FMD viruses across the continent which makes vaccination difficult. To address this, the researchers will sample wildlife, mainly buffalo and livestock - domestic cattle, sheep and goats - to map the genetic diversity of viruses across Tanzania. The international team will also study livestock herds adjacent to the Serengeti National Park to investigate FMD outbreaks in more detail, assess the risk of the disease spreading from wildlife to livestock and determine whether and how the immune response to one type of virus can protect against other types of viruses.

The researchers will use a variety of new techniques that have been developed by scientists in the UK, such as using genetic changes in the virus to track the spread of the disease, and apply these for the first time to the study of FMD in East Africa.

Collaborations

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Blood samples from cattle will provide information about which types of foot and mouth disease virus are occurring in different parts of Tanzania





A smallholder in the Democratic Republic of the Congo transporting a pig to market

Developing rapid tests to prevent pig deaths from African swine fever

African swine fever (ASF) is a severe viral disease of domestic pigs which causes the death of almost all infected pigs. The disease is present in Africa, Sardinia and the southern Russian Federation and Caucasus region from where it could potentially spread to the high pig producing regions of South East Asia and China and also into the European Union.

ASF has a devastating economic impact in affected countries and limits pig production in Africa depriving the local communities of a cheap, high quality, source of protein. Currently there is no vaccine against ASF and the only way to control the disease is through quarantine and slaughter of infected animals. However, many outbreaks, especially in Africa go undiagnosed as the facilities for diagnosis are not available locally or even nationally, in some cases samples are sent to overseas reference laboratories.

Researchers from the UK and South Africa aim to identify the different proteins exposed on the surface of the virus and use this knowledge to develop rapid diagnostic tests which can be carried out in the field, such as a dip-stick where blood is dropped on one end and if the virus is present a positive band will appear at the other end. Over the next three years, the researchers also plan to identify virus proteins which can be used to produce vaccines by studying the surface proteins on the virus and how they aid the virus entering into the cells of the animal.

Collaborations

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Tackling wildebeest disease to save cattle

The wildebeest migration in Africa is a great annual spectacle, with over one million wildebeest migrating over 1,800 miles every year. However, for local farmers this natural wonder endangers their livelihood as the 400,000 wildebeest calves born each year harbour a viral disease deadly to livestock.

The disease - malignant catarrhal fever (MCF) - is a major concern for farmers whose cattle are essential to their economic and social welfare. To avoid MCF, they move their cattle to poorer upland grazing where they are exposed to other serious diseases.

Researchers from the UK and Tanzania have developed a MCF vaccine, the next step is to test it in field conditions. Over the next three years, the researchers will test the vaccine in Tanzania, develop it further as required and then look to make a new vaccine for a sheep virus which is very similar to the wildebeest virus and causes MCF in livestock in other parts of the world, including Europe, Indonesia, Australasia and the Americas. Successful MCF control will have a major impact on the quality of life of farmers and their communities as well as on the ecology of the plains where wildebeest and cattle co-exist.

Collaborations

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The wildebeest calving season on the Serengeti plains





Horro sheep feeding

Looking at traditional healing methods for Ethiopian livestock

Annual economic losses due to worms, lice, mites and ticks in Ethiopian small ruminant livestock exceeds \$100 million. For generations, smallholder farmers and pastoralists in countries like Ethiopia have used medicinal plants to try to control these parasites, often because chemical drugs to treat these parasites are too expensive.

However, little is known about whether using plants works, how they work and if there are any side effects of these plant-based treatments.

Researchers from the UK are joining forces with Ethiopian researchers to work with traditional healers and smallholder farmers to look at how and if plants are able to provide useful anti-parasitic treatment for sheep. If the researchers find that plants can successfully be used in either a preventative or treatment way, the researchers will then look at ways to promote this among smallholders.

The approaches used and expected demonstration of effective plant-based parasite control strategies could in principle be applied to any country that has native plants that show promise for possible animal disease control. The expectation is that the results of this project would provide countries like Ethiopia with the knowledge required to use their own natural resources to control animal parasites as much as possible, either in isolation or combined with other disease control strategies.

Collaborations

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Controlling worms to increase production of sheep and goats

Worms are a major cause of production loss among sheep and goats in sub-tropical regions of India and Africa. The worms attach to the stomach walls of the animals causing anaemia, severe dehydration and ultimately death.

Parasitic worm infections are conventionally controlled using drugs, but these are expensive for smallholder farmers especially as they need to be administered regularly and increasingly worms are becoming resistant to these drugs.

Researchers from the UK, India, South Africa and Canada will spend the next three years looking at developing ways to enable farmers to control parasitic worms. The researchers will do this by looking at ways of developing cheap, effective vaccinations which could be produced locally, and getting a better insight of the extent of the problems caused by parasitic worms. The researchers will also look at refining dosing strategies, making the use of drugs cheaper by targeting animals least able to cope with infection, and will then look at informing farmers of such strategies using web-based decision support tools accessible via mobile phones.

Collaborations

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Parasitic worm (Haemonchus contortus) with characteristic 'barber's pole' appearance and filled with host blood





A buffalo liver infected with liver fluke

Developing a vaccine to control deadly liver fluke

Tropical liver fluke worms cause serious losses in cattle, buffaloes, goats and sheep and are a serious threat to the livelihood of farmers in many areas of Asia and Africa. In India alone, this worm inflicts estimated losses of up to \$4.7 billion a year and milk yields in infected buffalo fall by around 30 per cent. Infected animals are less healthy and show poor feed conversion efficiencies and reproduction, representing a huge burden to the largely agricultural Indian economy.

In the developed world liver fluke worms are mainly controlled using drugs which kill them. However, drug resistance is spreading, meaning that these drugs are becoming less effective, and thus undermining their potential as a long-term, liver fluke control strategy. Instead, a new cost-effective, single-treatment control strategy based on vaccination is urgently needed and this is exactly what researchers from the UK and India are looking to develop over the next three years.

Key to the development of an effective vaccine will be the careful selection of a suitable vaccine target from within the worm. The vaccine target must be important to the survival of the worm so that vaccination will trigger the immune system of the infected animal to attack the target and kill the fluke. Researchers will use new molecular technologies to select these vaccine targets. One such technology is gene silencing, whereby potential targets are temporarily removed from the worms and their importance to worm survival determined. Based on this strategy, the researchers will systematically select vaccine targets that when removed (or silenced) have the most negative impact on liver fluke worm survival.

Following the selection of the best vaccine targets in the UK, researchers in India will carry out field trials in livestock to identify the most suitable vaccine candidates for commercial development to control liver fluke disease. This new technology-based strategy of vaccine target selection will be directly transferable to other parasites of animals and humans such as blood flukes and tapeworms.

Collaborations

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Diagnosing and treating contagious bovine disease

Contagious bovine pleuropneumonia (CBPP) is a devastating disease of cattle in sub-Saharan Africa that is spreading throughout the sub-continent, with 26 countries currently affected. Caused by a Mycoplasma bacterium, the disease manifests in a variety of ways, ranging from acute pneumonia and chronic breathlessness to wasting and death.

Infection almost invariably results in a prolonged carrier state, so that apparently recovered cattle remain sources of infection for other animals. This feature of the disease is fundamental to its spread, particularly in pastoralist livestock systems. Control of CBPP is undertaken by national veterinary services, largely through the use of live vaccines, but these have limited efficacy and, because control programmes are a state responsibility, are not directly available to farmers.

The use of antibiotics for control of the disease is discouraged or banned in most affected countries, because of the belief that treated cattle are more likely to become persistent carriers of the disease. Nonetheless, farmers continue to use antibiotics, as they lack confidence in government vaccination programmes. Researchers from the UK, Switzerland and Africa are joining forces to address this issue. Over the next three years they will apply advanced pharmacological methods, based on laboratory studies of drug efficacy and computer modelling, to evaluate three antibiotics for control of the CBPP bacterium and develop effective dosage regimens that impede its persistence. The project will also develop a diagnostic test capable of recognising cattle in the early stages of infection, using a format applicable in the field, to inform decisions to treat.

Collaborations

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Cow with acute CBPP, showing the characteristic posture adopted by these animals





A healthy Boran bull - an East African Bos indicus breed of cattle

Preventing East Coast fever with improved vaccine

Over 20 per cent of people in sub-Saharan Africa are classified as living below the poverty line and many of these people reside in rural communities that are heavily dependent on livestock for their livelihoods. One of the most important diseases of cattle in this region is East Coast fever (ECF) caused by a tickborne parasite *Theileria parva*.

This disease is present in 16 countries in eastern and southern Africa and is the most economically important cattle disease in 11 of these countries. Estimates of economic losses due to ECF exceed 300 million US dollars annually. Imported breeds of cattle, which are increasingly being used to satisfy demands for milk production, are particularly susceptible.

Although treatment of infected animals with antiparasitic drugs and application of chemicals to prevent tick infestation can be used to control ECF, these methods are difficult to apply and generally are unaffordable by poor farmers. Vaccination offers a more sustainable means of controlling the disease.

Cattle can currently be immunised against the disease by infection with live parasites and simultaneous drug treatment but, because of differences between parasite strains, vaccination requires the use of a mixture of strains. Although a vaccine using three parasite strains has been used locally in some countries with some success, its widespread application has been hindered by difficulties in quality control and distribution, and there remain questions about whether the parasite strains are the best mix for providing robust immunity.

Researchers from the UK and Kenya will build on recent advances in identification of antigens recognised by the protective immune response to investigate the nature and extent of variability in these antigens between parasite strains and to understand the factors that determine the parasite strain specificity of immunity following vaccination.

The researchers aim to provide methods for improving quality control of the current live vaccine, identify parasite strains that could be incorporated into an improved second generation live vaccine as well as provide data which could be used to design a new vaccine that would avoid the use of live parasites.

Collaborations

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Improving the quality of foot and mouth disease vaccines

Foot and mouth disease (FMD) is global problem affecting cloven-hoofed domestic and wild animals. It has been largely eradicated from the developed world, but remains widespread in developing countries including those of sub-Saharan Africa and South Asia, where it seriously affects livestock productivity through weight loss, decrease in milk yield and loss of draught power.

Indeed, FMD is considered the single most important constraint to international trade in live animals and animal products. FMD can be controlled by restricting animal movements, slaughtering affected animals and vaccination; the latter being used continuously in endemic countries and as an emergency measure if disease is newly introduced. The massive culling of animals that was required to control the FMD outbreaks in the UK in 2001 has led to calls for more reliance to be placed on vaccination as the primary means of disease control in developed countries.

However, control of FMD by vaccination is not straight forward. Current vaccines only protect animals for about six months and are serotypespecific and sometimes strain-specific. Each batch of the vaccine also needs to be tested in animals with live FMD virus to ensure quality and potency. This requires very expensive high containment facilities that may not be available or may pose a risk of virus escape if inadequately maintained. Researchers from the UK, South Africa and India are working together to overcome these constraints by developing effective vaccine-based control strategies in developing countries. They plan to do this by adding new agents (adjuvants) to increase the potency and duration of immunity offered by current vaccines and looking at more targeted ways to match the vaccines against circulating strains.

The researchers will also look at safer, cheaper ways of testing vaccines using artificial methods (*in vitro assays*) rather than having to test on animals carrying the virus; such new techniques could provide a significant breakthrough in the cost-effectiveness of vaccine use and FMD control in sub-Saharan Africa and South Asia.

Collaborations

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Sample collection from FMD infected cattle in Zimbabwe





Backyard rearing of indigenous poultry in Tamil Nadu where birds are bred for meat and eggs

Saving chickens by uncovering the genetic diversity of a killer parasite

Chickens are widely farmed in rural poor households, providing an important source of dietary protein and a currency for local marketing and trade. Diseases that compromise the health or survival of poultry have major impacts on the livelihoods of the world's poorest people.

Coccidiosis is a devastating poultry disease caused by seven species of protozoan parasites which attack the digestive system. Cost-effective, cross-species vaccines are a realistic prospect due to recent research that has identified key antigens and new technologies for vaccine delivery that include genetic modification of parasites. However, the parasites become resistant to drugs fairly rapidly and this is also a major consideration in the development of new vaccines to control the disease.

Researchers from the UK and India are working together to overcome this by developing new multiantigen vaccines. As part of this, the international team will look at the prevalence of different parasites responsible for coccidiosis and chart the frequency with which multiple infections and genetic exchanges occur between parasites and examine the effect this has on the growth and spread of parasites in infected chickens. Based on this, the researchers will develop vaccines and test them against field parasites to predict the likely efficacy and longevity of such vaccines.

Collaborations

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Looking at ticks in the spread of lumpy skin disease virus

Lumpy skin disease (LSD) is a serious disease of African cattle. The disease has a high impact on animal productivity such as a sharp drop in milk yield, a loss in body weight, permanent damage to hides and reproductive problems. As a whole, this results in considerable economic losses particularly for smallholders across Africa.

Researchers from the UK and South Africa will investigate the transmission of the virus by three common tick species in sub-Saharan Africa. Laboratory-bred clean larvae, nymphs and adult ticks will be placed to feed on the skin of cattle experimentally infected with LSD virus. These potentially infected ticks will then be transferred to feed on the skin of non-infected animals. The recipient animals will be closely monitored for clinical signs and tested regularly for LSD virus. Detailed studies will be carried out on the persistence of the virus in different cell types of larvae, nymphs and adult ticks and tick eggs.

The three year study will provide new and fundamental data on the transmission of the virus and improve the understanding of the epidemiology of LSD and will have direct impact on the welfare of farming communities, the preventative health care of cattle and the export and import policies for live domestic and wild ruminants in Africa. Researchers on the project will also gain invaluable tick dissection skills and an experience in the establishment and maintenance of tick colonies which will be useful in studying other tick transmitted viruses.

Collaborations

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A cow showing severe generalized lumpy skin disease





Nomadic Fulani Herdsman carrying a young calf to keep up with the herd

Using community based interventions to beat sleeping sickness

Animal sleeping sickness (Trypanosomiasis) is a serious parasitic disease which causes severe production losses in cattle with an estimated three million deaths and \$4 billion in lost income annually across Sub Saharan Africa. The disease can be fatal in humans too.

The parasites are transmitted by tsetse flies feeding on blood from infected mammals. While sleeping sickness is difficult and expensive to treat in people (treatment has a high risk of death of up to five per cent) elimination of these parasites from domestic livestock is affordable and effective.

A single treatment with an injectable drug can clear the animal of all circulating trypanosomes but it is not appropriate or possible to continuously treat every animal without the risk of resistance to the drugs developing, and risking the efficacy of the limited armoury of human treatments.

Researchers from the UK and Nigeria are joining forces to address this and develop ways to target interventions at high-risk carriers of the disease amongst livestock over the next four years. Focusing on the Jos Plateau in Nigeria the researchers aim to maximise livestock health by assessing the risk of trypanosomiasis spread by livestock movements and by developing effective disease control options including restricted application of insecticide, strategic prophylactic treatments and training farmers on rational drug use.

The project will enable policy makers, public institutions, communities and individual smallholder farmers to identify appropriate and cost-effective methods for sustainable farmer based control.

Collaborations

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For more information about the initiative, please contact Amanda Read: amanda.read@bbsrc.ac.uk Details of DFID supported research can be found at: www.research4development.info Details of BBSRC funded research can be found at: www.bbsrc.ac.uk

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