Economic and Social Impact of Science at the Institute for Animal Health

BACKGROUND

The Institute for Animal Health (IAH) has the mission *'to deliver high quality fundamental, strategic and applied science into infectious animal diseases that currently affect or threaten the UK and, from that knowledge, to advance veterinary and medical science, enhance the sustainability of livestock farming, improve animal welfare, safeguard the supply and safety of food, and protect public health and the environment.*

The core activities of IAH relate not to growing the livestock market *per se*, but to protecting current activity levels. We do this by working to prevent or assist in controlling outbreaks of disease and qualitatively improving animal health. This is part of the Governments intervention in animal health where the market on its own cannot deliver all objectives. IAH is the 'voice at many tables'.

Work at the Pirbright Laboratory is especially relevant to the needs of Government as it houses Reference Laboratories that focus on surveillance of viruses that are not endemic within, but pose a threat to, the UK. Such viruses include foot and mouth disease virus (FMDV) and bluetongue virus (BTV). Thus significant activity within IAH is to help the UK to monitor current and future threats from exotic viruses, to inform national and international government and non-governmental agencies and to lead with efforts to best control exotic viruses if and when they arrive in the UK.

IAH targets much research towards the fundamental and strategic ends of the science spectrum. Once an idea is developed to a near market proposition, licences are obtained by the private

sector to allow commercial development. Thus, the main financial benefits of commercialisation of vaccines, for example, are competitively reaped by the private sector rather than accruing directly to IAH.

In 2005 the market value of UK meat, milk and eggs was ~£8 billion from more than 150,000 farm businesses producing 10, 35, 6 and 800 million cattle, sheep, pigs and poultry, respectively. The overall costs of animal diseases to the UK over the past 15 years may have exceeded £15 billion through impact on production losses and implementation of control strategies. Outbreaks of diseases such as FMD have huge financial and societal impacts but fortunately they occur infrequently. Under ideal circumstances, IAH research on exotic viruses provides an insurance to the UK and impacts overtly only at infrequent intervals.

CONTROLLING DISEASES OF LIVESTOCK

Global eradication of rinderpest virus, the cause of cattle plague

"Never before in the memory of man, or by the voice of tradition, have the cattle died in such numbers; never before has the wild game suffered". Anon, circa 1890.

Rinderpest (cattle plague) is an infectious viral disease that spread across the African continent as a pandemic in the late 1880s killing 80-90% of cattle, buffalo, eland, giraffe, wildebeest, kudu and various species of antelope and in Kenya, the Masai people suffered starvation and their numbers were severely reduced.

A campaign to eradicate rinderpest (the Global Rinderpest Eradication Programme, GREP) was launched formally in 1994 by the Food and Agricultural Organisation (FAO) using IAH to develop surveillance technologies; training and technology transfer and provision of advice to policy groups. IAH scientists introduced serological and diagnostic tests into Africa, the Middle East and Asia through an IAE-funded Rinderpest Laboratory Network. These kits were supplied worldwide through an IAH commercial collaboration with Biological Diagnostic Supplies Ltd. The IAH laboratory at Pirbright was designated as the FAO World Reference Laboratory for Rinderpest in 1994 to provide a world-wide diagnostic service and was later designated as the World Reference Laboratory for Morbilliviruses in 2002. Through its work, IAH identified the last rinderpest-positive sample from the Kenya border with Somalia in 2001 and sero-surveillance continues to provide final confirmation of global eradication. If the GREP proceeds through the final stages as expected, by around 2010 rinderpest will become the first veterinary virus disease to have been eradicated globally, and only the second disease after smallpox.

Elimination of rinderpest through large scale vaccination and surveillance campaigns stands as one of the greatest successes for veterinary science, and can be regarded as producing a net economic benefit to the African region alone of at least $1 billion per annum.

Foot and mouth disease

The outbreaks of foot-and-mouth disease (FMD) in Europe in 2001 identified the vulnerability of the intensive agricultural industries in Europe and North America to the economic consequences of the introduction of this disease. Economic losses due to FMD arise from the direct effects of the disease on production (primarily dairy and pig production systems), costs of disease control, restriction of trade and indirect losses such as a reduction in tourism income.

A ‘market failure’ exists in relation to threats to UK livestock from exotic diseases. The livestock sector, by itself, has not and cannot be expected to deliver outcomes to some activities, and this provides a rationale for Government intervention and hence IAH support - particularly for outcomes which are qualitative in nature and cannot be readily quantified into currency.

An excellent example of IAH addressing a market failure is the statutory surveillance and diagnostic activities at the Pirbright Laboratory. International data are time-consuming to collect and difficult to analyse but they are made available across a range of final industrial users to promote public benefits. Were a private company to invest the same time and effort in production of this output, they would have no incentive to share their “intellectual property” as it would reduce their potential incomes – this could lead to replication of effort and thus sub-optimal resource use at the national or international level. Whilst specific figures on the economic savings arising from IAH work on FMD are not available, the huge financial costs of FMD outbreaks (the total loss to the UK economy through the outbreak in 2001 is estimated at ~£7 billion, equivalent to ~ 0.2% of GDP) provide an effective commentary on the importance of surveillance activities and improving UK responsiveness and preparedness. The FMD work at IAH thus provides the UK with a contingency for laboratory diagnosis and expertise, as well as a mix of international surveillance, and applied and basic research that informs both national and international disease control measures (e.g. vaccine selection) and will provide improved tools for future control and eradication of the disease (e.g. new vaccines, diagnostics, and antivirals.

Since the FMD outbreak in 2001, IAH has further developed tests. and reagents for faster diagnosis and surveillance of disease including:

- A rapid on-farm test for FMD, which became commercially available in May 2008.
- Validated, high throughput, rapid, laboratory-based real time RT-PCR for FMDV detection in a variety of sample types with capability to devolve testing to regional laboratory to bring tests nearer to animals and reduce delays in sample transit to labs.
- New saliva test (for FMDV-specific IgA antibodies) developed and partially validated to identify persistently infected cattle regardless of vaccination status.
- International network of FMD Reference Laboratories established to improve information on the threats posed by FMDV circulating worldwide.
- Full genome sequencing of FMD viruses shown to be able to identify the order in which farms become infected within a complex outbreak.
- Enhanced capability for the prediction of airborne disease spread.
- A key approach to controlling diseases by vaccination is the critical ability to differentiate between animals that have been actively vaccinated and those infected naturally.
  IAH work to distinguish FMD-vaccinated animals from infected animals opens the way for a vaccinate-to-live policy that has the potential to save the UK millions of pounds in compensation, lost trade and tourism. A mass slaughter policy is now regarded as being unacceptable politically.

In 2007, the outbreak in Surrey was quickly contained with minimal numbers of animals slaughtered. Working with IAH scientists, Defra acted swiftly and efficiently to impose movement restrictions that limited economic losses to between £100-200 million. As a result of research and development within IAH since the UK outbreak of FMD in 2001, IAH scientists were able to confirm infection in suspected animals within one hour of receipt of samples into the Pirbright Laboratory, with results from two further confirmatory tests usually available to Defra within about four hours. [more….] Genetic fingerprinting analyses of virus from each Infected Premises speedily and unequivocally confirmed that all viruses examined were related very closely and that it was possible to ‘track’ the movement of the virus across Surrey. RT-

PCR tests developed at Pirbright proved especially useful because infected animals were identified in the absence of early clinical signs.

Transmissible spongiform encephalopathies (TSEs) and the national scrapie plan (NSP)

The Neuropathogenesis Unit (NPU) based in Edinburgh is a vital part of the UK effort to understand the biology of transmissible spongiform encephalopathies (TSEs) (the cost to the UK of BSE in 1986/7 is estimated to be £2.3 billion) and its scientists are a key component of the National Scrapie Plan (NSP). Until April 2007, the NPU was part of the IAH, but is now within the Roslin Institute/Easter Bush Research Consortium, Edinburgh.

The aim of the NSP is to increase the level of resistance to TSEs in the national sheep flock with the eventual eradication of all TSEs. As a consequence, the theoretical risk to human health arising from the possible presence of bovine spongiform encephalopathy (BSE) in sheep will also be removed. Indeed, scientists at the NPU were the first to describe the sheep, goat and cattle PrP gene and discovered the association between sheep PrP polymorphisms and scrapie. This was a significant contribution to the both the NSP and to EU regulations for scrapie eradication programmes.

The NSP has been developed jointly by the Agriculture and Rural Affairs Departments for Great Britain as part of the Rural Development Plans for England and Wales and the Agriculture Strategy for Scotland and takes a long-term perspective with policies based on the best scientific advice available and using a precautionary principle to minimise the theoretical risk to human health. Scrapie was made a notifiable disease in 1993. By law, every animal suspected of having scrapie must be reported to the local Defra animal health office. Since 1998, sheep with suspected scrapie have been subject to compulsory slaughter and compensation is paid by government to the farmer.

Targeting the genotyping programme at pure-bred flocks should, within 10 years, increase the prevalence of the most scrapie resistant allele to 80% in the ram population and to 85% in the slaughter population but it is likely to be several years before a significant impact is made on the incidence of scrapie.

IAH research at the NPU has led to licences with the Laboratory of the Government Chemist and Orchid Biosciences Europe Limited (Cellmark) for a patented invention for determining the susceptibility of sheep to scrapie and this technology is being used as part of the science underpinning the NSP.

With the discovery of ‘atypical scrapie’, IAH scientists were quickly approached by Defra to undertake studies to establish the potential for the presence of this “new” TSE in the British flock and the work of the NSP has been further reassessed with IAH scientists providing assessments of the variation in risk for sheep of differing genotypes.

A vaccine against Marek’s disease virus helped to transform the modern poultry industry

Marek's disease virus is a highly contagious herpesvirus of chickens and it induces rapid-onset tumours involving lymphoid cells. The disease has many manifestations, including tumours in the heart, ovary, tests, muscles and lungs. Marek’s disease alone was responsible for enormous losses in the poultry industry, with mortality rates up to up to 80%.

Research at the forerunner of IAH in identifying the causative agent and methods of control led directly to the first vaccines against the disease in the 1970's. This vaccine helped to transform dramatically the developing poultry industry into the highly effective and efficient food-producing industry of today. Today, around 40 billion chickens are reared annually worldwide and more than 800 million birds are kept for their meat in the UK. The economic impact of control of Marek's disease by vaccination and the contribution of the UK government-funded research is truly colossal and can be measured in £ billions as it helped facilitate growth of a global industry.

Marek's disease still has a worldwide distribution as the causative virus has changed genetically with time and the emergence of highly virulent strains in the face of vaccines remains a problem to the poultry industry. IAH now has 'Reference Laboratory' status for its work on Marek's disease virus and remains a key organisation at the forefront of research and is currently helping to provide a new generation of vaccines based on manipulation of the viral genome.

A unique vaccine for controlling coccidial parasites of poultry

For several decades, the poultry industry worldwide had an almost total reliance on chemical drugs (given in-feed) to control infections by intestinal, coccidial, parasites. Around 25 years ago IAH looked beyond the immediate needs and interests of the industry and initiated work to develop an alternative control strategy that would be based on a safe vaccine.

In 1989 the first live attenuated vaccine, *Paracox*-8, was developed from IAH research with additional financial support from the British Technology Group and Schering-Plough Animal Health. The *Paracox* vaccine provided the poultry industry with the first non-chemical method to safely protect valuable breeding flocks against coccidiosis and it is now used throughout the European Union (and beyond) to protect virtually all the highly valuable chickens kept for breeding purposes. Moreover, the vaccine is regularly exported to more than 30 countries globally and has created over 30 new jobs in the UK for its manufacture.

Such has been the worldwide success of *Paracox*-8 that a new product, called *Paracox*-5, was launched in 2000 for the control of coccidiosis in birds kept for their meat. In total, the two products are now used to protect ~1 billion chickens per annum. The economic benefits generated by the Paracox vaccines to date are hard to calculate, but could be around ~£50+ million given that the total cost of coccidial infections to the UK poultry industry remain at ~£40 million per annum. The IAH's success at basic research and then translating it into such a useful tool for improved health in the poultrty industry was acknowledged in the "Biosciences Biomillions" event.

By providing a way forward for the production of chickens in the complete absence of drugs, the availability of *Paracox* vaccines stimulated debate within the EU on the complete elimination of dietary anticoccidial drugs. Legislation is now anticipated to ban the use of these drugs in the feedstuffs of poultry in 2012.

A vaccine against bovine respiratory syncytial virus (BRSV)

BRSV is the most important cause of respiratory disease in young calves in Europe and North America. It is estimated that in the U.K. up to 1.9 million cattle are affected by respiratory disease each year, at a cost to the cattle industry of £54 million per annum. Furthermore, approximately 160,000 calves, which have a potential market value of £100 million, die

annually as a result of pneumonia and related illnesses in the U.K. Vaccination against BRSV provides a sustainable method of disease control and *Torvac RSV* was developed at the IAH with additional financial support from the British Technology Group and produced by Novartis Animal Vaccines Ltd.

Preparing the UK in readiness for a new disease of sheep and cattle: bluetongue

During 2007, and for the first time ever, disease caused by bluetongue virus became a problem in sheep and cattle of parts of the UK.

IAH scientists enabled UK government departments to prepare for the new incursion by critically identifying climate change as being linked to the spread of BTV in Europe, by confirming the UK midge as a potential carrier of the virus, and, from meterological studies by Dr John Gloster, being able to identify exactly when infected midges were blown across the English Channel to establish the infections in East Anglia.

Diagnosis of bluetongue in the UK is performed by IAH, which is also the Reference Laboratory for the European Community and OIE (World Organisation for Animal Health).

During BT2007, IAH provided advice to policy makers to facilitate proper informed decision-making processes. For example, IAH met regularly with Defra through specific committees set up to develop policies and strategies for controlling a possible country-wide outbreak of BT during 2008. IAH has shared with stakeholders and government the belief that vaccination is the only protection against BTV and unless a minimum of 80% of the country's ruminant livestock are vaccinated then the economic consequences are likely to be severe. In 2007, an outbreak in Belgium led to 42% mortality in sheep. IAH is also working with commerce both to develop new diagnostic tests for BTV and with vaccine producers. IAH has contributed to a number of bluetongue videos produced for farmers.
http://www.fwi.co.uk/Articles/2008/05/08/110429/watch-4-may-2008-edition-of-farming-sunday-again-on.html
http://www.nfuonline.com/x27172.xml
http://www.farmersguardian.com/hybrid.asp?typeCode=254&pubCode=1

Diagnostic kits and research resources allied to control measures

The Pirbright Laboratory produces a range of kits and reference reagents for the diagnosis of several ‘list A’ viral infections of livestock (including FMD, African swine fever, rinderpest, bluetongue) which are exported to many developing countries with an annual revenue to IAH of approximately £550K.

The IAH has produced monoclonal antibodies to respiratory syncytial virus (RSV) which have been licensed for use in kits for the diagnosis of RSV in human infants. IAH has also commercialised monoclonal antibodies specific for bovine leukocytes and cytokines through AbD Serotec, enabling others in the scientific community to undertake their research. The bovine tuberculosis (TB) research group at Compton has filed a patent for a rapid diagnostic test for bovine TB that will help control bovine TB in the UK.

A TSE Resource Centre located at the Compton Laboratory has commercially provided more than 500 samples to laboratories around the world during the past four years to ensure that

common standards of diagnosis of TSE diseases are established and maintained.

TRAINING THE NEXT GENERATION

Post-graduate training

IAH has provided post-graduate training to more than 120 students from across the globe during the past 10 years. A high proportion of students are from developing countries and after completion of their studies around 70% have continued with scientific research as a career in the government or industrial sectors.

Livestock disease specialists

For more than 30 years IAH has provided training to poultry health specialists wishing to learn about diseases of commercially-reared poultry, vaccination regimes and other methods of control. IAH typically attracts young veterinarians and scientists both from countries with developed or developing livestock industries and during the past five years delegates have attended from more than 40 countries worldwide, including Australia, Cuba, Denmark, Indonesia, Kuwait, Japan, Malaysia, Saudi Arabia and Sweden.

Diagnosis of disease

Effective surveillance is a key tool to maintaining disease-free status in many countries. IAH remains at the cutting edge of developing new technologies for the molecular and immunological detection of viruses. During the past 20 years the Pirbright Laboratory has trained hundreds of researchers and technicians from across the globe in the diagnosis of diseases caused by economically very important pathogens such as FMDV, swine vesicular disease, BTV, rinderpest and pox viruses. This has been accomplished both through formal training courses held at IAH Pirbright and multi-national training courses and workshops held in developing countries.

Overseas courses have been held throughout Africa, Asia and the Middle East funded through FAO-IAEA and the EU as part of the Rinderpest Network and GREP. Scientists who benefited from these annual workshops have all now attained influential roles in their veterinary services and act as independent consultants, not only in their own country but world-wide.

A ‘generic’ course on ELISA technology covering basic principles through to specific assay systems, test optimisation and development to trouble-shooting and interpretation of results has been an important component of technology transfer to many countries, especially in Eastern Europe funded through the EU on the FAIR programme and Africa, the Middle East and Asia funded by the British Council and IAEA.

In 2007 alone, IAH hosted 24 scientists, most from developing countries, to learn how to utilise the latest procedures to identify different types and sub-types of viruses, with an additional course for UK government veterinarians.

Multi-media disease information discs on rinderpest and FMD were developed as part a consortium formed between IAH, FAO, OIE and Telos ALEFF Ltd. More recently these have

become internet-based and, during the 2001 FMD outbreak in the UK, the FMD modules were made freely available and received more than one million hits.

INFORMING A BROAD USER COMMUNITY

IAH has close relationships with a number of Government Departments, including Defra, and provides scientific resources and advice on different aspects of livestock diseases, including threats from 'exotic' viruses of farm animals. During the 2001 and 2007 FMD outbreaks, IAH worked closely with Defra in terms of carrying out diagnostic assays, providing reagents and training for other laboratories to carry out serological testing and providing scientific advice to Defra on dealing with the outbreak. IAH scientists were involved in visiting the early outbreaks on farms and in providing training for Departmental veterinary surgeons on recognising animals with the disease. IAH also provides scientific advice for policy development on the control of diseases such as FMD and bluetongue.

Outside of the UK, IAH veterinary scientists provide advice and guidance to international bodies, such as the FAO and the OIE which is integrated into their policy development, for example, review of control measures for FMD in the UAE; outbreak of bluetongue in Spain; outbreak of swine vesicular disease in Portugal.

IAH scientists are invited by overseas Governments to give advice on control policies for diseases in livestock and origins of disease outbreaks

PUBLICATIONS

IAH science on important diseases has, just over the past 10 years alone, resulted in more than 1500 primary scientific papers in key biological, agricultural and livestock-orientated journals with a world-wide readership.