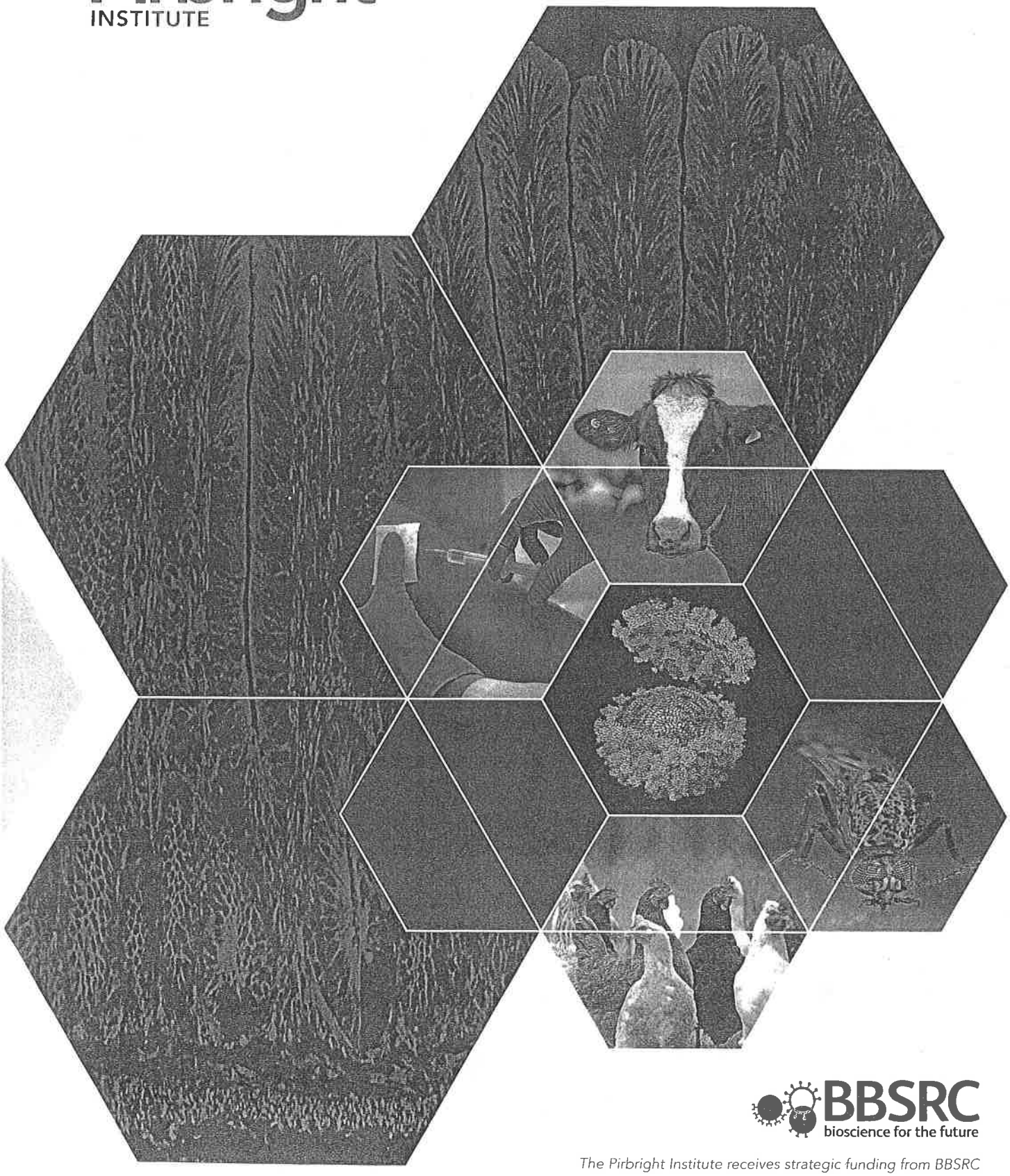
Preventing and controlling viral diseases

THE Pirbright INSTITUTE



BBSRC bioscience for the future

The Pirbright Institute receives strategic funding from BBSRC

Foreword

Professor Joe Brownlie CBE

Chair of the Trustee Board

The Pirbright Institute is a company, limited by guarantee, with charitable status. It is the role of Trustees to ensure its proper governance and financial probity whilst also supporting the Institute's Executive Team in their endeavour for excellent science and surveillance.

The Institute has a long history of service; in fact, a 100 years of service. There have been a number of highlights during this time, notably its crucial role in the global elimination of cattle plague (rinderpest) and the provision of exceptional expertise and support during the foot-and-mouth outbreaks of 1967, 2001 and more recently 2007. However, by 2007/8, it was recognised that there had been serious under-investment in the facilities and an unsustainable programme of research across both the Compton and Pirbright sites. This necessitated some hard decisions and some visionary investment. It is very much to the credit of both the Biotechnology and Biological Sciences Research Council (BBSRC) and latterly of the Department of Business Innovation and Skills (BIS) that both vision and investment were found. The hard decisions were to focus our research on only viral diseases and to concentrate our operations on one site – the Pirbright site in Surrey. However, having done that, we have, with the support of both BBSRC and BIS, made some extraordinary progress in the last five years.

The design and building of new state-of –the-art high security animal housing and laboratories on the Pirbright campus will have both national and global importance. The Phase 1 buildings, which permit research on high impact viral diseases such as foot-and-mouth disease and bluetongue, will be completed in 2014, with occupation in 2015. Phases 2 & 3 will follow and provide facilities for avian research and further infra-structural development of the site. Such excellent facilities will allow us to study viral diseases, both those presently of concern but also any future new and emerging diseases, in a bio-secure environment. We also know that the vast majority of the new human diseases emerge from animal hosts – for this reason, Pirbright scientists will now be well appointed to contribute, with their medical colleagues, to the 'One Health' agenda.

Of course, an Institute is only as good as its staff. The Trustees are thus delighted to have appointed a new and dynamic Director – Professor John Fazakerley. John has already made his mark and provides leadership and vision in equal measure. He has been the first to acknowledge the excellence of the present researchers within The Pirbright Institute and has, through establishment of a 'Fellowship' scheme, made some exciting new appointments. There are still some further appointments yet to make.

The next 2-3 years will see the completion of the new facilities and the consolidation of the viral-disease research programme. We will need to take care during this time; it will set the direction of The Pirbright Institute for the next two decades. There can be little doubt, if we get this right, we can look forward to another 100 years of outstanding and exciting science of global significance.

Professor Joe Brownlie CBE
Chair of the Trustee Board

Porcine tongue epithelium infected with foot and mouth disease virus showing areas of virus replication (red), host cell tubulin (green) and nuclei (blue).

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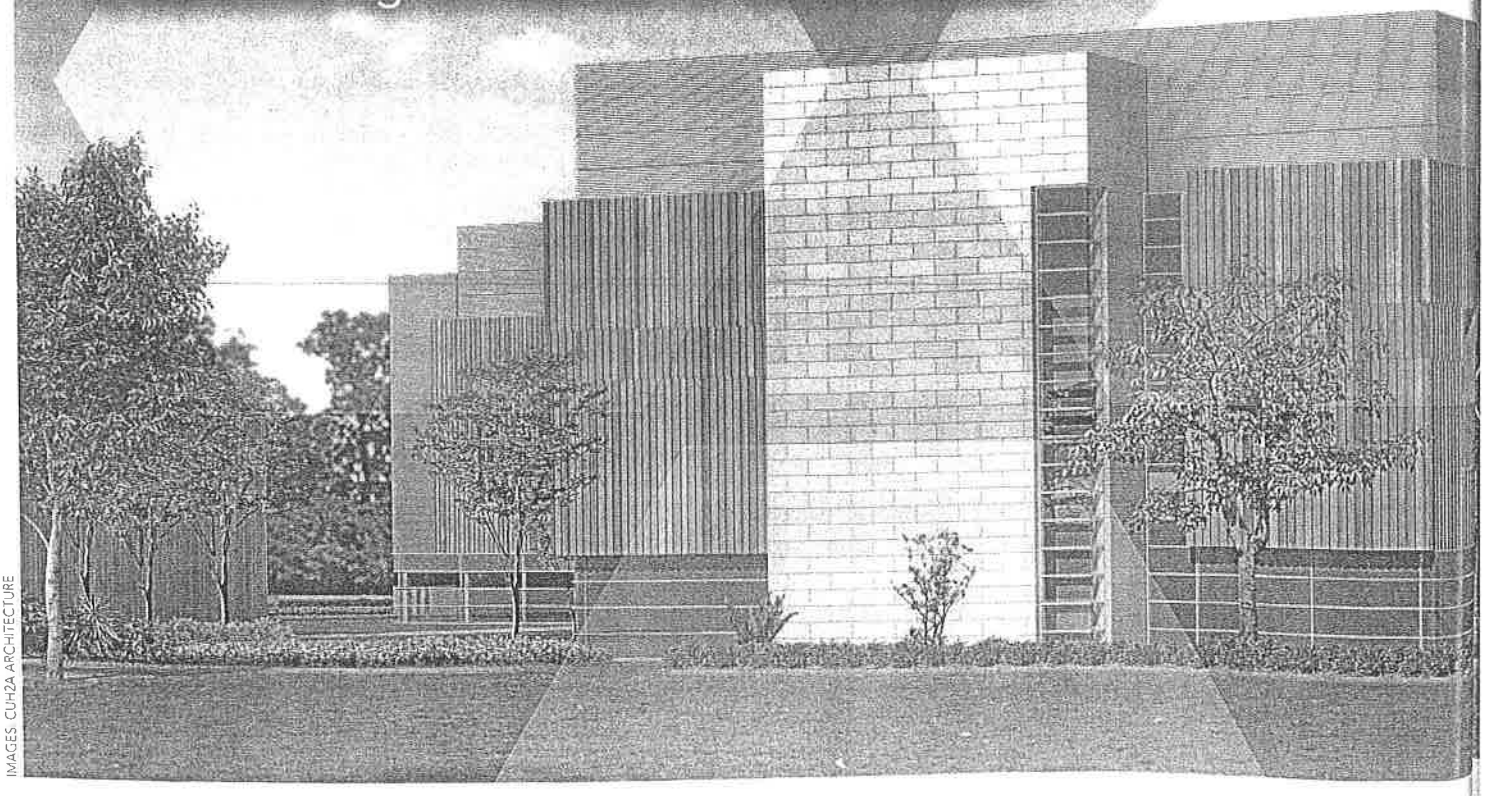
01 About the Institute

The Pirbright Institute is a world leading centre of excellence in research and surveillance of virus diseases of farm animals and viruses that spread from animals to humans. Through fundamental and applied research, the Institute aims to ensure global health and wellbeing and economic and food security by improving understanding and control of virus diseases.



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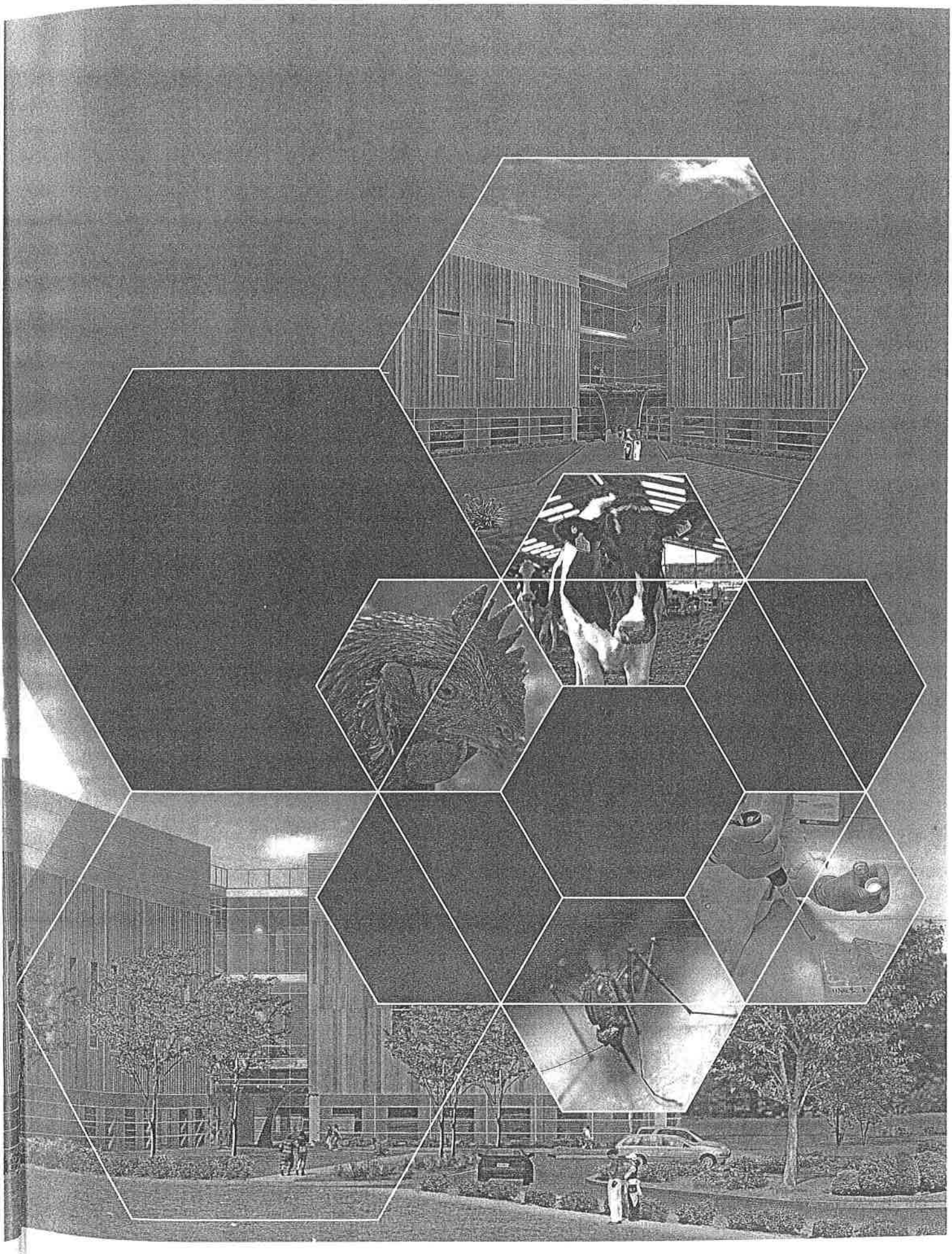


Vision, Mission, Values

Vision

In the context of changing environments and an increasing human population, understanding and controlling virus diseases of livestock and viruses that spread from animals to humans will promote global health and wellbeing and economic and food security.

Mission

Research and surveillance to prevent virus diseases of livestock and virus transmission from animals to humans.

Values

The Pirbright Institute and its staff value leadership, respect, cooperation, collaboration and professional development and take pride in being a world-class institution where knowledge, expertise, facilities, professional excellence and rigorous academic, biosecurity and ethical standards combine to generate global health and economic impacts.

Welcome

Now, in the 21st Century, we are experiencing great global challenges; not least, how to be healthy and well-nourished in the context of a rapidly increasing population, a changing environment, globalisation, and economic uncertainty.

By employing the best bioscience to control and eliminate virus diseases of farm animals and transmission of viruses from animals to humans, The Pirbright Institute is in a unique position to strengthen the UK's resilience to these challenges.

We have the best people and the facilities to provide the knowledge, tools, technologies and advice to monitor, predict, advise and meet new threats that emerge. This will ultimately achieve our vision of mitigating the effects of virus diseases on global food security, health and wellbeing and economic security.

The Pirbright Institute has a proud history dating back to the end of the nineteenth century and we have operated under various guises and on several sites. In 2009 it was announced that we would consolidate on our site in Pirbright, Surrey. This site has been in constant use for farm animal heath surveillance and research for a hundred years. In late 2012 the Institute for Animal Health became The Pirbright Institute and adopted the Pirbright campus as its registered office and headquarters.

Our work is supported by strategic funding from the Biotechnology and Biological Sciences Research Council (BBSRC) and Defra (the Department for the Environment Food and Rural Affairs), and many competitively won grants.

With considerable capital investment from BBSRC and the Department for Business Innovation and Skills in new state-of-the-art buildings and facilities, we are developing a research and innovation campus at Pirbright where our high containment facilities, biological collections and expertise combine to provide a world-leading hub for disease surveillance, fundamental and applied research and commercialisation.

Among the Institute's achievements, we played a major role in the global eradication of rinderpest virus, which is the cause of cattle plague and, after smallpox, only the second virus disease to be eradicated globally. Confirmed in 2011, rinderpest eradication has been estimated to save the economies of Africa around one billion pounds per annum. In 2007-8, The Institute prevented a serious outbreak of bluetongue disease in the UK, saving the UK economy an estimated £485 million per annum. We are currently working on foot-and-mouth disease, African horse sickness, African swine fever and influenza viruses; these are amongst the viruses mostly likely to cause problems for the UK in the future. The Institute continues to develop effective and innovative vaccines and diagnostic tools to protect livestock, poultry and human health worldwide.

As an organisation we are looking forward and evolving; the future is tremendously exciting for us and we are grateful for the support we receive from our funders, partners and collaborators.

This publication provides details of the Institute and examples of its scientific, social and economic impacts, I hope you will find it interesting and inspiring.

Professor John K Fazakerley
Director
The Pirbright Institute

Corporate governance

The Pirbright Institute is an important national capability, under corporate governance from the UK Biotechnology and Biological Sciences Research Council (BBSRC) - one of seven Research Councils that work together as Research Councils UK and are funded by the Government's Department for Business, Innovation and Skills.

The Pirbright Institute is both a charity and a company limited by guarantee, governed by two trustee directors; a corporate trustee director – the Biotechnology and Biological Sciences Research Council (BBSRC), which also provides core funding for the Institute's strategic programmes and national capabilities – and a 'natural' trustee director. Trustee directors are appointed by the member(s) for a period of three years, after which they are eligible for re-appointment.

BBSRC fulfils its role as corporate trustee director through a team of individual representatives appointed by BBSRC Council, collectively the Corporate Trustee Team (CTT). The 'natural' trustee director is Mr Tim Key MBE, who is appointed for three years to 27th March 2015 and the Board is chaired by Professor Joe Brownlie CBE, also Chair of the CTT, for a period of three years to 27th September 2015.

The Trustee Board operates through the Institute's memorandum and articles and the Institute Grant Agreement. There are regular Board meetings, every two months, and in attendance are the Institute Director and Director of Operations/Company Secretary, together with other members of the Institute executive as appropriate.

At its meetings the Trustee Board considers standing reports from the Institute Director and Directors of Science and Operations, together with compliance and risk management updates. The Trustee Board has also constituted a Finance and General Purposes Committee dealing primarily with financial matters and sustainability, as well as audit activity.

There are representatives of the Trustee Board on the Institute's infrastructure development programme and on the Farm Advisory Group. The Chair of the Trustee Board also sits on and contributes to the Science Advisory Board*, which advises the Director and the Trustee Board on the Institute's science activities. In addition to its regular formal meetings, Trustee Board members also attend Business Partnership Meetings held with the Institute's strategic funder, BBSRC.

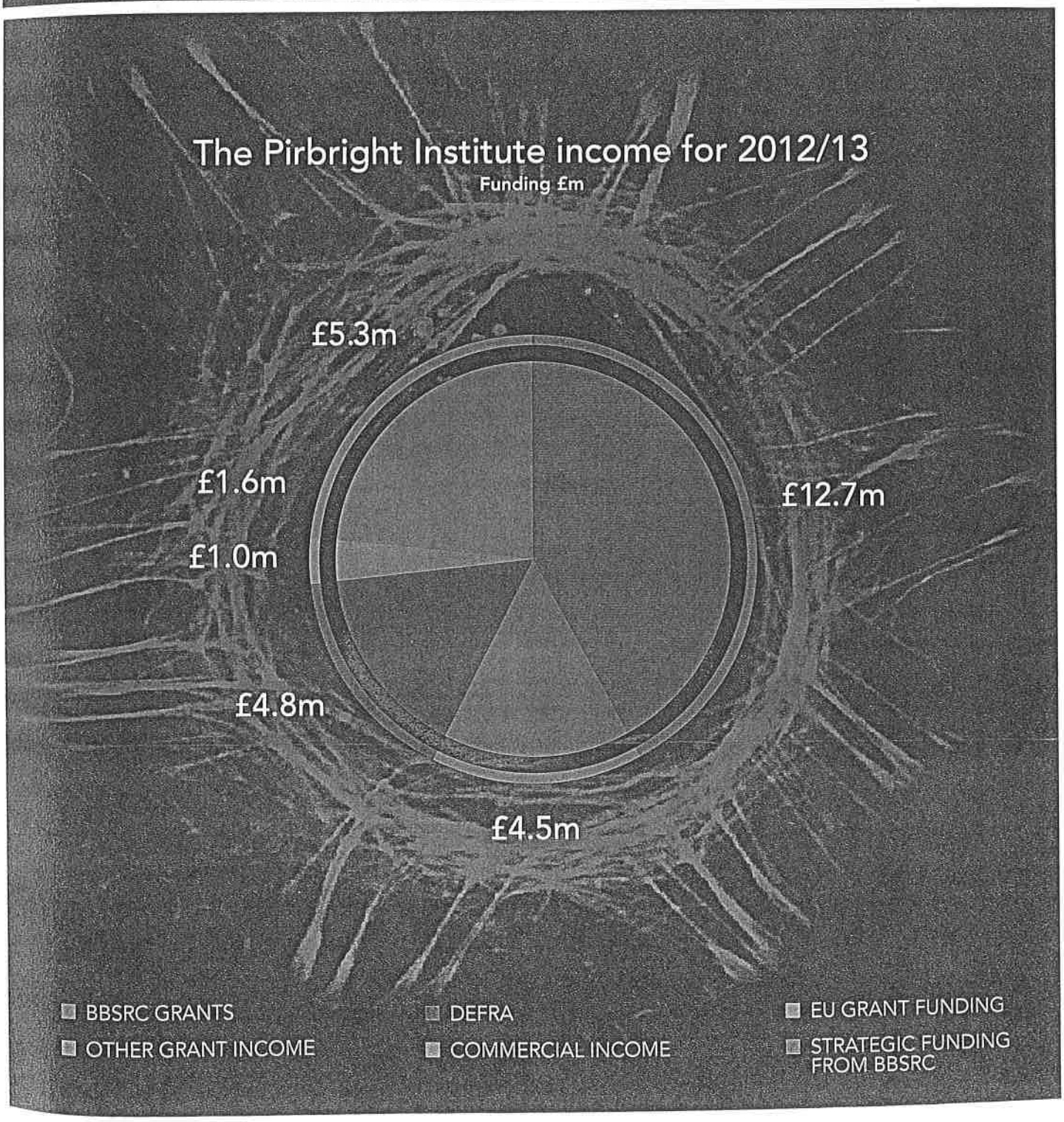
The Institute continually reviews its practices for induction and trustee training. Trustee directors are encouraged to attend appropriate external training events where these will facilitate the undertaking of their role.

BBSRC
bioscience for the future

*The Institute's Science Advisory Board comprises a group of pre-eminent scientists who meet The Pirbright Institute's science executive four times a year to consider science direction and how well the Institute is delivering its science.

Funding

The Institute has aggregate funding of £29.9 million per annum from the following sources:



Strategic direction

Research and surveillance to prevent virus diseases of livestock and transmission of viruses from animals to humans.

The global population is expected to increase to nine billion by 2050 and during that time there will be changes to our environment. Food consumption is changing worldwide and developing countries in particular are consuming vastly more animal protein. At the same time, the threat of emerging diseases is rising, not least because of the volume and speed of human and animal movements; changes in the distribution of animals and disease vectors and reservoirs; and ever closer contact between animals and humans.

As scientists we have the opportunity to make a significant impact on the ability of the UK and other countries to withstand the threat of emerging diseases. The Pirbright Institute has the expertise, facilities, resources and experience to bring science to bear on issues of food security, health and wellbeing of humans and animals, and protecting economies from the devastating effect of a major disease outbreak. We do this by employing fundamental through to applied research into viruses, the animals that become infected, and the relationships between the two.

Exotic and emerging diseases

The Pirbright Institute focuses on virus diseases, contributing to the UK's defences against the unpredictable and sometimes unknown threats of virus disease. For example, bluetongue virus, which is spread by midges and is endemic in tropical regions, was considered a potential threat to the UK and Europe and many years ago a research team was established at Pirbright to study it. When bluetongue arrived in the UK in 2007 the Institute was prepared, and when Schmallenberg virus, another midge-transmitted virus, was first detected in the UK in 2012 the same expertise was rapidly mobilised to study that new virus.

Zoonoses

The majority of new human pathogens identified in the past 25 years have been zoonotic – that is they have originated from animals. Influenza virus, West Nile virus, SARS virus, chikungunya virus and even HIV are examples of viruses causing disease in humans which originated in animals. Some of these viruses also cause disease in animals. The cost of a global pandemic of, for example, virulent influenza affecting pigs, poultry, or humans would be enormous and incalculable and is considered by the UK government to be one of the most important risks we face. In 2009 the Institute redefined its strategy to focus on virus infections of livestock and zoonoses.

A global hub

The Pirbright Institute is based on a rapidly evolving campus with national biocontainment facilities that act as a hub with collaborative spokes to other institutes, universities and the commercial sector. This provides the UK with the capacity to respond rapidly to new and emerging threats and is supported by a worldwide reputation for excellence, rigorous academic standards, a science-enabling culture, unique scientific possibilities and high profile, high impact scientific outputs. Pirbright is fast becoming a scientific destination of choice.

Collaborations

Close collaborations with many other organisations in the UK and worldwide are key to the success of the Institute. Strategic research partners include the Animal Health Veterinary Laboratories Agency, the

BBSRC Genome Analysis Centre, the University of Edinburgh (Roslin Institute), the University of Glasgow (Centre for Virus Research), the University of Oxford (Jenner Institute), the Royal Veterinary College, and the University of Surrey.

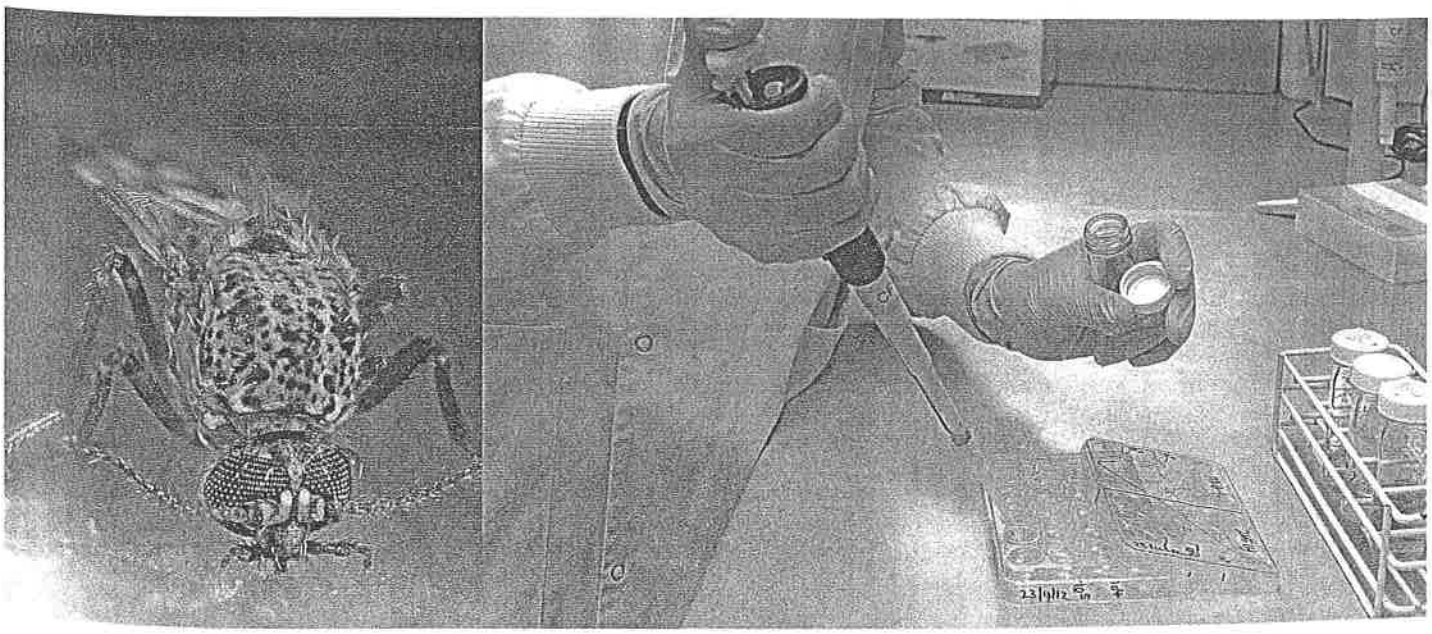
Joint staff appointments offer excellent opportunities for close strategic links and promote the sharing of expertise. The availability of the Institute's national facilities at marginal costs, thanks to dedicated funding in the form of a national capability grant from the Biotechnology and Biological Sciences Research Council (BBSRC), also strengthens these links. Through sharing of expertise and best practice in biocontainment, the Institute also has special relationships with other high containment laboratories worldwide, including the Australian Animal Health Laboratory, Geelong; the Friedrich Loeffler Institute, Germany; and the Plum Island Animal Diseases Centre, USA.

Making the most of research

Much of the research at The Pirbright Institute has clear avenues for application and responds to the hopes, fears, concerns and aspirations of people in the UK and beyond. A clear commercial strategy ensures that end users benefit from the knowledge generated by researchers and creates income that can be ploughed back into research and development. There is also the advantage that a number of national and international reference laboratories for diseases such as African swine fever, bluetongue, foot-and-mouth, Marek's disease and peste des petits ruminants are incorporated into the Institute. The Institute is a leading player in monitoring the distribution and transmission of viruses; provision of early warning of emerging threats; and identification of gaps in preparedness and research needs. Diagnostic laboratories throughout the world receive support and training at the Institute and The Pirbright Institute's World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) coordinates foot-and-mouth laboratories around the world as part of the OIE (The World Organisation for Animal Health) and FAO (Food and Agriculture Organisation) global strategy on foot-and-mouth disease.

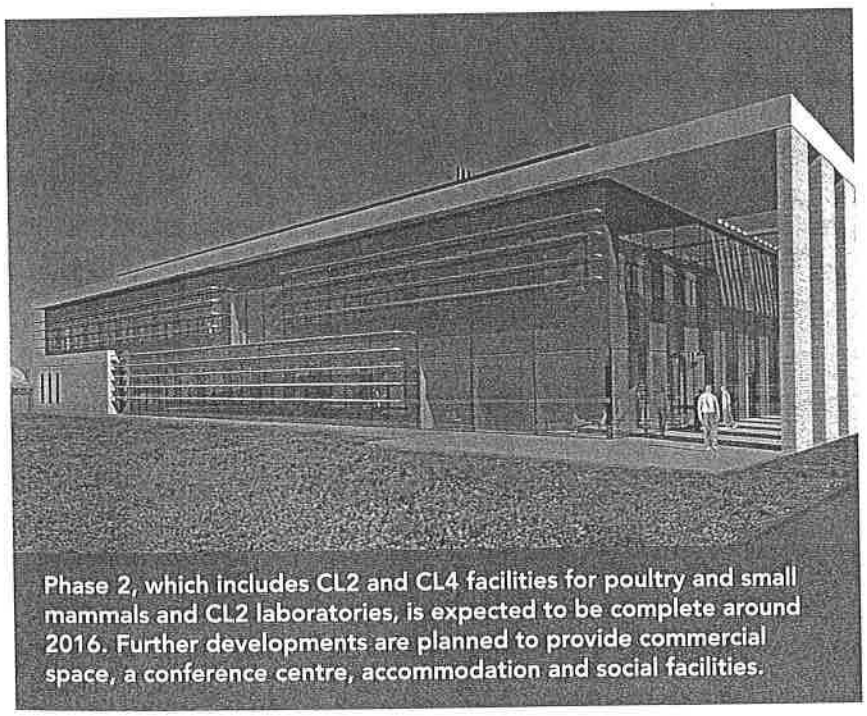
Enabling science

The Institute has a strong brand and reputation, which is supported by excellent communication and relationships with a very wide range of stakeholders. The Institute's training, quality assurance, compliance, biosecurity, health and safety, engineering and security functions ensure the integrity and robust performance of The Institute's highly specialised operating environment. Information systems support and enable all staff and provide research infrastructure for in silico experiments, data management and data sharing. Strategic human resources and rigorous financial management ensure the necessary resources are available across the organisation and the Institute has a firm commitment to training the next generation of scientists and supporting the professional development of all its staff.



The Pirbright campus

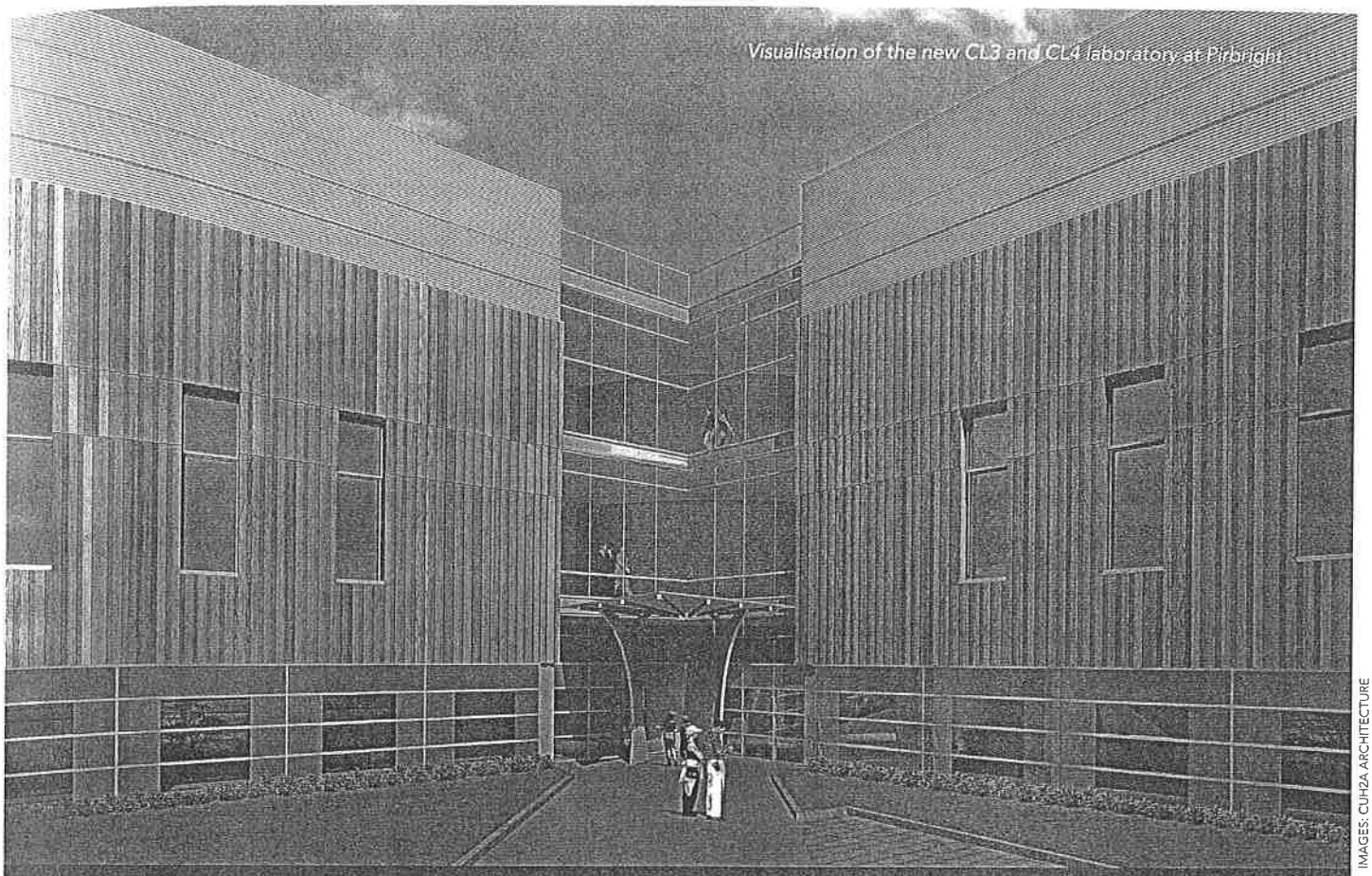
The Institute's main campus at Pirbright is undergoing a renaissance thanks to significant financial investment from the UK government via the Biotechnology and Biological Sciences Research Council (BBSRC). The transformation will establish The Pirbright Institute as the foremost state-of-the-art institute in the world for fundamental and applied research on some of the world's most devastating viruses of farmed animals, including viruses that can spread from animals to humans. It is already unique in the UK as a single centre where viruses can be studied at the bench and in the host animal under the highest levels of bio-containment.



Phase 2, which includes CL2 and CL4 facilities for poultry and small mammals and CL2 laboratories, is expected to be complete around 2016. Further developments are planned to provide commercial space, a conference centre, accommodation and social facilities.

Work on livestock and poultry viruses that are not normally in this country requires high-tech laboratories to contain the viruses. The redevelopment of the site is essential to keep pace with the scientific strategy of the Institute.

In the first stage of redevelopment the Institute constructed two state-of-the-art CL4 large animal facilities. These are for work on virus diseases such as foot-and-mouth and came on-line in late 2011. Phase 1 of the site redevelopment will be completed with construction of a high bio-containment (at level 3 and level 4 as defined in the Specified Animal Pathogens Order 1998– CL3 and CL4) laboratory complex. This is expected to be handed over from the contractors sometime during the first half of 2014 and will house 150 scientists and support staff.



Visualisation of the new CL3 and CL4 laboratory at Pirbright.

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In order to facilitate high containment work until the new large laboratory complex comes on stream, a smaller interim high-containment laboratory that operates at Defra SAPO 4 containment level has been constructed. This came into use in late 2011 and ensures that, together with other laboratories, all current Pirbright research and diagnostic activity can continue until the new laboratories are ready for occupation.

CL3 and CL4 laboratory

Phase 1 of the redevelopment was confirmed in 2009 when the Government (Department of Business, Innovation and Skills) and BBSRC made over £100M available for the construction of a high bio-containment laboratory complex. Building commenced in September 2010.

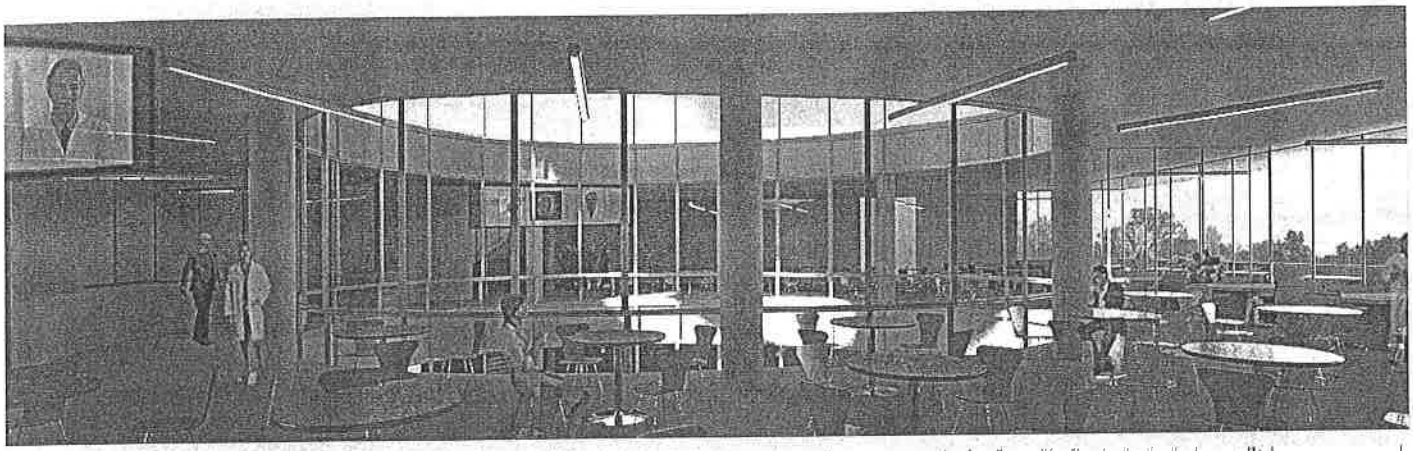
The building reached its maximum height in October 2011, just a year after construction commenced. This was celebrated with a 'topping-out' event, attended by the Minister for Universities and Science, the Right Honourable David Willetts MP.

Viruses that will be worked on in the new laboratory complex include those that cause African swine fever, highly pathogenic avian influenza, foot-and-mouth disease, and goat plague (peste des petits ruminants).

The Institute's work on avian viruses is expanding and much of the avian research formerly carried out at the Compton laboratory will be done on the Pirbright campus in future. The Government and BBSRC have committed £100M+ to the second phase of redevelopment. The CL2 laboratories will not only accommodate scientists working on poultry viruses such as Marek's disease and avian infectious bronchitis viruses but also those working on immunological and entomological projects that do not require CL4 containment.

The plan is that in the future The Pirbright Institute will become an anchor tenant on a diverse and productive multipurpose campus for research and innovation in virus diseases that affect livestock and poultry.

One of the great advantages of The Pirbright Institute is that its advances in the understanding of diseases and development of vaccines and diagnostics are underpinned by studies of the species (cattle, poultry, sheep, pigs) that will ultimately benefit.



Top: Visualisation of open plan area surrounding the glass atrium of the new high containment laboratory complex at Pirbright.

Bottom: One floor of the new complex.

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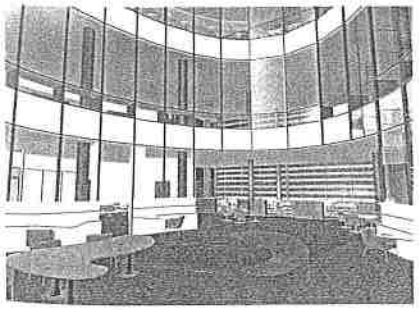
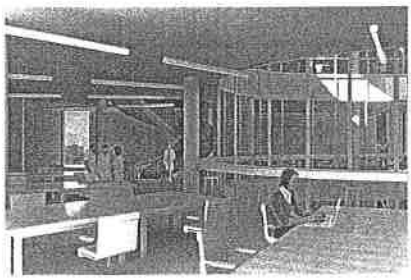
The Pirbright Institute: a unique national capability

The Pirbright Institute is a unique national centre that works to enhance the UK's capability to contain, control, and eliminate endemic and exotic virus diseases of livestock and viruses that can spread from animals to humans. This requires a unique combination of expertise; high bio-containment laboratories and animal facilities; exclusive biological resources, including extensive reference virus collections, arthropod vector colonies, and genetically defined farm animal host species; and diagnostic services. The Institute serves as a hub with research links radiating out to other centres of expertise within the UK and overseas.

The Pirbright Institute provides the UK with:

- High bio-containment laboratories (CL4) for investigating viruses that are not usually found circulating in the UK.
- Genetically defined lines of poultry, cattle and pigs to analyse immune responses and to study susceptibility and resistance traits.
- High bio-containment animal facilities (CL3 and CL4) for work involving poultry, cattle, sheep, pigs and small animals.
- Insectary for the production and maintenance of colonies of arthropods that spread viruses, including midges, mosquitoes and ticks.
- Reference collections of exotic viruses, including foot-and-mouth disease virus, bluetongue virus, African horse sickness virus, African swine fever virus and peste des petits ruminants virus.
- Expertise in the handling of endemic, exotic and zoonotic viruses.
- Diagnostic and surveillance capability for eleven exotic diseases, provided for Defra, the UN's Food and Agriculture Organisation, the World Organisation for Animal Health (OIE) and the EC.
- Advice to farmers, government and international organisations.
- Training in exotic viral diseases and virus handling for the upcoming generation of scientists, technicians and diagnosticians for the UK and overseas, and for Defra veterinarians.





A major strength of the Institute is that it is possible to study infectious diseases in the natural, farm animal hosts – cattle, poultry, sheep and pigs. Consequently, discoveries are directly applicable to farm animals whose health the Institute seeks to maintain and improve.

The Institute studies the insect and tick vectors that spread some virus diseases. Understanding transmission may lead to prevention.

Studies on virus structure, replication and pathogenesis provide fundamental knowledge applicable to both animal and human virus diseases.

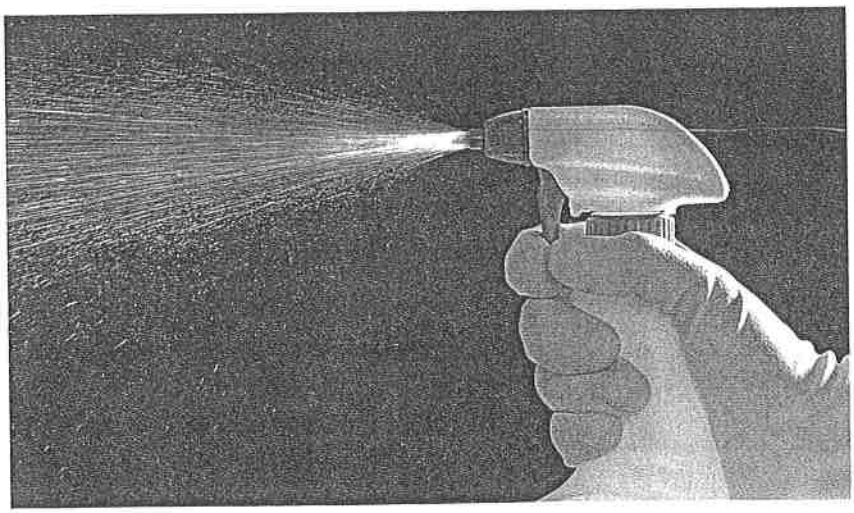
Compliance, Regulatory Affairs and Risk

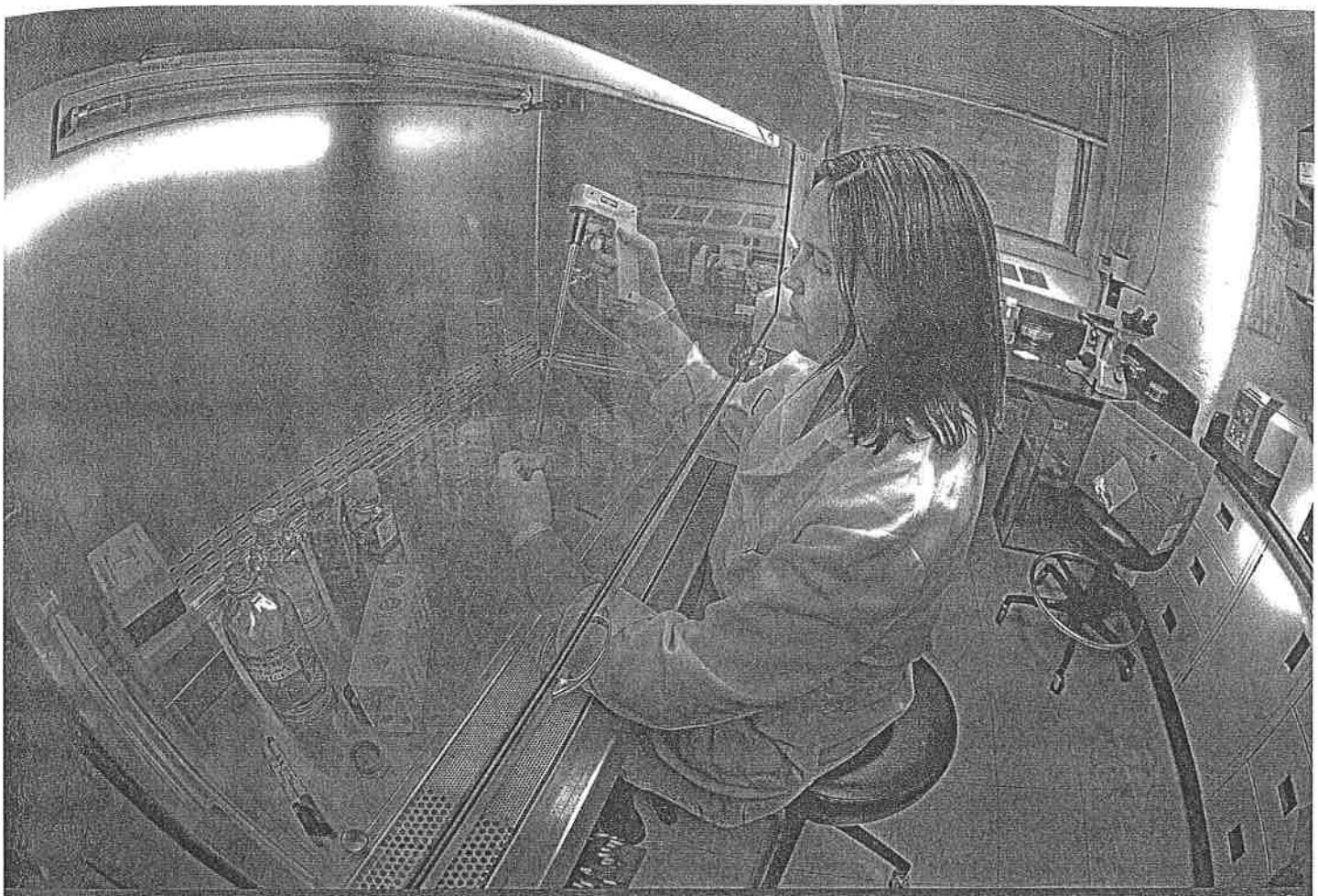
World leading research and surveillance of virus diseases necessarily means working with the viruses and host animal species of interest in controlled environments. This makes The Pirbright Institute a unique working environment and with this comes a special responsibility to protect workers, contractors, the general public and the environment.

The Pirbright Institute, with leadership from the Institute Executive Board and Trustee Board, has developed facilities, processes and practices that are designed and supported by a team of professionals in biosafety and biorisk management; health, safety and the environment; risk management; and quality assurance. The team works together with the leadership and workforce of the Institute to implement a system of risk management with the clear aspiration of causing zero harm. Members of the team are also in high demand externally for their advice on best practice in biosecurity.

Compliance

The Institute is under constant scrutiny from regulatory authorities and the role of the compliance team, through the Institute's governance structure, is to provide assurance to the workforce, funders and government that potential risks have been reduced to as low as reasonably practicable. To this end the compliance team have built strong links with authorities such as the Department of Food and Rural Affairs, the Health and Safety Executive, and the Environment Agency. In addition, as the Institute's mission involves work with pathogens of high consequence there are also strong links with the national anti-crime and terrorism security office.



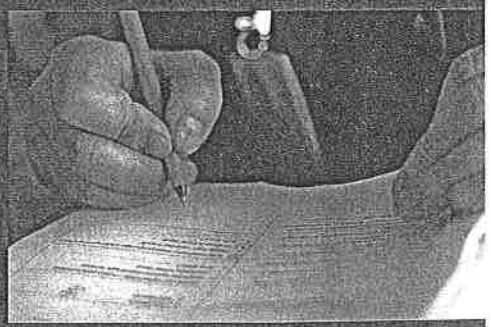


Health and Safety, Environment, and Biorisk Management

The Institute's positive health, safety and environment culture is based on mutual respect and trust. By continuing to reduce risks, the Institute's vision and mission statement is supported; costs are reduced; and business continuity is ensured. Mandatory training for all staff and specific training for those with general management or biorisk management responsibility ensures that the workforce has the necessary knowledge and practical guidance to deal with potential hazards to people and the environment.

Achieving a system of risk identification and risk management requires strong and effective leadership, the involvement of workers through constructive engagement and ongoing assessment and review. To this end the Head of Compliance is a member of the Institute Executive Board and reports directly on matters of health and safety and biosafety to the Director. Health and safety and biorisk management are considered core values of the organisation and the Director chairs the Institute Health and Safety and Environment committee which also oversees biorisk management activities. The Institute has found that addressing health and safety provides opportunities to improve business efficiency as well as safeguarding the health and safety of workers.

By maintaining and reviewing an effective risk register senior management have an accurate picture of the risk profile of the organisation which allows them to plan and implement a preventative approach to risk management.

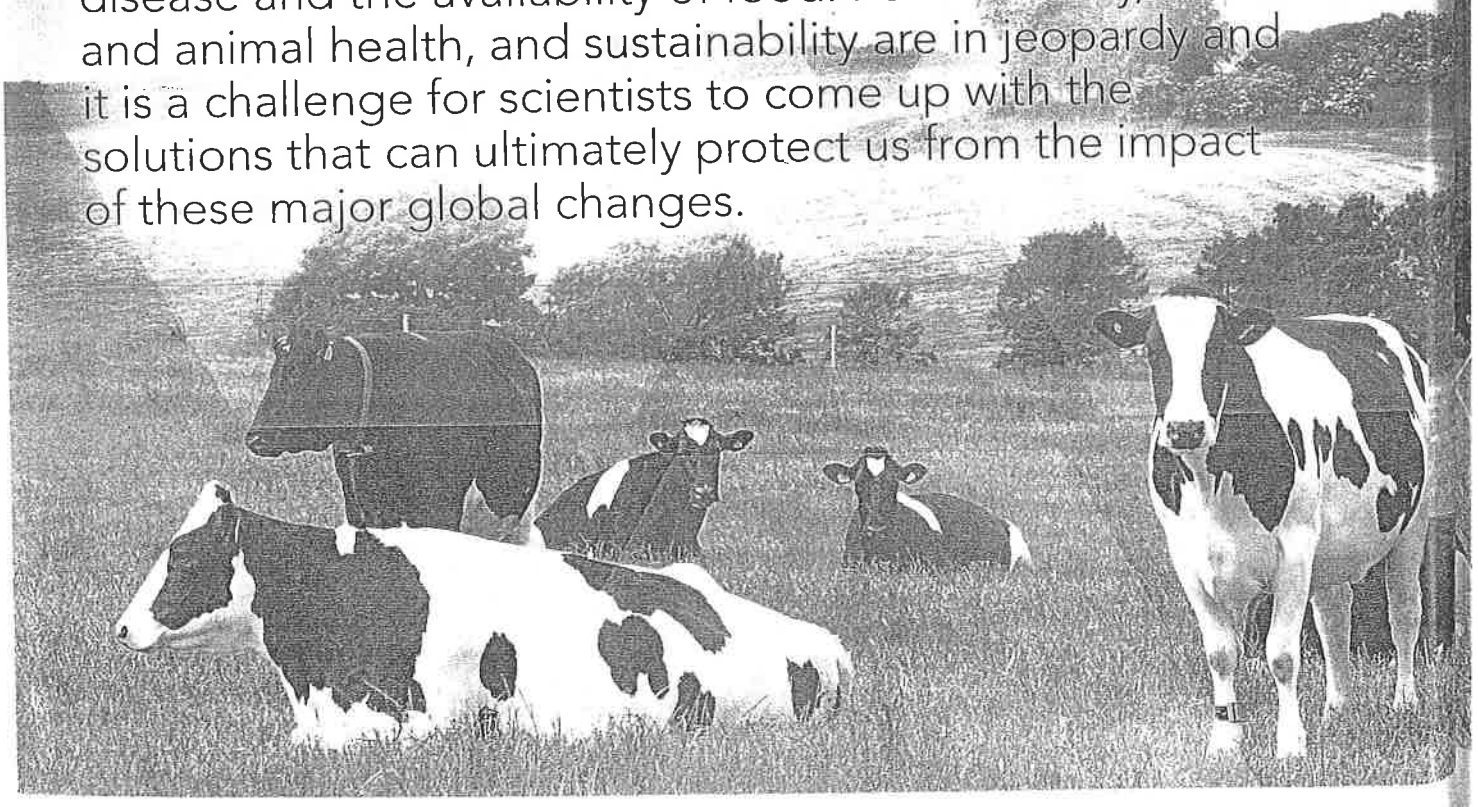


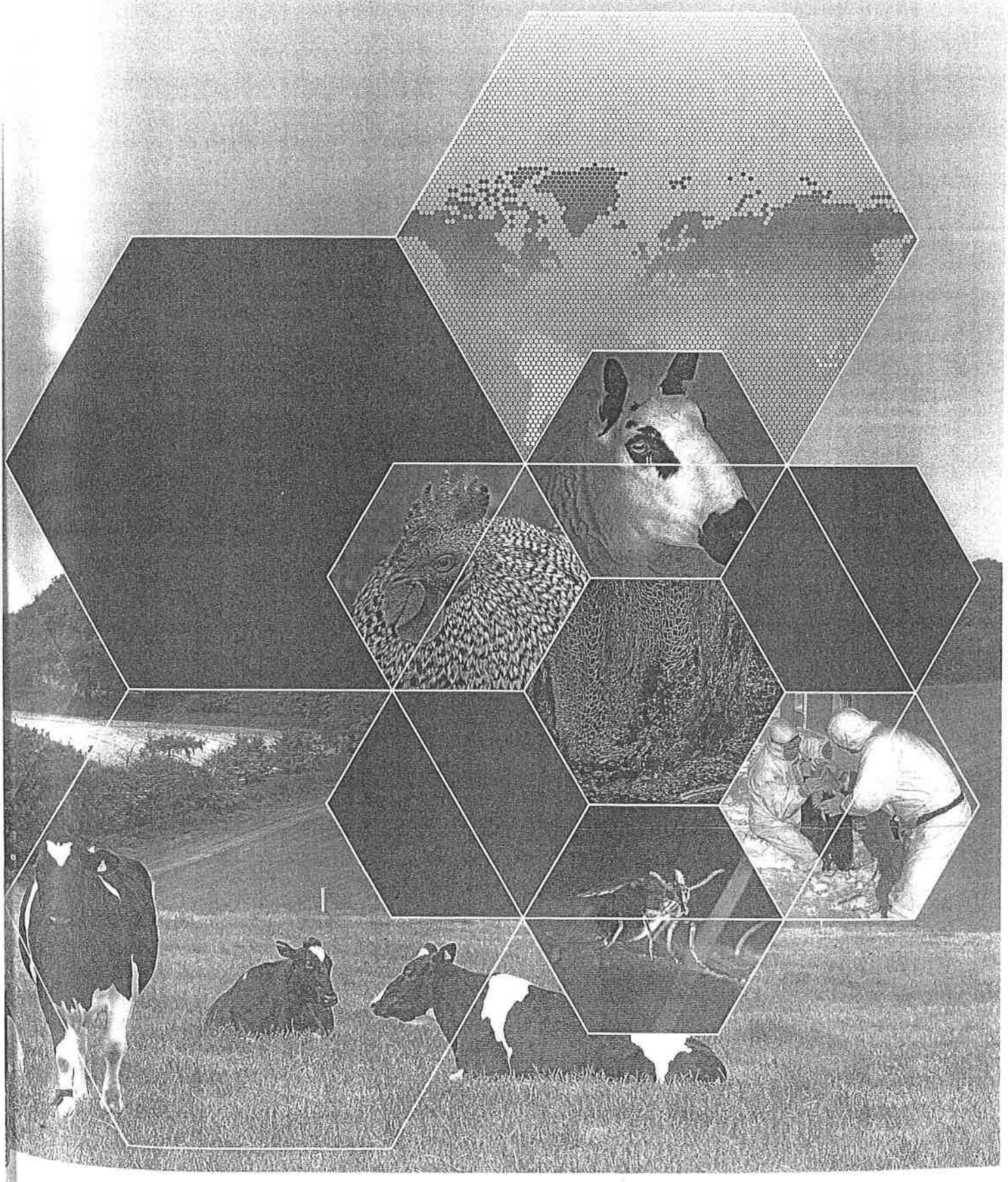
Quality Assurance

The quality assurance function is critical to all the Institute's work. Policies and procedures have been put in place to ensure compliance with the Funders Code of Practice for Research. The Pirbright Institute reference laboratory services and disinfectant testing laboratory are also accredited to internationally recognised accreditation schemes (ISO IEC 17025).

02 Meeting global challenges

The Pirbright Institute is in a unique position to provide knowledge, tools, technologies and advice that contribute to addressing some of the greatest global challenges of our time. Our environment is changing; the population is increasing; major changes in patterns of travel, trade, and consumption are having an impact on the spread of disease and the availability of food. Food security, human and animal health, and sustainability are in jeopardy and it is a challenge for scientists to come up with the solutions that can ultimately protect us from the impact of these major global changes.





Food security

One of the greatest challenges faced globally is that of food security. With a global population set to rise to nine billion by 2050, it is vital to improve the quantity, quality and sustainability of the food that we produce and to do so in the context of a changing environment and increasingly limited resources.

Meat consumption around the world is rising – particularly poultry. This means that as well as responding to the issues of environmental change and increasing population we also have to respond to changes in the patterns of consumption. The Pirbright Institute is working to improve food availability, rural prosperity and animal welfare by focussing on some of the most damaging of the viruses that affect livestock, with notable successes. In this way, the Institute safeguards the supply of meat, eggs, and dairy products to feed everyone.

The virus diseases worked on at the Institute include:

DISEASE	ANIMALS AFFECTED	CHRONICALLY AFFECTED REGIONS
African horse sickness	*Equidae e.g. horses, donkeys*	*Africa*
African swine fever	*Pigs*	*Caucasus (since 2007), Sardinia, Africa*
Avian influenza	*Poultry, ducks, sometimes people*	*Asia and beyond*
Bluetongue	*Ruminants e.g. cattle, sheep*	*Africa, Asia, Australia, North America, southern Europe*
Bovine pneumonia	*Cattle*	*Worldwide*
Foot-and-mouth disease	*Cloven-hoofed e.g. cattle, sheep, pigs*	*Africa, Asia, Middle East*
Goat pox	*Goats*	*Africa, Asia*
Infectious bronchitis	*Chickens*	*Worldwide*
Lumpy skin disease	*Cattle*	*Africa*
Marek's disease	*Poultry e.g. chickens, turkeys*	*Worldwide*
Nairobi sheep disease	*Sheep, goats*	*Africa*
Peste des petits ruminants	*Sheep, goats*	*Africa, Asia (increasingly)*
Rinderpest	*Bovines e.g. cattle*	*Eradicated globally*
Sheep pox	*Sheep*	*Africa, Asia*
Swine vesicular disease	*Pigs*	*Asia, Southern Italy*

The Institute made major contributions to the recently announced global eradication of rinderpest (cattle plague), the greatest scourge of cattle for centuries, and to the elimination of bluetongue virus from the UK following its introduction in 2007. Researchers at the Institute have developed diagnostic tests for most of the diseases listed above, and provide diagnostic services for Defra, the European Food Standards Agency, the Food and Agriculture Organisation, and OIE (the World Organisation for Animal Health). In addition, our epidemiological studies result in viral isolates being transferred to animal health companies for vaccine development.

'One Health, One Medicine': research that benefits animal and human health

'One Health, One Medicine' is the idea that the biology of human health and the biology of animal health are sufficiently similar that scientific and medical advances in one can inform, and may be applicable to, the other.

The value of this approach is clear for zoonotic diseases – those that can spread from animals to humans – but a broadening of the idea to include synergistic approaches that employ knowledge and expertise across both fields can have added impact to improve health for humans and animals alike. This has a history as much of our knowledge of viruses in humans is predicated upon earlier research of related viruses in animals and birds. At The Pirbright Institute the pool of knowledge on viruses, immunity, and insects and other vectors of disease could be a vital tool to improving human health. Researchers are also examining zoonotic diseases such as some influenzas and vector-borne viruses such as West Nile virus, chikungunya virus and Rift Valley fever virus. The Institute has considerable expertise on mosquitoes and ticks which can transmit both human and veterinary viruses.

Avian influenza

Within the Institute there are several lines of research on avian influenza viruses (AIV), partly because of their immense potential for harm to poultry, and also because of their potential to spread from poultry to pigs and humans. The Institute is doing research that will underpin a new generation of vaccines against the disease in poultry, based on using another avian virus, herpesvirus of turkeys. Researchers at the Institute are also examining the use of human virus vectors to develop a 'universal influenza vaccine', able to protect chickens against several virus subtypes.

Marek's disease in poultry: Cancer in humans

Marek's disease herpesvirus causes tumours in poultry. It was the first oncogenic virus to be controlled by vaccination. Current research on this virus at the Institute is not only of relevance to the improved control of the disease in poultry but also to the development of novel approaches to the control of cancers in humans.

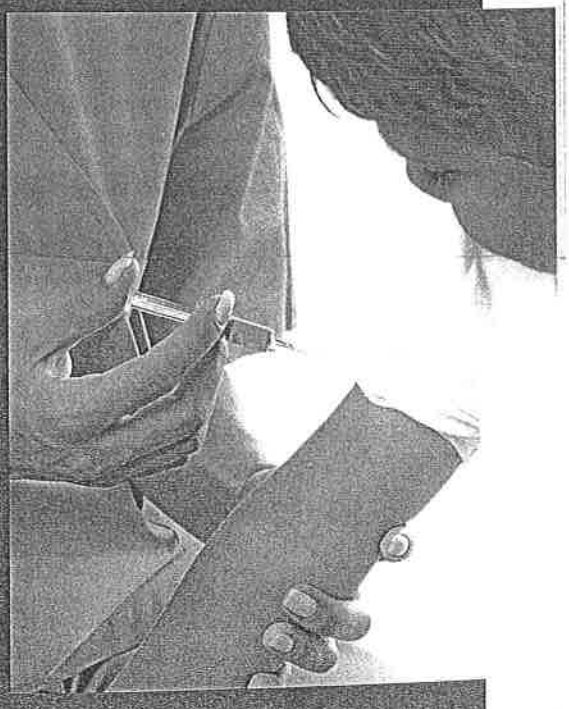
Respiratory syncytial virus

Both cattle and humans are affected by respiratory syncytial viruses – in humans this is the single most important cause of bronchiolitis and pneumonia in infants. At The Pirbright Institute, bovine respiratory syncytial virus (BSRV) is studied with a view to improving vaccination of cattle. This work advances understanding of the interaction between BSRV and the cattle immune system and yields results that should also be of benefit to human health.

The Jenner Institute

The Jenner Institute was founded in November 2005 to develop innovative vaccines against major global diseases. It is a partnership between The Pirbright Institute and the University of Oxford, focussing on diseases of humans and livestock and testing new vaccine approaches in parallel in different species.

For more information see www.jenner.ac.uk



The Institute's research on viruses that affect animals can have an impact on approaches to human health research.

Living with environmental change

The environment we live in is changing. Changing climate and land use alter the suitability of many regions for the transmission of livestock and zoonotic viruses, potentially broadening their impact. This, in the context of growing global trade and the subsequent rise in movements and extent of travel of animals and animal products, increases the potential for viruses to emerge and spread internationally.

Some of the viruses most susceptible to environmental change are those transmitted by insects, such as midges and mosquitoes. Many insects are capable of rapid population growth, allowing them to capitalise rapidly on favourable environmental changes. Some can be introduced over long distances, for example by transport on the wind. Mosquito larvae have been transmitted to many parts of the world by the trade in used tyres and lucky bamboo. Lastly, insects are cold-blooded, meaning that warmer environments accelerate the incubation of viruses within them. Climate change could therefore result in the emergence of new viruses in the UK and elsewhere. At Pirbright, scientists have been investigating the potential for insects and ticks to be involved in the spread of outbreaks in previously unaffected regions. This includes studies on the competency of indigenous arthropods to be infected by and to transmit specific viruses.

Bluetongue virus

Wind and temperature have proven to be critical to the spread of bluetongue virus. First, the midge species responsible for transmitting bluetongue in most of Africa spread to Southern Europe on the wind. The species was able to become established due to changes in the climate of Southern Europe. This meant that subsequent virus introductions could spread. As a result, bluetongue cases have occurred in Southern Europe every year since 1998. Before 1998 only two outbreaks had occurred (excluding Cyprus, where bluetongue is endemic).

Circulation of the virus in Europe may have allowed bluetongue strains to adapt to be spread by local species of midge.

In 2006, bluetongue was introduced into Northern Europe, probably by international trade. It subsequently spread to the UK in the summer of 2007, when infected midges were blown on the wind from the continent.

Zoonotic diseases

Zoonotic mosquito-borne viruses – i.e. those that affect people as well as animals – have been emerging in Europe, with outbreaks of West Nile virus in Spain, Portugal, Greece and Italy in the last few years and cases of chikungunya in Italy and Southern France. At Pirbright researchers have established colonies of mosquitoes from UK populations in order to be able to study the transmission of these viruses.

It is predicted by the European Centre for Disease Prevention and Control, that the vector of dengue fever and chinkungunya fever, the mosquito *Aedes albopictus* will eventually colonise much of Western Europe, perhaps as far north as the Scottish borders. Cases of chikungunya have already occurred in Italy and Southern France.

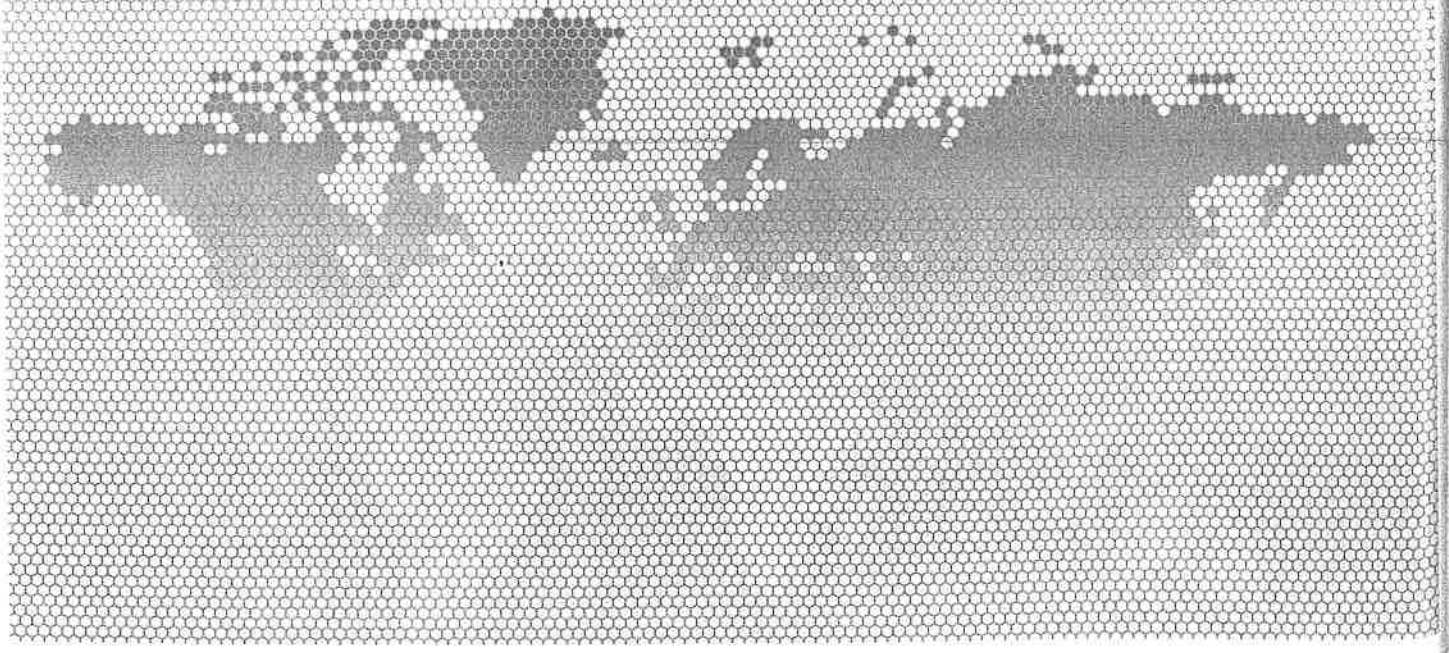
Responding effectively to emerging diseases requires the early identification of potential threats. In partnership with the Animal Health Veterinary Laboratories Agency and funded by Defra, the Institute recently assessed the threat to the UK of 70 arthropod-borne livestock viruses, as well as the national capability to respond to them. Analysis of this kind allows the Institute to direct its resources to efficiently tackle key threats facing UK agriculture and health. The Institute is also a member of several large international networks that aim to identify future threats to UK farming.

Emerging viral threats

The Institute contributes to both national and international efforts to prevent and control viral diseases by the global reach of its world-class bioscience and expert advice. This is in the context of the ever-changing nature of viral disease threats stemming from the globalisation of trade and travel, environmental change, expanding human and animal populations, the intrinsic mutability of some viruses, and differences in disease resistance between breeds of animals.

Below are just some of the viral diseases that moved huge distances to new continents and then spread within them, within the last decade or so.

- Avian influenza virus subtype H5N1 spread globally, by migrating birds, from China (1997).
- West Nile virus arrived in New York in 1999. Within four years it had crossed the continent, spread by mosquitoes.
- Foot-and-mouth disease virus arrived in the UK from the Far East in 2001.
- Bluetongue virus serotype 8 arrived in Northern Europe in 2006, probably from Central Africa, and then spread widely in Northern Europe, including the UK, carried by biting midges.
- Bluetongue virus serotype 1 entered Europe in Spain, from North Africa (2006) and then spread into France, carried by biting midges.
- Peste des petits ruminants virus spread from the Arabian peninsula to Northwest Africa (2008), from Central to Eastern Africa (2006, 2008), and from India to China (2007).
- African swine fever virus was transported from eastern Africa to the Caucasus (2007), and was subsequently spread to North-Western Russia (2009, 2011).
- Schmallenberg virus was introduced into northern Europe from an unknown source (2011), after which it was disseminated widely, including to the UK.
- Chikungunya virus is endemic in Africa, probably in monkeys. Between 2005 and 2010 it spread across the Indian Ocean islands and the Indian subcontinent into South East Asia.



International development

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. Diseases of livestock and crops can reduce output by as much as 50%. The World Bank estimates that, for the world's poorest people, Gross Domestic Product growth originating in agriculture is about four times more effective in reducing poverty than any other sector growth.

The Institute's research, surveillance and diagnostics work has, for many years, included viruses that are not usually present in the UK livestock population but which are endemic on other continents e.g. rinderpest (now eradicated), foot-and-mouth disease (FMD), and bluetongue.

Research and development on these viruses has had a twin benefit: contributing to the nation's preparedness for outbreaks in the UK, and to international development by helping developing countries to control the diseases within their own borders. Moreover, diminishing these diseases in endemic overseas areas reduces the risk of the causative viruses coming to the UK.

The Institute has considerable expertise and international standing in this area. This was recognised by the OIE (World Organisation for Animal Health) and the FAO (Food and Agriculture Organisation of the UN) in 2012 when the Pirbright-based World Reference Laboratory for FMD was appointed coordinator of the world's FMD reference laboratories as part of the OIE and FAO strategy on FMD. The Pirbright Institute was also an obvious partner in many of the research projects within the Biotechnology and Biological Sciences Research Council's CIDLID (Combating Infectious Diseases of Livestock for International Development) programme:

- Development of vaccines against multiple diseases to save sheep and goats.
- Dip-stick test for goat plague.
- Providing tools for monitoring and controlling bluetongue virus outbreaks in India.
- Comparing foot-and-mouth disease in wildlife and livestock.
- Developing rapid tests to prevent pig deaths from African swine fever
- Improving the quality of foot-and-mouth disease vaccines.
- Looking at ticks in the spread of lumpy skin disease virus.

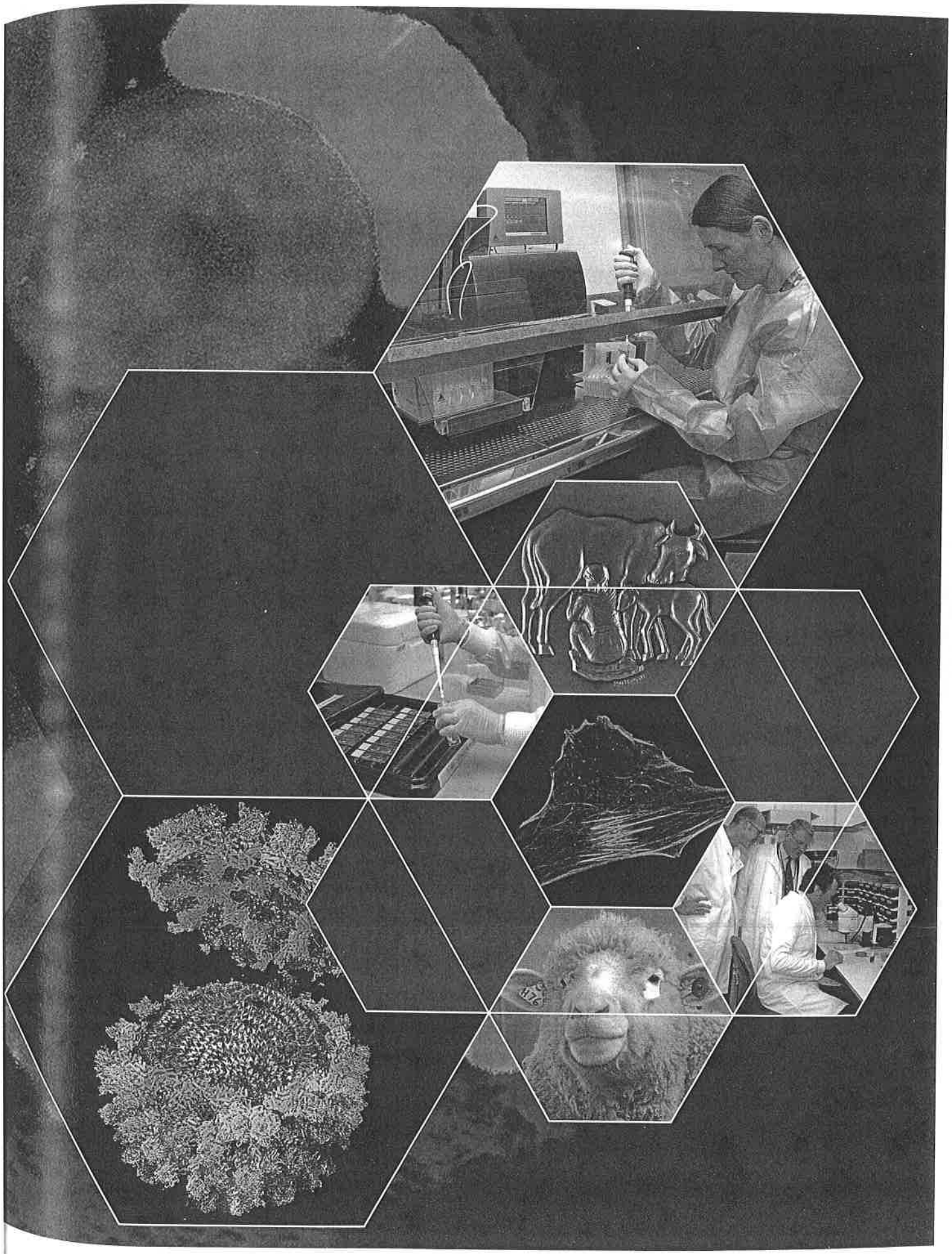
The Institute's contribution to international development extends much further than Africa and the Indian sub-continent as the viruses that we study, monitor and advise on are also present in many parts of Asia, the Middle and Far East and, in the case of FMD, South America.

Reference laboratories twinning programmes

The Institute supports the development of diagnostic capabilities within laboratories in developing countries through twinning programmes. At the time of writing, active programmes include laboratories in Morocco and Uganda.

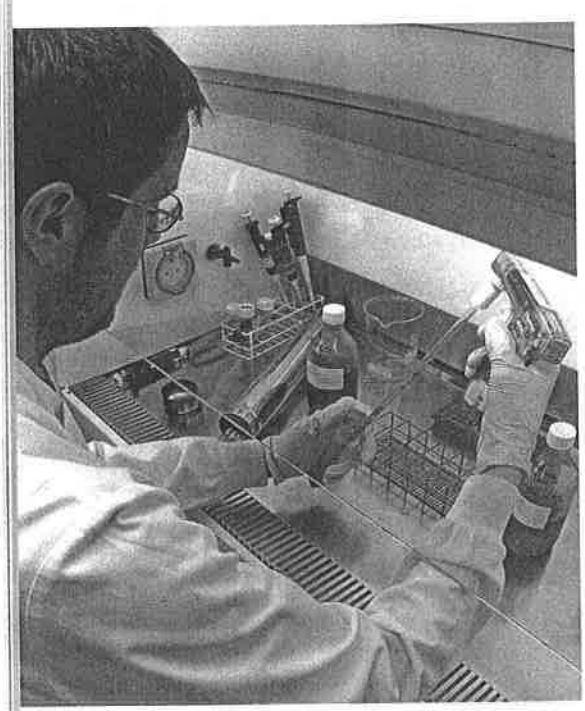
03 Social and economic impact

The Pirbright Institute provides knowledge, tools, technologies and advice to a variety of end users in science, agriculture, veterinary medicine, pharmaceutical industries and policy. Fundamental science underpins practical solutions to many of the challenges faced by farmers, vets, and policy makers and it is through public engagement, knowledge exchange and commercialisation that the Institute creates opportunities for social and economic impact. The benefits can be world-changing: The Institute has played a role in eradicating rinderpest, which is estimated to save the economies of Africa around US$1 billion per year; closer to home, advice from the Institute led to a successful voluntary vaccination programme against an incursion of bluetongue virus in 2007, saving the UK around £485 million per annum and protecting around 10,000 jobs.



Diagnostic services and Surveillance

The Pirbright Institute provides diagnostic services, early warning and advice on eleven exotic animal virus diseases to numerous stakeholders including governments in the UK and elsewhere, industry bodies and international agencies. The outputs from the Institute's reference laboratories, supported by the research that underpins them, provide tools and advice to help minimise disease overseas and thus lower the threat to the UK.



The Institute maintains the capacity to provide rapid diagnosis and emergency response, and carry out specific tests in support of national and international disease surveillance. Facilities and expertise are in place to:

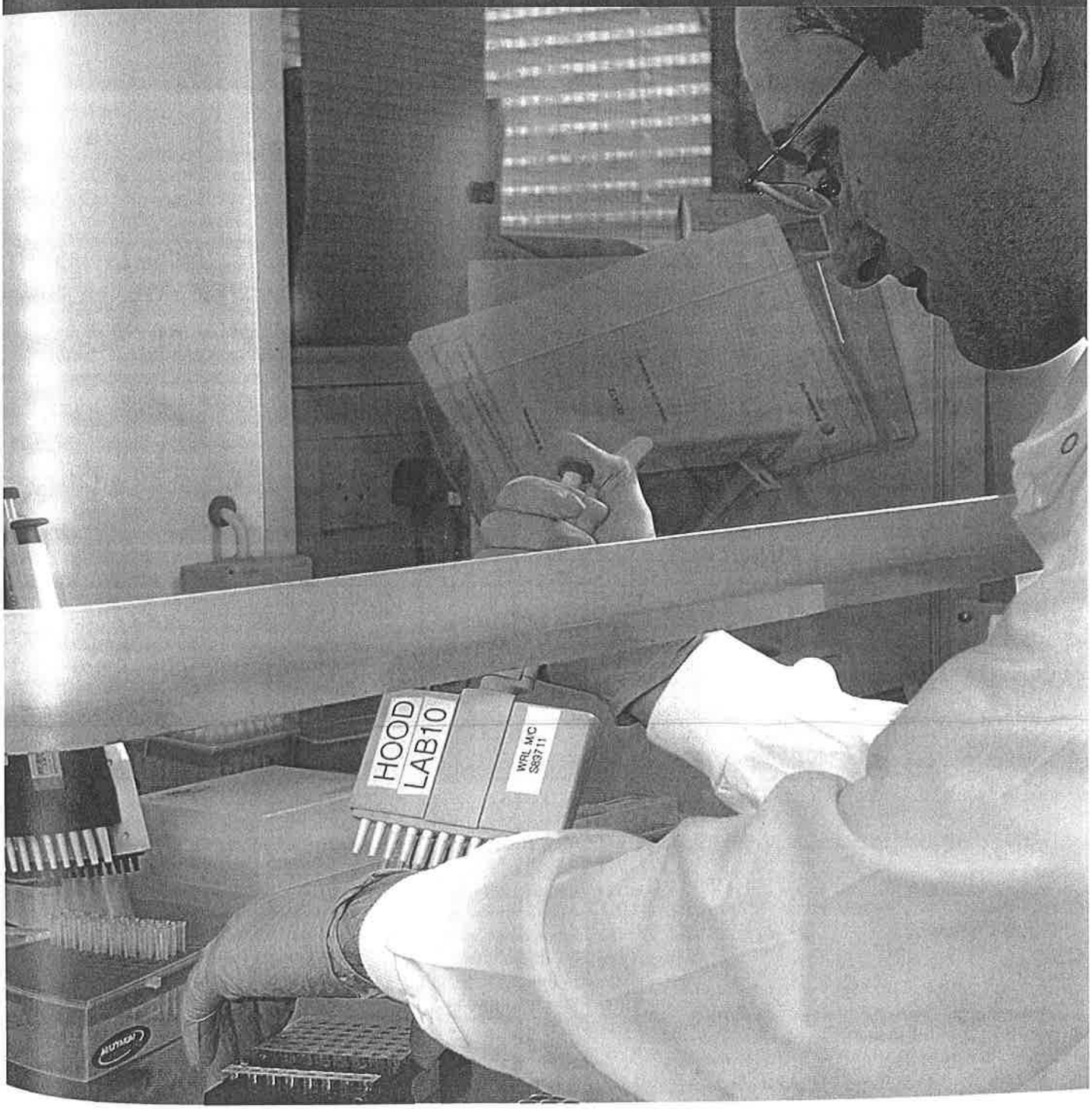
- Characterise viral pathogens in vitro and in vivo.
- Produce comprehensive reports.
- Offer vaccine evaluation and recommendations.
- Give expert advice on control strategies.
- Undertake statutory testing in support of animal trade.
- Maintain unique reference collections and sequence databases.
- Influence OIE/EC regulations for livestock trade.
- Improve international laboratory capability and capacity through extensive networks, twinning projects, highly successful proficiency testing schemes, and supply of diagnostic reagents and kits.

Stakeholders include Defra, FAO (the UN's Food and Agriculture Organisation), OIE (the World Organisation for Animal Health), and the European Commission. The Institute provides official and ad hoc training courses for these organisations and for the Animal Health Veterinary Laboratories Agency and the International Atomic Energy Authority.

Monitoring and controlling outbreaks

In 2001 the UK experienced a major outbreak of foot-and-mouth disease. Through the course of the outbreak, the Institute's reference laboratories tested around 15,000 samples for the presence of foot-and-mouth disease virus. This provided vital information to policy makers and veterinarians working to control the outbreak.

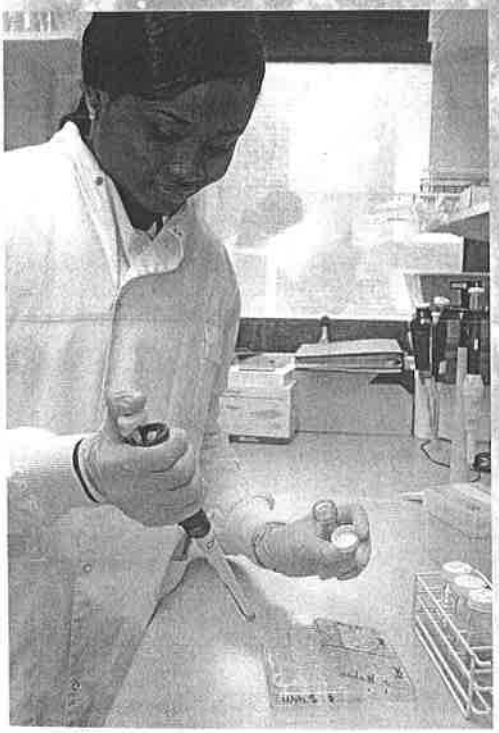
The Institute's reference laboratories provide a vital service in real time during outbreaks of disease, both nationally and internationally.



Expert advice

The Pirbright Institute is in a strong position to advise governments and policy makers on the control of virus diseases of farm animals and the transmission of viruses from animals to humans. This is particularly true of the Institute's reference laboratories.

The Institute is a centre of expertise that is unique in the UK and it is a key player at international level. Experts are called upon to advise not only the British Government and farmers, but also pharmaceutical and diagnostics companies, international agencies including the UN's Food and Agriculture Organisation (FAO), the World Organisation for Animal Health (OIE) and the European Commission, national governments, and other research, surveillance and diagnostics facilities.



For example, foot-and-mouth-disease (FMD) experts advise on the composition of millions of pounds worth of vaccine stocks being maintained by the EU, and other international FMD vaccine banks around the world.

Between 2006 and 2008 bluetongue disease experts from the Institute advised that development and rapid deployment of a vaccine against bluetongue virus type 8 was crucial if the disease was to be contained and ultimately eliminated. This advice was followed, with a very successful outcome preventing outbreaks of bluetongue in the UK in 2008. Advice from the Institute also contributes to the Government's contingency plans in the event of future FMD or bluetongue outbreaks and Institute experts are members of many international forums.

In addition, the Institute maintains a number of websites detailing much of the information generated by reference and research laboratory activities. As well as recent results and epidemiological information, regular disease reports circulated to a broad range of stakeholders are available from these sites. This is an essential information source that is regularly accessed from all over the world highlighting the truly international nature of the information and advice that the Institute provides.

Maintaining a high security biocontainment facility requires a variety of skills and capabilities in facility design, engineering and maintenance, biosecurity, biosafety and facility management. The Institute is a world leader in providing experts and accumulated knowledge on these matters to others wishing to construct new high security buildings. Such advice has recently been provided to laboratories in the USA and Europe, and a programme of knowledge exchange has begun with Public Health England and the Animal Health and Veterinary Laboratories Agency in the UK.

The Pirbright Institute provides both statutory and independent commercial disinfectant testing services. Veterinary disinfectants play an essential part in the prevention and control of endemic epizootic animal diseases and in the UK and its devolved administrations only approved disinfectants can be used where required in the Animal Health Act 1981 and in orders issue under the act. The Approval Process is regulated through The Diseases of Animals (Approved Disinfectants) (England) Order 2007 (S.I. 2007/448) and parallel statutory instruments in the devolved administrations. The Institute offers efficacy testing for disinfectants against foot-and-mouth diseases virus and swine vesicular disease virus.

Knowledge Exchange and Commercialisation

The Pirbright Institute is committed to realising the economic and social benefit of its science and has developed a strong culture of translational research where understanding biological processes can lead to benefits in science, veterinary medicine and policy.

With an emphasis on collaboration and cooperation with end users, the knowledge generated by research into the biology of animal diseases is turned into valuable advice, tools and technologies.

When appropriate, the Institute protects knowledge and patents inventions. As a publicly-funded charity, intellectual property that arises from research is properly protected to encourage its use for the benefit of society.

Knowledge is also shared through training and professional development, access to specialist facilities and biological collections, publication of academic papers, policy guidelines, seats on governmental and NGO working parties, and conferences.

The Pirbright Institute is currently focussed on virus diseases. However, past research has also included bacteriology and parasitology.

The Institute continues to work with collaborators on management of knowledge exchange and commercialisation in these fields.

Global strategy

Diseases that are exotic to the UK can be endemic elsewhere in the world, particularly in less developed countries. The Pirbright Institute works extensively to improve disease control across the globe and thus protects the UK's borders from the threat of emerging viruses. When an exotic disease does arrive, the tools, technology, and policy advice offered by the Institute is instrumental in ensuring the best possible outcome for UK farmers, the economy and animal welfare.

The state-of-the-art high containment facilities at Pirbright offer the opportunity to scientists from around the world to study viruses of interest that cannot be worked on in their home countries.

Former Institute Director Professor Martin Shirley developed a successful vaccine against Eimeria, the parasite that causes coccidiosis, which is still in production some years after the patent expired.

Commissions

Major advances in vaccines against some of the world's most economically important animal viruses have been made by the Institute, often on the basis of non-commercial endeavours that are aimed purely at delivering a public good. Many of these are commissioned by UK, European and World agencies for health and agriculture.

A programme supported by the EU, DfID, and FAO, among others, resulted in the development of effective diagnostic test kits for rinderpest – an advance that contributed to the eradication of the virus.

The Pirbright Institute is part of a £13 million plus investment by the Biotechnology and Biological Sciences Research Council (BBSRC) and the UK Department for International Development (DfID) into the Combating Infectious Diseases of Livestock for International Development (CIDLID) programme.
See www.pirbright.ac.uk/CIDLID

Knowledge Exchange and Commercialisation continued

Collaborative development

The Institute develops reagents, tools and new techniques for diagnosing viral diseases and for research into species-specific responses to viral infection. This important work is done in-house, in collaboration with other research institutes, and via public-private partnerships.

Staying ahead of new threats from virus diseases means developing diagnostic reagents, assays and kits where the commercial potential is currently unknown but the consequence of an unmonitored, uncontrolled outbreak of disease could be devastating. As soon as there is a need, these are developed in house, sold, or licensed to companies for bespoke development on proprietary platforms as well as sales and distribution. The Institute's kits and reagents are supplied all around the world.

Facilities and biological collections

The Institute has a comprehensive archive of viruses that are partially or fully characterised. These are available to the animal health community for academic and commercial research into e.g. novel vaccines; development of new vaccines for emerging variants; and the evaluation of vaccines against a range of variants from around the world.

The Institute developed a diagnostic kit for 24 different serotypes of bluetongue virus, which has been launched by global assay technologies company, QIAGEN as the *cador* BTV RT-PCR kit.

In house, these collections are used to build our understanding of viral evolution and the global distribution of viruses; and to test diagnostic kits and assays. This enables the Institute to advise governments and animal health agencies on the most effective control approaches elsewhere in the world.

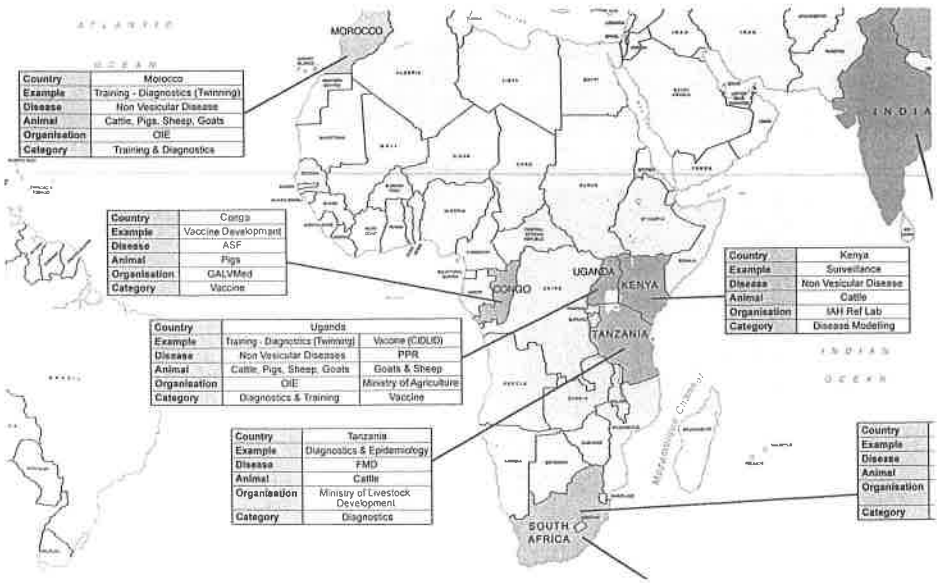
The Institute also provides access to specialist facilities via contract research and services as well as public-private partnerships.

Professional development

Institute scientists and students as well as visiting researchers and diagnosticians from academic institutions, government agencies, and commercial companies benefit from a range of educational access programmes. These include specialist disease or discipline training programs such as in biosecurity.

There is an extensive diagnostics training programme at Pirbright. Institute scientists also support and train researchers and diagnosticians overseas. Animal health professionals from around the world are trained by the Institute and disseminate knowledge and best practice in their home environment to improve disease control and animal welfare worldwide.

Excellence in research and training is heavily supported through doctoral and masters programmes and visiting scientist fellowships. Formal educational and training qualifications are supported by partnerships with UK universities as awarding bodies.



In 2012 the Institute received samples from an outbreak of foot-and-mouth disease (FMD) in Egypt. This was the SAT2 strain, which hadn't been seen in Egypt for decades. Advice from the World Reference Laboratory for FMD, based at Pirbright, included identifying the appropriate vaccine to be used to control the outbreak.

International training

The Institute provides annual training courses in livestock and poultry health for Defra's Animal Health veterinarians and for diagnosticians, technicians and veterinary scientists from around the world.

The Institute has a wealth of knowledge on livestock disease stemming from both its fundamental research and the diagnostic and surveillance activities of its 11 reference laboratories.

As part of their remit, the reference laboratories at Pirbright provide detailed annual training programmes which include hands-on practical training for technicians and veterinary scientists from overseas. These two-week courses concentrate on technical aspects for the laboratory diagnosis of foot-and-mouth disease virus, bluetongue, capripox and peste des petits ruminants viruses. In recent years, attendees have come from many countries, including Sudan, Morocco, Argentina, Ethiopia, Indonesia, Iran, Iraq, Israel, Jordan, Malaysia, Mongolia, Russia, and Yemen, as well as from Europe. Institute experts also provide lectures on aspects of disease epidemiology and control. This training is very much a two-way process, enabling the Institute to make international contacts and foster links with diagnostic laboratories around the world.

The Institute also provides a two-day training programme for veterinarians from the Animal Health Veterinary Laboratories Agency. This course provides updates on all aspects of the viral diseases that are worked on at The Pirbright Institute.

Animal Health vets are amongst the attendees at the annual two-week Poultry Health Course organised by the Institute. This also serves vets from the UK and internationally who work for poultry producers, breeding companies and pharmaceutical companies.

Additionally, Pirbright hosts trainees on an ad hoc basis on request from international organisations such as the International Atomic Energy Agency (IAEA), the United Nations Development Programme (UNDP), the Food and Agriculture Organisation (FAO) and the European Commission (EC). These training visits may last anything from two weeks to six months.

The reference laboratories are occasionally 'twinned' through a scheme fostered by the OIE (World Organisation for Animal Health) with national reference laboratories from other countries. The aim of these three-year twinning projects is for the Institute to help in the development of diagnostic capabilities for key diseases within laboratories in developing countries.

Communications and Outreach

The Pirbright Institute receives strategic funding from the UK Biotechnology and Biological Sciences Research Council (BBSRC) and is in receipt of grant income from BBSRC and other public, taxpayer-funded, organisations. The setting of science strategy and plans for delivery of research objectives must therefore respond to a changing environment to deliver fundamental and applied science that is for the public good and responds to the hopes, fears, concerns and aspirations of people in the UK. Openness, transparency and accountability in the spending of public money are also vital.

To this end, the Institute has a programme of communications and outreach that ensures it is responsive to its publics and maintains a high profile and excellent reputation amongst a wide variety of stakeholders.

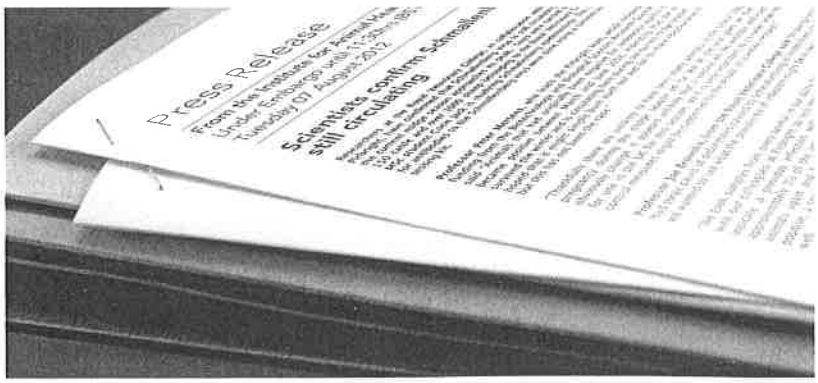
Website

The Institute's corporate website (www.pirbright.ac.uk) offers a range of information for academic colleagues, commercial collaborators, customers of diagnostics and testing services, end users of research, students, and the general public, among others. The site is evolving and will become increasingly dynamic with time.

Media relations

A combination of reactive and proactive media relations ensures the Institute has a high profile in relevant media, including outlets local to its two campuses in Pirbright, Surrey and Compton, Berkshire. The communications team also works to create opportunities for researchers to communicate via the media and to support journalists with information and interviewees in order to promote high quality science reporting.

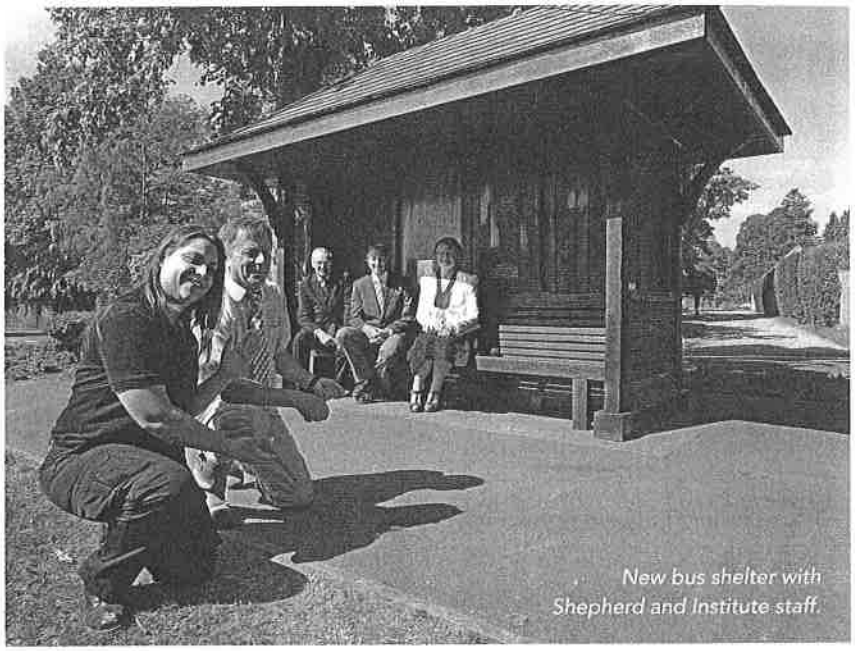
During 2012 the Institute has featured prominently in reports about the arrival of Schmallenberg virus in the UK from mainland Europe. There has been considerable interest from national news media as well as farming and veterinary outlets. Professor Peter Mertens and other members of the vector-borne viral diseases programme have featured in reports.



Local community engagement

The Institute is in regular contact with local communities around both sites; staff have contributed to local development projects, sometimes in collaboration with contractors. Formal and informal research and consultation ensure that the Institute can respond to the hopes, fears, concerns and aspirations of its close neighbours.

The Institute contributed to a project led by Shepherd Construction Ltd. (the lead contractor in the building of a new high containment facility at Pirbright) to restore a historic bus shelter in the village of Pirbright.



New bus shelter with Shepherd and Institute staff.

Politicians and policy makers

The Pirbright Institute receives strategic funding from BBSRC, which is in turn funded by the UK government. A combination of events and visits ensures that interested ministers, parliamentarians, and local councillors are kept informed of the Institute's activities.

The Institute was pleased to welcome local MP for Woking, Jonathan Lord, to the Pirbright campus in 2012. In late 2011 David Willetts, Minister for Universities and Science, attended to welcome news of £80 million funding for the Institute announced in the Chancellor's autumn statement.

Minister for Universities and Science, David Willetts (second from right) with BBSRC Deputy Chief Executive, Steve Visscher (far left), BBSRC Chief Executive, Professor Douglas Kell (second from left) and Institute Director, Professor John Fazakerley (far right).

Public engagement

Perhaps the most powerful way to ensure research questions and practices take account of, and respond to, the public is for Institute staff to participate in public engagement activities. These can be dialogue-focussed i.e. two-way discussions around an area of research or an issue, with the aim of informing research direction, policies or strategy. Or it can involve extractive opinion gathering through public attitude studies or consultation exercises to help understand public views, values and attitudes around an area of research.

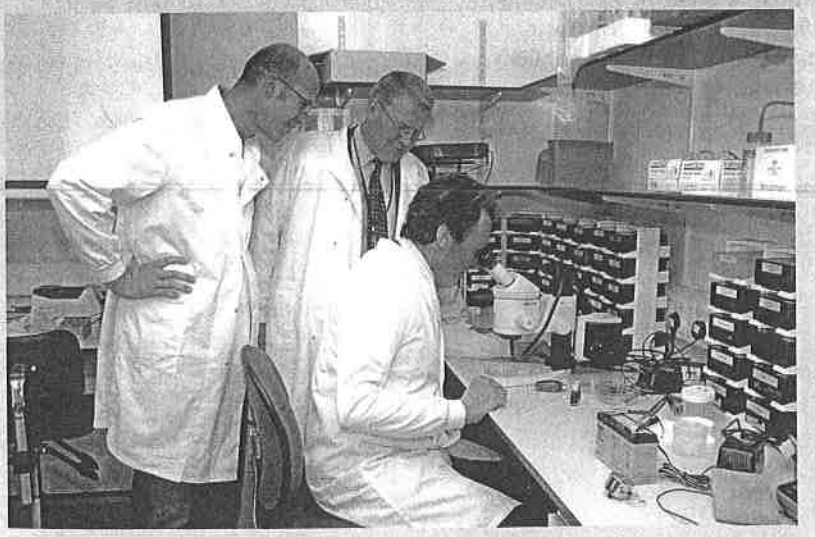
There is also an important role for researchers to play in equipping members of the general public, including school children, to engage in future debates around science and technology.

Communications and Outreach continued

Institute staff take part in trade shows and events where they speak with agricultural professionals about the broader social issues that impact on their experience with animal health.

Institute researchers speak with attendees at Sheep 2012.

When engaging with end users of science, Institute researchers often find themselves discussing the factors affecting emergence of disease. This was never more true than in 2006 when bluetongue first appeared in the Maastricht region of the Netherlands. UK farmers were desperate to know more about this disease, how could it have arrived in the Netherlands, and what was the risk to the UK. Thanks to sustained funding from Defra and BBSRC, the Institute has a core of world-leading experts on bluetongue who understand how midge-borne diseases can be impacted by climate change, weather conditions, and global movements of people and animals; along with colleagues at the UK's Met Office they were able to model disease spread and predict the arrival of the virus in the UK during 2007. These early initial discussions with the farming community in the UK established a relationship that ultimately led to a very successful voluntary vaccination programme. Bluetongue was eradicated from the UK in 2008. The same multidisciplinary team has recently been researching Schmallenberg virus and has been working with the National Farmers Union from the outset.



Dr Simon Carpenter shows NFU President, Peter Kendall and Vice President Adam Quinney midges in the Institute's insectary. Copyright: National Farmers Union.

Science communication

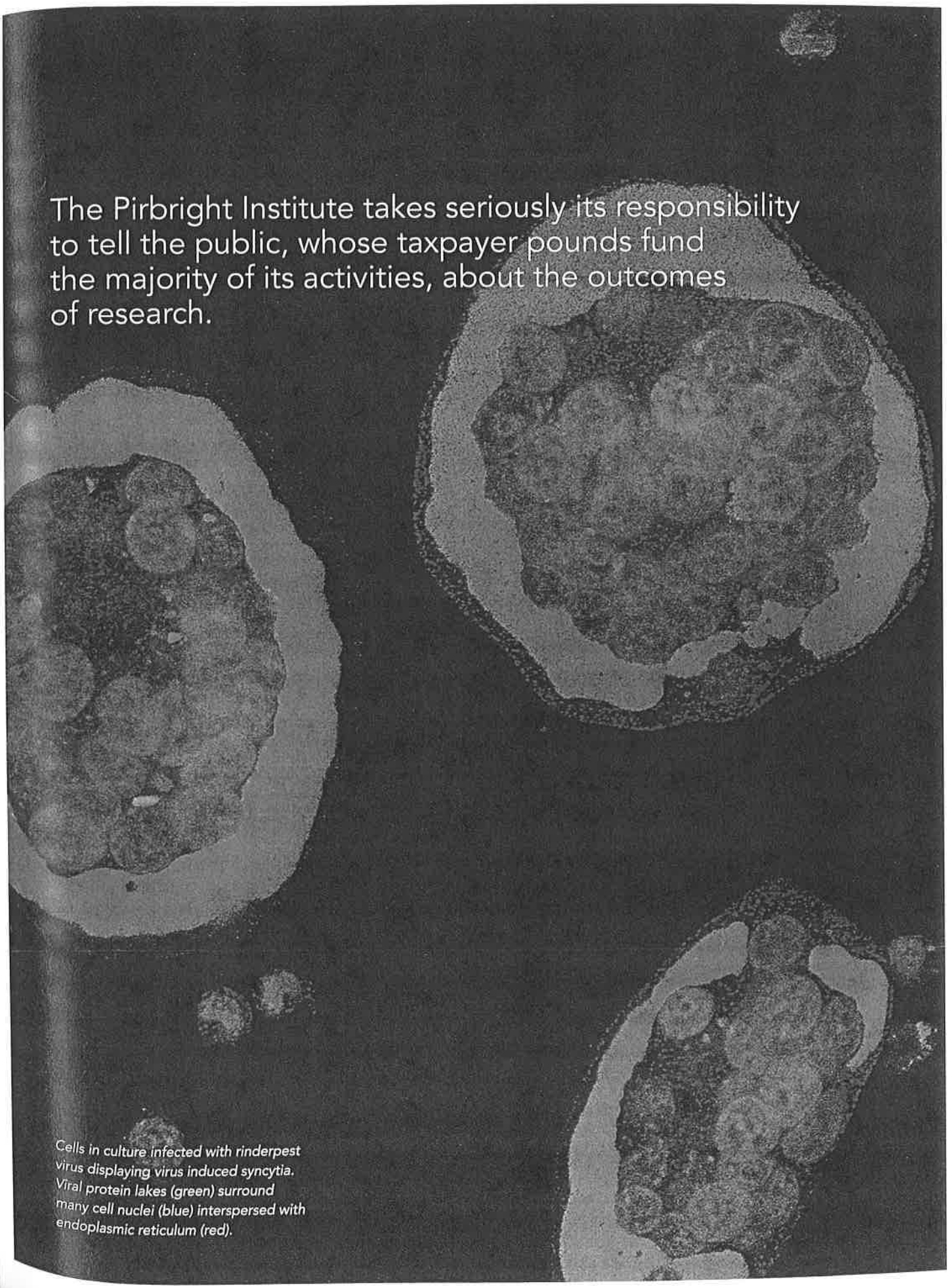
The Pirbright Institute has a responsibility to tell the public, whose taxpayer pounds fund the majority of its activities, about the outcomes of research. Staff do this through a variety of activities including media relations, public exhibitions and lectures, science festivals, newsletters and websites.

Inspiring the next generation

The Pirbright Institute has developed partnerships with a number of local schools around Compton and Pirbright. Staff take part in careers events and science demonstrations that are designed to inspire the next generation of practicing scientists.

Demonstrating a key laboratory technique like polymerase chain reaction where young people can have a hands on experience is one way to encourage students to choose biosciences for their future careers. A proportion of Institute staff are STEM Ambassadors and the Institute works with organisations including STEMNET and Surrey SATRO to engage with schools.

A scientist from the Institute demonstrates polymerase chain reaction to sixth form biology students.



The Pirbright Institute takes seriously its responsibility to tell the public, whose taxpayer pounds fund the majority of its activities, about the outcomes of research.

Cells in culture infected with rinderpest virus displaying virus induced syncytia. Viral protein lakes (green) surround many cell nuclei (blue) interspersed with endoplasmic reticulum (red).

Eradication of rinderpest
The first animal virus to be eliminated

The fight against viral diseases can seem never-ending, given the sheer complexity and evolutionary flexibility of viruses. Once in a while we do lift up our eyes a little higher; we allow ourselves to believe that there may one day be a final victory against one or other of our opponents. Just such an ambitious target was achieved in 2010 with the completion of work on the Global Rinderpest Eradication Programme (GREP), to which the Institute made major contributions.

Rinderpest was for centuries the most economically devastating of all cattle diseases. Caused by a virus closely related to measles virus, the disease was highly infectious and resulted in very high mortality (80%-90%). The economic impact was estimated at US$1 billion per year in Africa alone.

Various national and regional control programmes in Africa and Asia took place in the 1970s and 1980s, and in the early 1990s rinderpest became the focus of a worldwide initiative to eliminate the virus from the wild, co-ordinated by the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE). In October 2010 the completion of the programme was announced by the FAO, and the disease was declared officially eradicated in the following year - making it only the second viral disease (after smallpox in 1979) to be eradicated.

The Institute became the FAO's World Reference Laboratory (WRL) for rinderpest in 1994, and several scientists played important roles in rinderpest eradication. Not least was Walter Plowright (d.2010), who, whilst working in Kenya, developed the safe, effective, rinderpest vaccine that was used in most countries during the eradication campaign. Other UK scientists who played leading roles include Dr Bill Taylor, who worked at Pirbright from 1978 to 1986. Bill, and another UK veterinarian Dr Peter Roeder, acted as advisors and co-ordinators for the eradication work in many countries.

Work on rinderpest diagnosis at Pirbright, led by Professor John Anderson MBE, resulted in the development of a simple rinderpest antibody-detecting ELISA test that could be used in the laboratories of developing-world countries. These tests were used in surveillance for rinderpest infection, and for checking the effectiveness of vaccination campaigns. John, in association with Dr Martyn Jeggo at the International Atomic Energy Agency (IAEA) in Vienna, also set up the Lab Network of training and support systems to standardise diagnostic tests for rinderpest internationally – a process that was crucial in enabling the global acceptance of test results from so many countries.

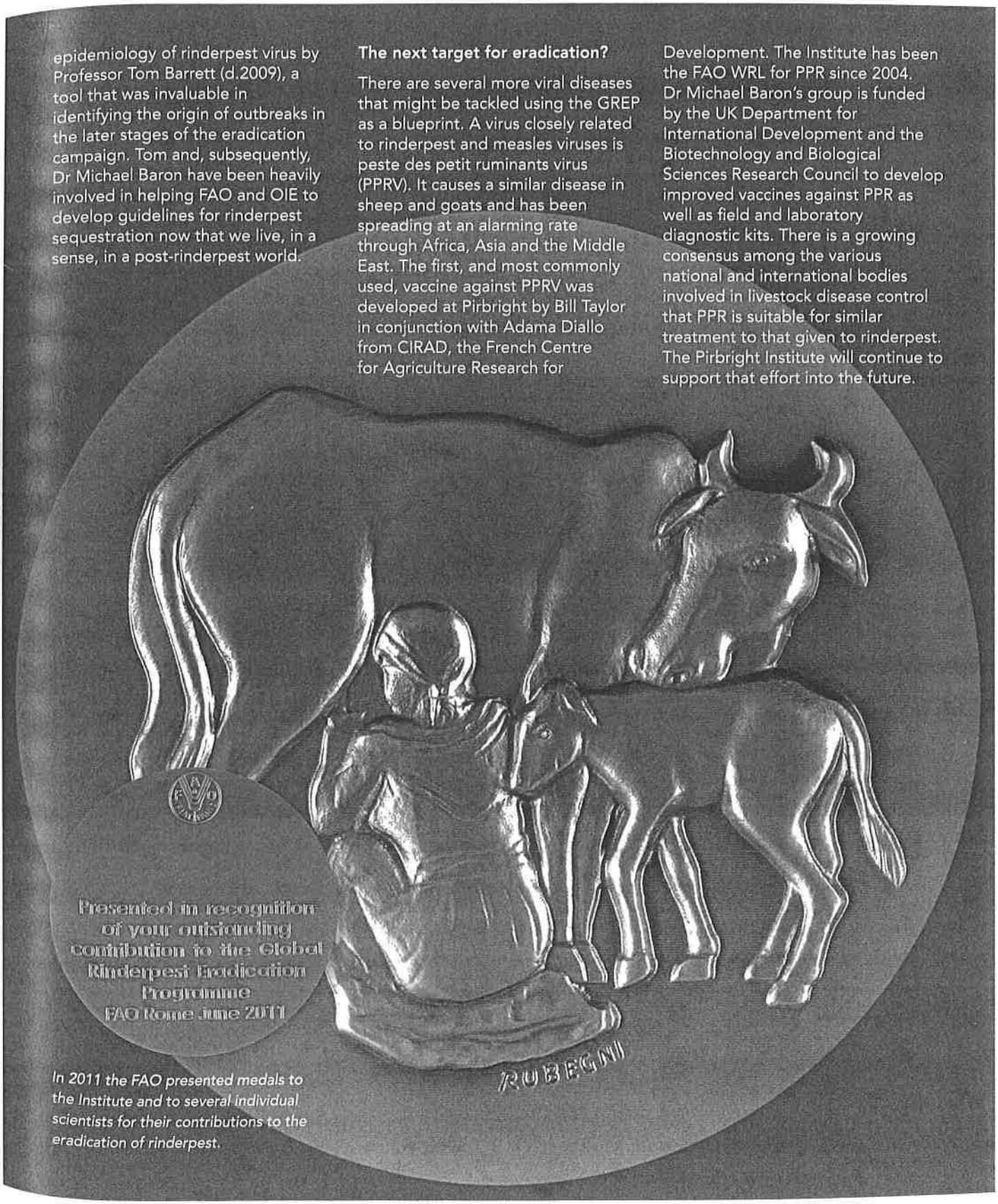
Subsequently, funded by the Department for International Development (DfID), John Anderson developed a simple, portable 'dip stick' test that could be used in the field to diagnose rinderpest, and led a number of training initiatives in the diagnosis and surveillance for rinderpest in the countries in which it was still endemic.

The complementarity of the research and diagnostic sides of the work at Pirbright was shown by the development of the molecular

epidemiology of rinderpest virus by Professor Tom Barrett (d.2009), a tool that was invaluable in identifying the origin of outbreaks in the later stages of the eradication campaign. Tom and, subsequently, Dr Michael Baron have been heavily involved in helping FAO and OIE to develop guidelines for rinderpest sequestration now that we live, in a sense, in a post-rinderpest world.

The next target for eradication?

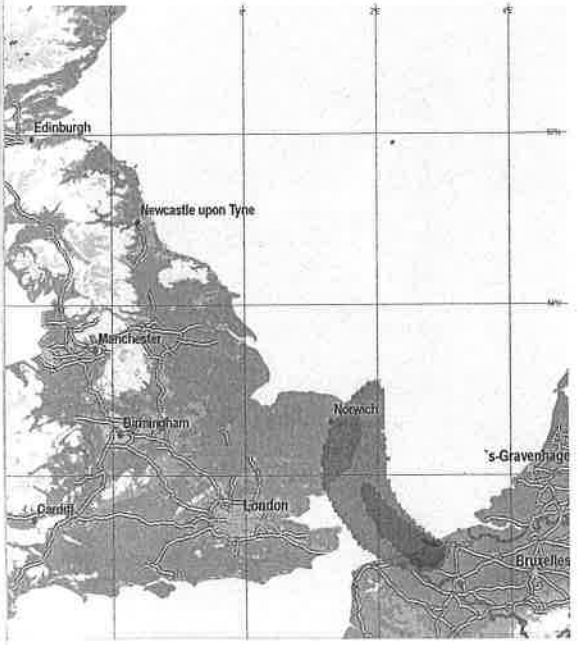
There are several more viral diseases that might be tackled using the GREP as a blueprint. A virus closely related to rinderpest and measles viruses is peste des petit ruminants virus (PPRV). It causes a similar disease in sheep and goats and has been spreading at an alarming rate through Africa, Asia and the Middle East. The first, and most commonly used, vaccine against PPRV was developed at Pirbright by Bill Taylor in conjunction with Adama Diallo from CIRAD, the French Centre for Agriculture Research for Development. The Institute has been the FAO WRL for PPR since 2004. Dr Michael Baron's group is funded by the UK Department for International Development and the Biotechnology and Biological Sciences Research Council to develop improved vaccines against PPR as well as field and laboratory diagnostic kits. There is a growing consensus among the various national and international bodies involved in livestock disease control that PPR is suitable for similar treatment to that given to rinderpest. The Pirbright Institute will continue to support that effort into the future.



In 2011 the FAO presented medals to the Institute and to several individual scientists for their contributions to the eradication of rinderpest.

Defeating bluetongue

The Institute played a pivotal role in the eradication of bluetongue virus following its first arrival in England in 2007, providing a unique array of experts for rapid and highly accurate diagnosis, and to advise Defra, the European Food Safety Authority, OIE (the World Organisation for Animal Health), British farmers, and pharmaceutical companies on a successful strategy for defeating the disease, based on virus surveillance and the development and targeted deployment of a new vaccine.



The Met Office's Numerical Atmospheric-dispersion Modelling Environment (NAME) helps to show how far, and in which direction, midges are likely to travel - blown by the prevailing wind.

When bluetongue virus (BTV) came to northern Europe for the first time in 2006, the Institute was fully prepared. There was a well established fundamental science programme on both the virus and the *Culicoides* biting midges that spread it. Based on this, researchers had developed rapid diagnostic tests and expert staff were on hand to put them into action.

The disease in Northern Europe was first observed in cattle in the Netherlands. Within 24 hours of receipt of samples at Pirbright scientists had not only confirmed that BTV was present but had also pinpointed that of the 24 types of BTV known at the time, it was type 8. Furthermore, gene sequencing indicated that sub-Saharan Africa was the origin of the virus.

Although BTV infects many ruminants, sheep are the most badly affected of livestock. The virus grows in the linings of blood vessels, the resultant damage leading to leakage of body fluids. This in turn leads to many clinical effects, including airways becoming full of liquid and froth, excessive salivation, swelling of the head, and occasional swelling of the tongue (which can turn blue, hence the name of the disease). Up to 30% of sheep that develop clinical signs die.

The Institute's research, funded by the Biotechnology and Biological Sciences Research Council and Defra, helped the UK anticipate the arrival of bluetongue, minimise its impact on food security and secure its eradication more rapidly than in any other affected country. Joint research with the Met Office predicted the introduction of bluetongue via windborne midges. Indeed, subsequent research indicates that this happened on the night of 4th/5th August 2007, precipitating the first outbreak of bluetongue in Britain, which is home to approximately 35 million sheep.

The Institute's midge surveillance network was incorporated into a risk assessment which resulted in approximately 85,000 livestock being moved without spreading the virus. Testing by the Institute's Defra-funded Bluetongue Reference Laboratory allowed international trade to

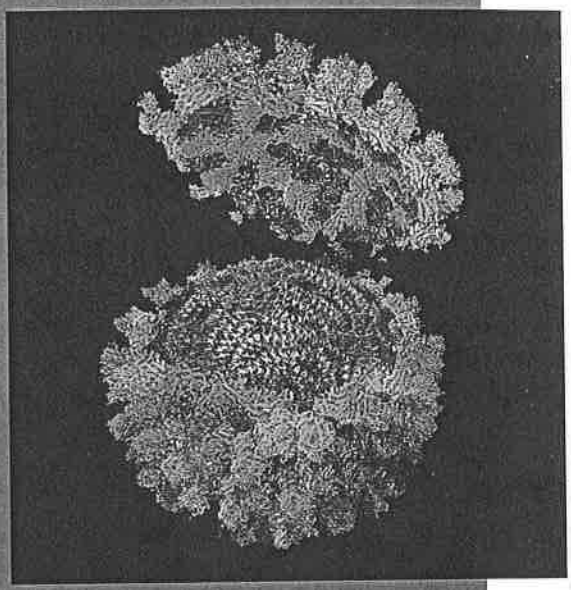
continue. Knowledge of bluetongue at Pirbright led the team to advise that the only feasible way of bringing the disease under control was to rapidly develop and deploy a BTV8 vaccine, as none that was suitable for European deployment existed at the time.

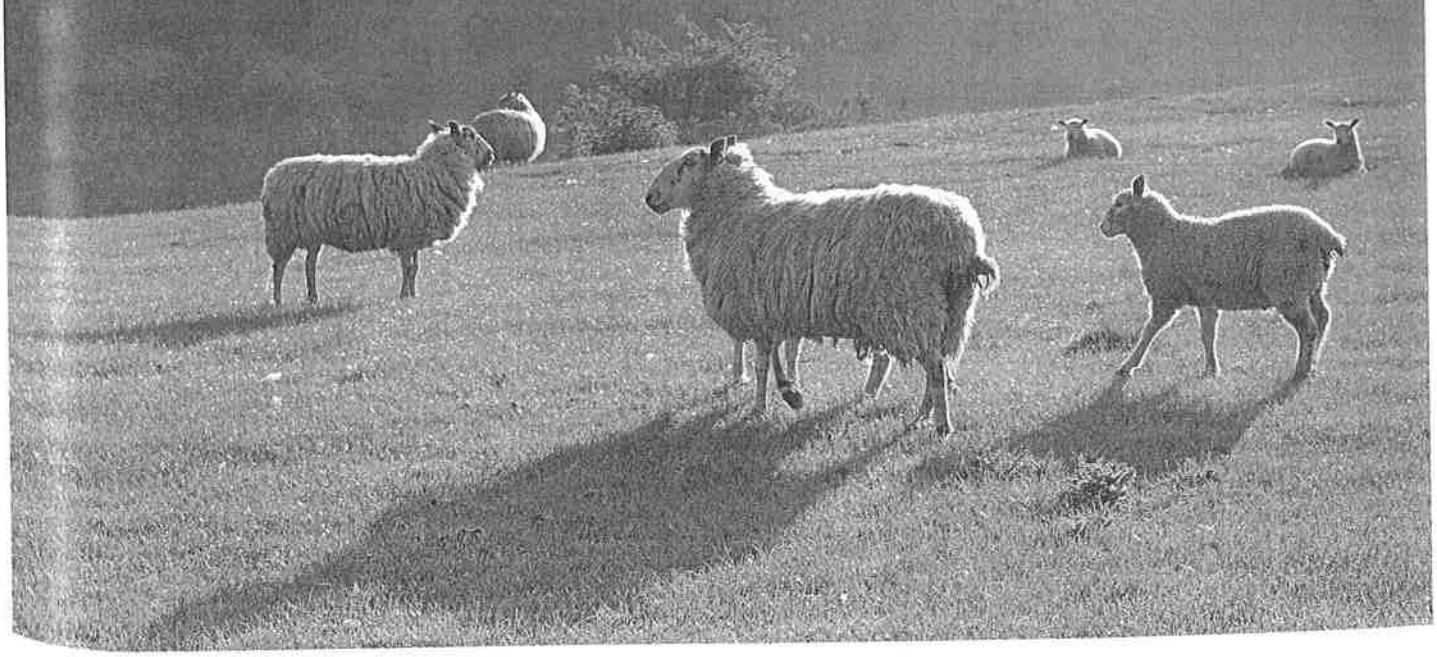
The Institute then took part in a very successful collaboration that involved farmers (with the National Farmers Union playing a prominent role), veterinarians, Defra and pharmaceutical companies which resulted in a very successful Joint campaign Against Bluetongue (JAB) campaign to persuade farmers and veterinarians to vaccinate.

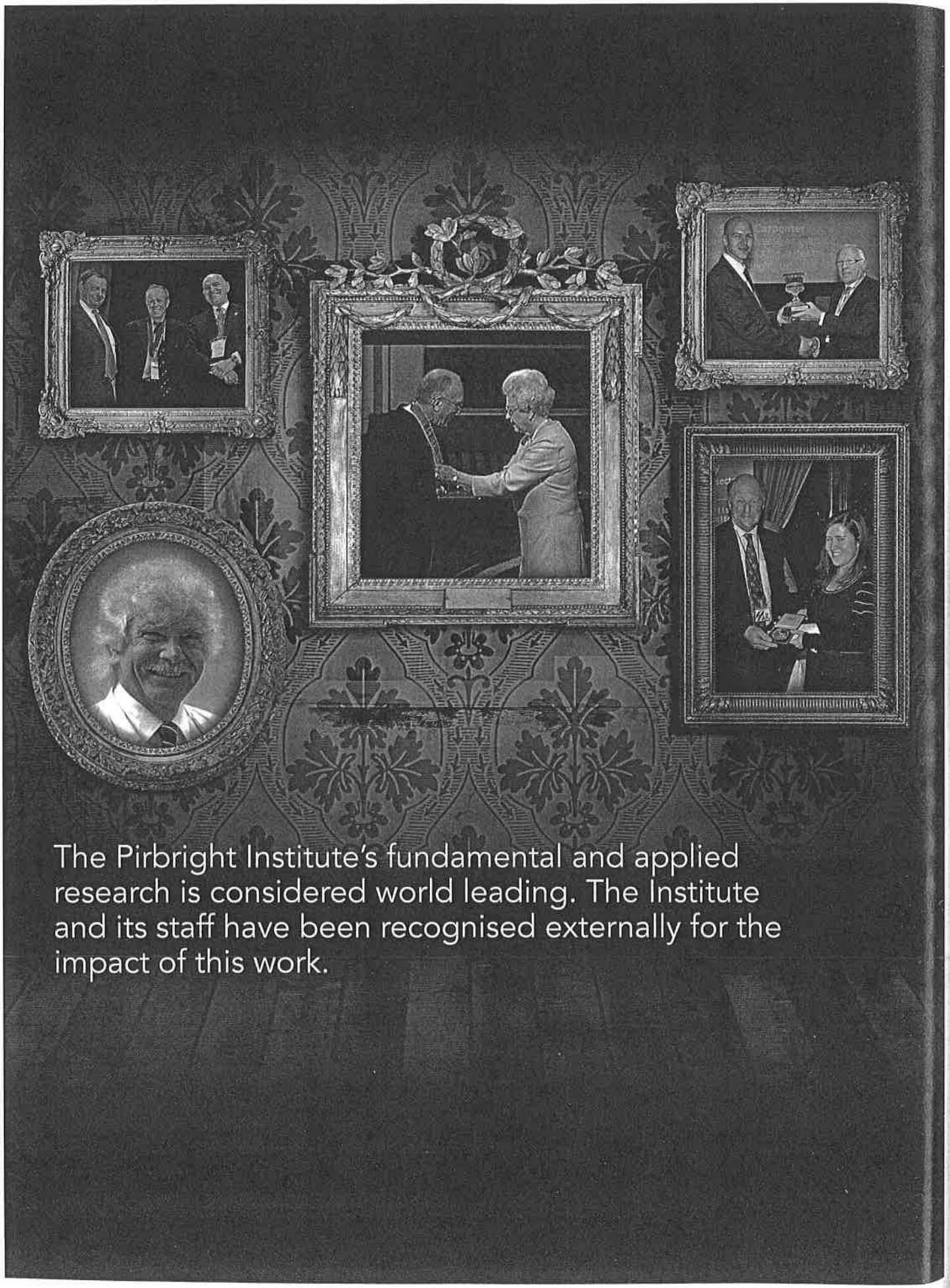
Pharmaceutical companies worked rapidly to produce an inactivated BTV8 vaccine, which became available in the UK in May 2008. As initial supplies were insufficient to distribute throughout the UK, The Institute used mathematical modelling to identify those counties most at risk of infection from virus that had survived (over-wintered) from 2007. Defra then used the predictions to make the first vaccine batches available where the risk of outbreaks was greatest. Subsequent batches were made available to the next most at-risk counties.

Thanks to a high take-up of vaccination by farmers, especially in southern counties of England and Wales, there was no incidence of bluetongue in British livestock in 2008, or since. This was despite the fact that some cattle imported from the Continent had bluetongue virus in them, sometimes in calves still within the womb. This was revealed by post-import testing at Pirbright, using gene-detection technology. Thankfully, the widespread application of BTV8 vaccine in England prevented the onward transmission of the imported virus to British stock. An independent assessment concluded that bluetongue research at the Institute saved £485 million and 10,000 jobs.

The recent arrival of BTV-1 as well as BTV-8 in France, and several other BTV types in Mediterranean countries (having arrived there from Africa, the Middle East and parts of Asia), underlines the dynamic nature of bluetongue epidemiology. Climate change and increasing international trade have contributed to the spread of bluetongue from its traditional hinterlands. There is every reason to believe that the spread of bluetongue to Northern Europe in recent years could happen again. The introduction of BTV by midges also demonstrated more generally that vector-borne viruses were more than just a potential threat. Indeed, Schmallenberg virus, which was first detected in Germany in late 2011 and which spread widely, including to the UK, is also at the time of writing thought to be insect transmitted.







The Pirbright Institute's fundamental and applied research is considered world leading. The Institute and its staff have been recognised externally for the impact of this work.

Awards and prizes

Institute staff and trustees have been honoured by Her Majesty the Queen and others for their contributions to science, innovation and technology transfer. A selection follows.

Professor Martin Shirley (Director of IAH from 2006 to 2010) receiving a CBE from Her Majesty The Queen, for Services to Science (centre). **Professors Philip Mellor** (bottom left) and **John Anderson** were awarded the OBE and MBE, respectively, for their service to science in the fields of bluetongue (Mellor) and foot-and-mouth disease diagnostics (Anderson).

Members of the Institute's trustee board have also received honours from Her Majesty The Queen: **Professor Joe Brownlie** (CBE), **Professor Quintin McKellar** (CBE), and **Tim Key** (MBE).

Professors John Anderson and **Tom Barrett** (d.2009) were awarded a medal by the UN Food and Agriculture Organisation for their contribution to the eradication of rinderpest, as was the Institute itself.

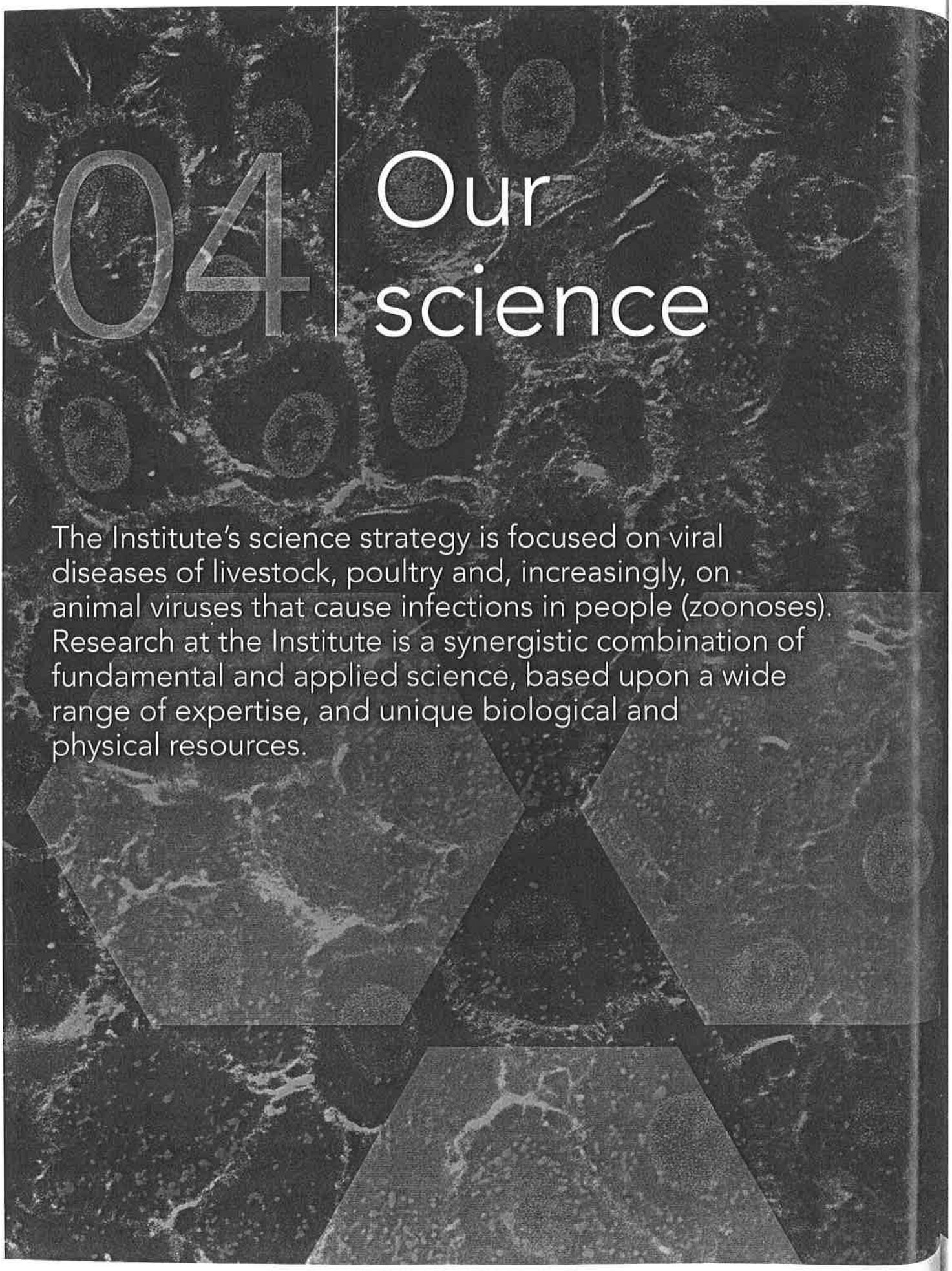
The World Organisation for Animal Health (OIE) recognised the foot-and-mouth disease research and development work of **Dr Nigel Ferris** MBE with the 2012 OIE Meritorious Award (top left image shows Dr Ferris (centre) receiving his award in Paris from **Dr Bernard Vallat** (left), Director General of OIE, and **Dr Carlos Correa Messuti** (right), President of the OIE).

The Institute, and **Nick Knowles**, individually, was awarded a medal in 2004 at the biannual Food and Agriculture Organisation meeting of the Executive Committee of the European Foot-and-Mouth Disease Commission, for outstanding contribution to monitoring the spread of FMD. Research students **Eleanor Cottam** and **Caroline Wright** were judged to have made the best presentations at the corresponding meetings in 2006 and 2010. Fellow research students **Teri Hodgson** and **Erica Bickerton** (bottom right) received the British Poultry Council's Scholarship Award, and research student **Francesca Culver** won the Poulter's Prize from the Worshipful Company of Poulters.

Dr Simon Carpenter (top right) received the first Rooker Award, for his research on the spread of viruses by arthropods from Lord Rooker during the International Veterinary Laboratory Agency Conference in 2009.

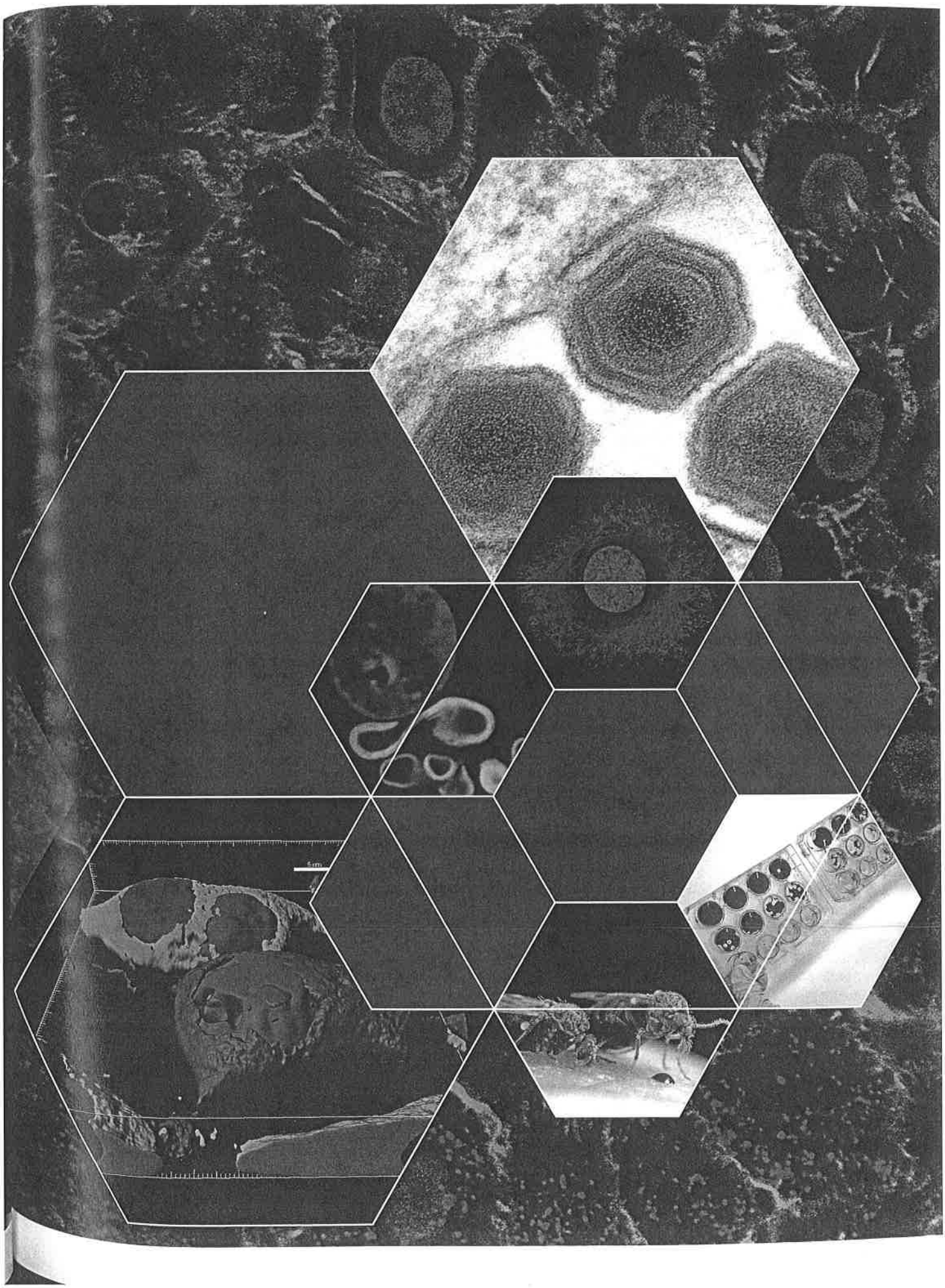
The Bart Rispens Award, for the best paper in the journal Avian Pathology in 2007 and 2008, was given to **Dr Sue Baigent** during the World Veterinary Poultry Association's Congress in Marrakech, 2009.

Dr Don King received a Technology Innovation Award from Genecom in 2009 for his work on the detection of foot-and-mouth disease virus.



04 Our science

The Institute's science strategy is focused on viral diseases of livestock, poultry and, increasingly, on animal viruses that cause infections in people (zoonoses). Research at the Institute is a synergistic combination of fundamental and applied science, based upon a wide range of expertise, and unique biological and physical resources.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Our science

We know from experience that the tools required for combating viral infections, including vaccines, diagnostics, and expert advice, are derived from sound, strategic fundamental science. Consequently the Institute's science strategy, which is delivered through three Institute Strategic Programmes, reflects this. Each programme comprises a platform of fundamental science projects that provide the new knowledge that is then translated, within the programmes, into applied science.

The three Institute Strategic Programmes are:

- **Avian Viral Diseases (AVD)**
- **Livestock Viral Diseases (LVD)**
- **Vector-borne Viral Diseases (VVD)**

These programmes are not mutually exclusive. The viral diseases that we study involve complex interactions between the virus, its host(s) and the environment. Consequently, in order to control them, we take a holistic approach, involving a broad range of sciences and technologies, many of which are common to all three research programmes.

Livestock and vector-borne disease research programmes encompass:

- African horse sickness.
- African swine fever.
- Bluetongue.
- Foot-and-mouth disease.
- Nairobi sheep disease.
- Peste des petits ruminants.
- Pestiviruses.
- Bovine and human respiratory syncytial viruses.
- Rotavirus.
- Swine influenza.
- Zoonotic arboviruses.

The avian programme, which will continue at Compton Laboratory until new poultry facilities have been completed at Pirbright, includes work on:

- Avian influenza.
- Infectious bronchitis.
- Infectious bursal disease.
- Marek's disease.

The infectious diseases situation is dynamic, due to various factors, including climate change, modern animal husbandry practices, livestock and human population increases, and the global nature of trade and travel. Consequently, the Institute continually reviews its research portfolio. For example, in response to the increasing threat of vector-borne diseases, the Institute is, at the time of writing, in the process of extending the VVD programme to include mosquitoes and a number of the viruses transmitted by them e.g. chikungunya virus.

Specialised fields at the Institute include bioimaging, bioinformatics, diagnostics, entomology, epidemiology, genetics, genomics, immunology, mathematical biology, molecular and structural biology, pathology, proteomics, vaccinology and virology.

The Pirbright Institute mission is research and surveillance to prevent virus diseases of livestock and virus transmission from animals to humans.

Avian Viral Diseases programme

Head of programme: **Professor Venugopal Nair**

Deputy Head of programme: **Professor Paul Britton**

Poultry production is an extremely efficient, relatively low carbon approach to producing the additional animal protein required for a rapidly expanding human population. However, infectious diseases remain a continuous threat to sustainable poultry production.

Vaccination against multiple avian viruses still remains the major means of protection against many of these diseases. However, the vaccination strategy is being threatened by the diversity and rapid evolution of the pathogens; microbial spread and evolution can be encouraged by the way that poultry are often kept in huge numbers and in close quarters. Currently, study of the following three viruses that are a threat to global food security is a major focus of the Institute's research:

- **Avian influenza**

Outbreaks caused by virulent strains of avian influenza virus (AIV) are relatively rare in developed countries but can be devastating when they do occur. Their threat is the greater because of the high prevalence of AIVs in South East Asia, their spread by movement of poultry and migrating wild birds, and their ability to produce new genetic forms, including those that can affect humans e.g. some of the H5N1 strains.

- **Infectious bronchitis virus**

Infectious bronchitis virus (IBV) is the major infectious cause of economic loss in the chicken industry in the UK. In addition to respiratory and kidney disease, which reduce weight gain and can kill young chickens, this virus can affect the reproductive organs, which also leads to poor egg production.

- **Marek's disease virus**

Marek's disease virus (MDV, a herpesvirus), which causes tumours in chickens and turkeys, is largely controlled by vaccines. However, there is increasing evidence of evolution of these viruses towards greater virulence – possibly driven by mass vaccination using conventional live attenuated vaccines. Although vaccination is still largely effective in protecting the birds against the disease, it has only marginal effects on preventing shedding of the virus, which is then a threat to any chickens or turkeys that have not been vaccinated.

The Institute's research, in partnership with vaccine producers, is aimed at developing new and more effective vaccines, and provides knowledge to the poultry industry to guide them in their use of vaccines and supplementary disease control measures.

Unique resource

The Institute has several lines of genetically defined specified pathogen-free chickens with differing susceptibility or resistance to a number of avian disease agents. These chicken lines, valuable in deciphering genetic determinants of resistance, are available to all researchers.

Scientific priorities are to understand:

- The attributes of the viruses that contribute to their ability to cause disease and to evolve.
- How virus and chicken cells interact to produce disease.
- How the avian immune system and genetic resistance factors contribute to protection against virus infections.

All of these priorities are with a view to exploiting knowledge for healthier poultry and sustainable production.

Research has additional impact arising from:

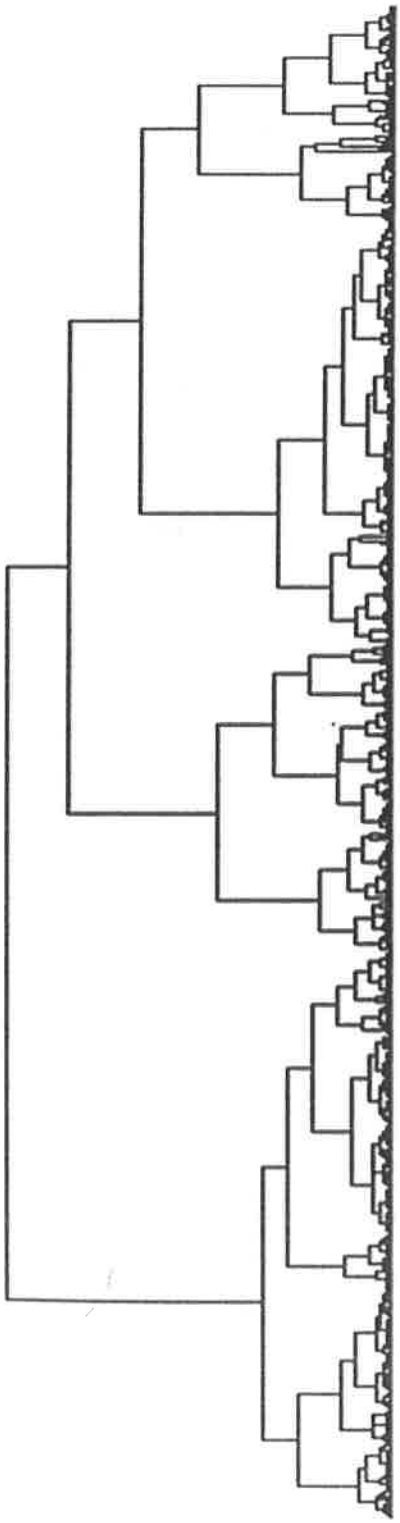
- Diagnostic and poultry health expertise.
- Development of diagnostic and investigative tools.
- Training of poultry industry professionals, diagnosticians and students through our annual Poultry Health Course.
- Chairing of the UK Poultry Disease Group, comprising many stakeholders in poultry health.

Recent and current supporters include:

BBSRC, British Egg Industry Council, British Poultry Council, Defra, European Commission, MSD, Merial Animal Health, Pfizer Animal Health, VH group, Aviagen.

More information: www.pirbright.ac.uk/ISPG/AVD.aspx

Avian Viral Diseases programme
Recent achievements



Tools and technologies

- Developed a recombinant infectious bronchitis virus that can be used safely to vaccinate birds before hatching (*in ovo*). As all the infectious bronchitis vaccines used hitherto are lethal to the embryos, this is a major finding that could revolutionise infectious bronchitis vaccination.
- Patented the technology of herpesvirus-mediated gene silencing using RNA interference, with significant potential for viral delivery of gene silencing cassettes.
- Patented the technology for growing infectious bronchitis vaccines in cell culture, a procedure that could revolutionise the vaccine manufacturing field.

Scientific achievements

- Demonstrated that Marek's disease virus (MDV)-encoded oncoprotein MEQ is the major determinant of oncogenicity of the virus.
- Contributed to the discovery of a number of novel microRNAs encoded by MDV, some of which were subsequently shown to be essential for the oncogenicity of the virus.
- Demonstrated the allosteric effects of the two IRES structures in a bicistronic MDV transcript, a feature of major significance in virus-host interactions and translational control.
- Demonstrated the potential for generating molecularly-defined vaccines against MDV by mutagenesis of the oncogenic determinants of the virus.
- Demonstrated differences in susceptibility to the same avian influenza virus between avian species such as turkeys and chickens.
- Demonstrated that virus-encoded accessory genes are not required for replication of infectious bronchitis virus (IBV) *in vitro*, a major finding in the field of coronavirus genetics.
- Showed that a sequence within the S2 subunit of the spike glycoprotein is a determinant for IBV growth in cell cultures, a major step towards the development of cell culture-derived IB vaccines.
- Determined the cell type-specific miRNA expression signature of avian cell types including B-lymphocytes, CD4+ T-cells and macrophages and embryonic stem cell lines, a finding of importance in understanding cell type-specific expression profiles.
- Developed an elegant system of proliferating chicken B-lymphocytes in vitro using recombinant chicken CD40 ligand (CD40L), a system that can aid in studying B-cell biology.

Avian Viral Diseases programme
People and key scientific questions

The AVD programme comprises three overlapping areas of research which are undergoing expansion and involve collaboration with the Roslin Institute in Edinburgh.

Research leaders within or contributing to the AVD programme	
Professor Venugopal Nair	Avian Oncogenic Viruses group, and Head of the AVD programme
Professor Paul Britton	Avian Endemic Virus group
Dr Colin Butter	Principle Investigator, Avian Immunology
Dr Nick Ciccone	Institute Fellow in Avian viral immunology
Dr Mark Fife	Genetics and Genomics group
Dr Munir Iqbal	Principle Investigator, Avian Influenza
Dr Holly Shelton	Institute Fellow in Influenza Viruses

Key scientific questions

What are the viral attributes that contribute to the virus biology, disease and diversity?

Objectives include:

- Understanding the functions of a diverse set of genes encoded by avian viruses with respect to biology, transmission and pathogenesis.
- Analysing the diversity of viral genes in relation to transmission dynamics, host range and evolution of viruses.
- Determining the viral genes associated with attenuation of viral phenotype for the rational development of molecularly-defined vaccines and diagnostic agents.

What are the molecular determinants of virus-host interactions that affect pathogenicity?

Objectives include:

- Analysing the dynamics of gene expression and protein interaction during infection by different avian viruses for understanding pathogenesis.
- Identifying the determinants associated with host range restriction, genetic resistance and diversity in viral infections.
- Determining the role of epigenetic mechanisms in virus-host interactions and immune responses to viral pathogens.

What are the distinct features of the avian immune system that enable it to respond to vaccines and combat viral infections?

Objectives include:

- Developing immunological tools, reagents and assays to analyse avian immune responses to viruses and vaccines.
- Analysing the role of innate immune responses, co-stimulatory molecules and B-cell repertoire in response to viral infections or vaccination.
- Developing new generations of vaccines against avian viruses using novel approaches.

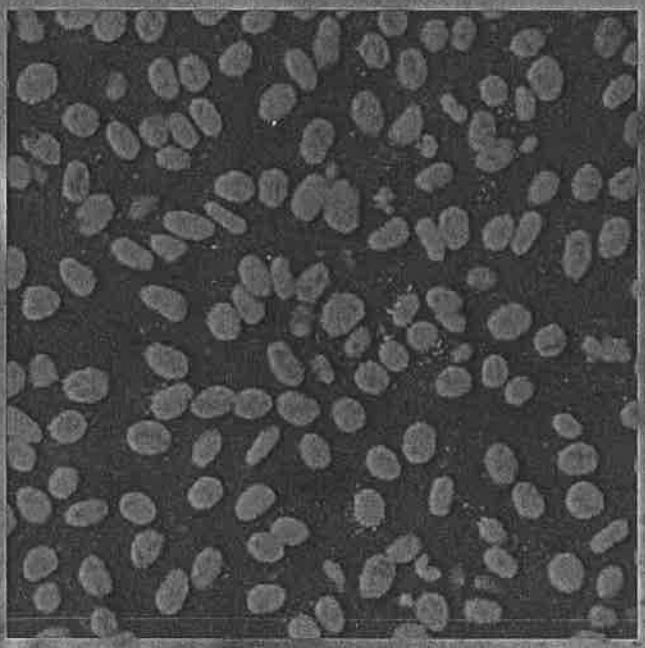
Case study
Producing vaccines against infectious bronchitis virus in cell culture

Infectious bronchitis virus (IBV) causes disease, welfare problems and major economic losses to the worldwide poultry industry and is a potential threat to food security. IBV vaccines are currently produced in embryonated chicken eggs. This is a cumbersome and expensive process, and is subject to the availability of embryonated eggs, which can be variable. Being able to produce IBV vaccines in cell culture would represent significant progress.

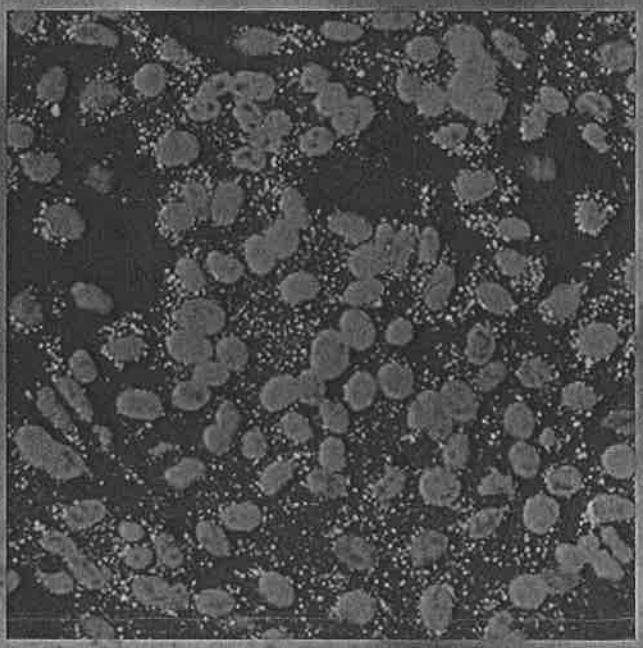
Viruses possess certain factors that allow them to infect specific cells and produce new copies of themselves. The ability of these factors to recognise different cell types widens the range of cells in which viruses can replicate, a feature known as cell tropism. Researchers at the Institute have been able to modify the cell tropism of IBV to develop a new approach to vaccine production.

Recent research in Professor Paul Britton's group, carried out by Dr Erica Bickerton, has shown that a short section of a surface protein of the Beaudette-R (Beau-R) strain of IBV enables replication of the virus in cell culture, in particular, in Vero cells; these cells are also used for the production of some human vaccines. This offers the prospect of being able to produce recombinant vaccinal strains of IBV in Vero cell culture rather than in chicken eggs.

Professor Britton's team is now looking at the potential for producing IBV vaccines against different strains of IBV that can be produced in cell culture.



IBV unable to grow on Vero Cells



Modified IBV that can grow on Vero Cells (virus shown in green)

Case study
Direct role for microRNAs in Marek's disease cancers

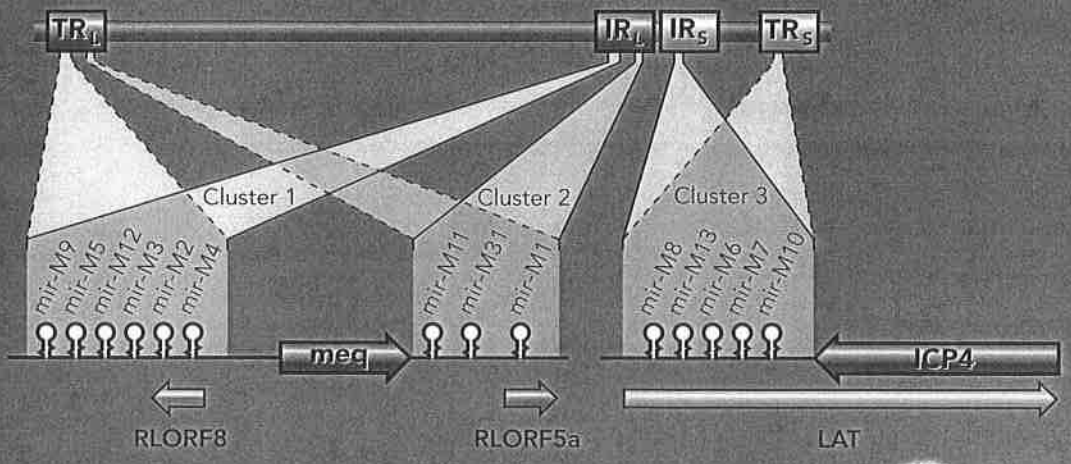
Marek's disease (MD) is caused by a type of contagious herpesvirus that induces tumours in chickens. It is a major cause of economic loss to the poultry industry. Although MD is controlled by the widespread use of vaccines, in the last 40 years emergence of viruses of increasing virulence is threatening the vaccination strategy.

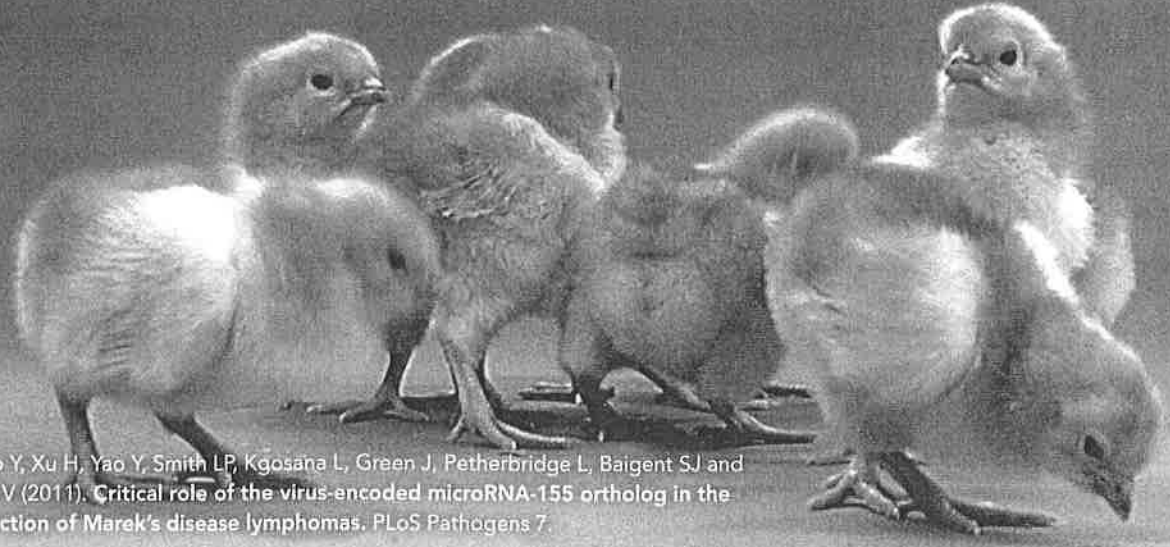
MicroRNAs (miRNAs) are short strands of genetic material 22-24 nucleotides long. They do not code for proteins but instead act to regulate the expression of multiple genes. Professor Venugopal Nair's group have shown that deletion of one part of the MD virus genome that produces miRNAs abolishes the ability of the virus to cause cancers.

This is the first direct evidence on the *in vivo* function of miRNAs in virus-induced cancer in their natural hosts.

Interestingly, one of the miRNAs associated with the induction of cancer in the chicken is closely related to at least two of the cancer-inducing miRNAs in humans, one expressed by human cells and the other by a human viral pathogen. Thus the study has wider implications in human cancer.

This study also led to a new approach for developing vaccines against MD. When chickens were vaccinated with the virus that was unable to cause cancer, because of the missing miRNAs, they developed protective immunity against challenge with oncogenic MDV to the same extent as chickens vaccinated with commercial MDV vaccine. Hence miRNA-deletion mutants of MDV have potential to be developed as novel molecularly-defined attenuated MDV vaccines.





Zhao Y, Xu H, Yao Y, Smith LP, Kgosana L, Green J, Petherbridge L, Baigent SJ and Nair V (2011). **Critical role of the virus-encoded microRNA-155 ortholog in the induction of Marek's disease lymphomas.** PLoS Pathogens 7.

Case study
A new approach to avian flu vaccines

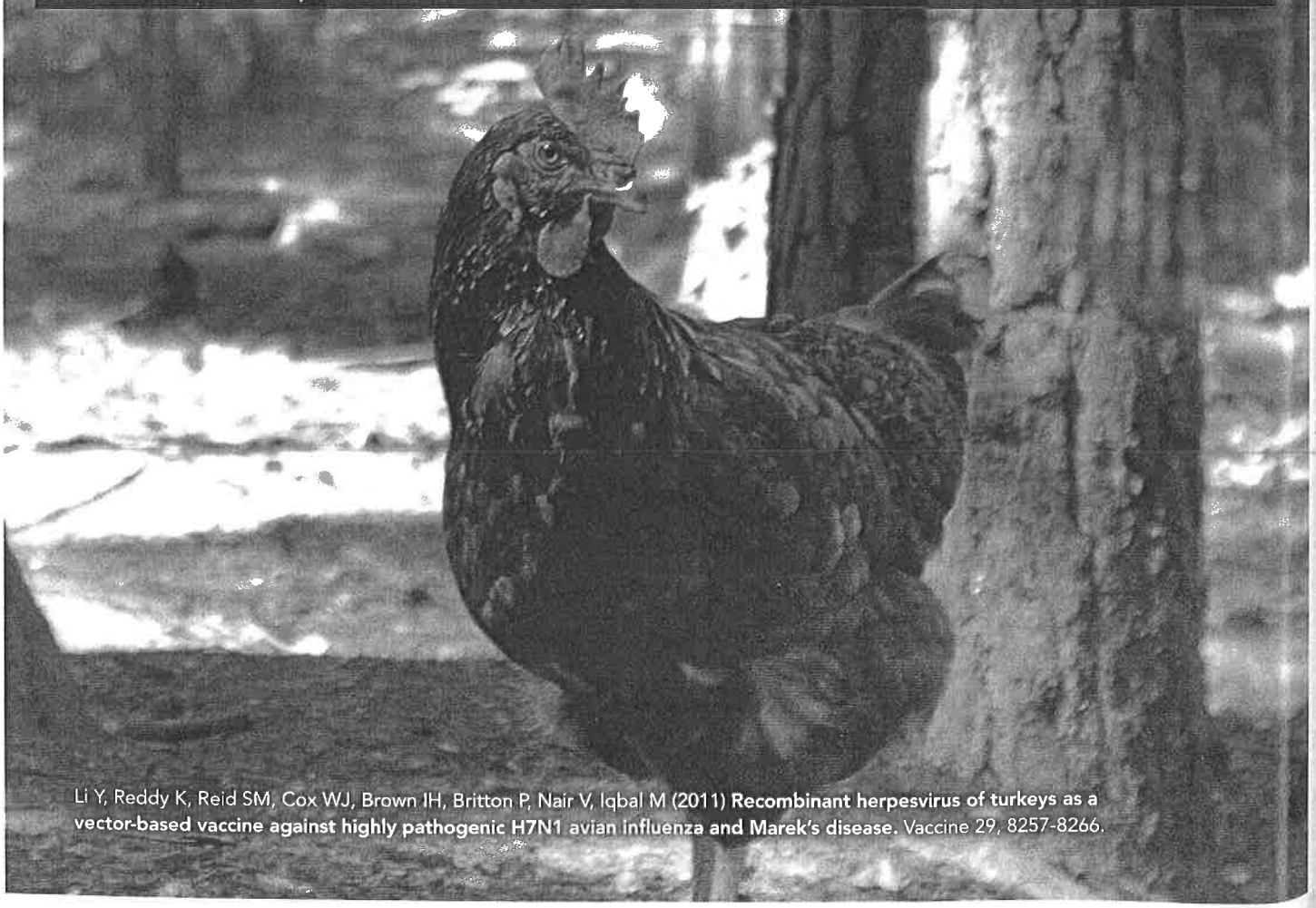
Highly pathogenic avian influenza viruses have increased in importance in recent years, in both poultry and human populations. Although effective vaccines are available, a new approach to vaccination that can offer safer and longer term protection would be of tremendous value. Recombinant herpesvirus of turkeys (HVT) can be used as a vector-based vaccine against highly pathogenic avian influenza virus (AIV) as well as Marek's disease virus (MDV).

HVT is a naturally occurring strain related to MDV that does not cause disease. It has been used extensively as a vaccine against MDV for several decades. It is possible to use this virus to introduce proteins from AIV and in particular haemagglutinin (HA), which is very effective to induce immunity. This method also removes the possibility of reversion of AIV to a form that that can cause disease, as can happen with traditional vaccines.

Using a bacterial artificial chromosome (BAC) vector for HVT developed in Professor Venugopal Nair's laboratory, Dr Munir Iqbal's group has constructed a recombinant HVT expressing the HA protein of a highly pathogenic H7N1 AIV.

Chicks were vaccinated with the recombinant HVT (HVT-H7HA) and then exposed to either H7N1 AIV or MDV. Five of the seven chickens resisted H7N1, compared to none that had been vaccinated with HVT alone. The lack of protection in two of the chickens vaccinated with HVT-H7HA indicated that successful vaccination against AIV is dose-dependent.
All the chickens vaccinated with HVT-H7HA were protected against very virulent MDV.

This recombinant vectored approach is promising for the production of vaccines against AIV that – in contrast to the use of conventional AIV vaccines - can be applied *in ovo* or in day-old chicks, give lifelong immunity, will not revert to virulence, and allow differentiation of AIV-infected from vaccinated chickens, as well as simultaneous vaccinatination against MDV.



Li Y, Reddy K, Reid SM, Cox WJ, Brown IH, Britton P, Nair V, Iqbal M (2011) **Recombinant herpesvirus of turkeys as a vector-based vaccine against highly pathogenic H7N1 avian influenza and Marek's disease.** Vaccine 29, 8257-8266.