



INSTITUTE FOR ANIMAL HEALTH

SCIENCE SUB-GROUP

REPORT

JUNE 2008

EXECUTIVE SUMMARY

1. BBSRC Council established a Science Sub-Group to consider the revised Institute for Animal Health (IAH) Research Strategy. The Sub-Group was also tasked with identifying the components of IAH science that must be retained in a single site based at Pirbright and activities that could or should be relocated elsewhere.
2. **Location and uncertainties:** When addressing the terms of reference the Sub-Group assumed that the location of the single-site institute would be Pirbright, but could be some other site. This position reflected a number of uncertainties and, in the event of the current Pirbright Site Redevelopment Programme not proceeding for strategic or financial reasons, BBSRC Council may wish to reconsider the advantages and disadvantages of a single site close to a university.
3. **Timeframe and mission:** The Science Sub-Group considered that the single site institute would be 7-10 years in development and, as such, discussions focused on facilities, skills and research appropriate for a 10-20 year timeframe. Emphasis was placed upon IAH's role to undertake high quality basic, strategic and applied research, appropriate to a Research Council institute. Discussion did not focus on other contracted duties such as preparedness for disease emergencies but the facilities requirements to fulfil these duties featured in the discussion.
4. **Response to IAH Strategy** The Science Sub-Group concluded that the IAH Research Strategy is framed around current scientific activity and planning in the short to medium term. Although some long term scientific goals are mentioned, it does not capture the change in capability and ethos that would be needed to establish a unified institute on a single site in the 10-20 year timeframe.
5. **Scientific strategy: Host capabilities** Recommendations from the Science Sub-Group are centred on the creation of a flexible, single-site institute that is built around core facilities, capabilities and skills for research on livestock disease that should initially be focused on poultry and cattle with potential to change to other large animals (pigs or sheep) as new challenges emerge. A flexible institute does not mean that IAH would cover 'everything, just in case', rather that the Director should be able to exercise flexibility in using the Institute's facilities and skills to respond to emerging research challenges and new strategic directions.
6. **Scientific strategy: Pathogen capabilities** While recognising the imperative for IAH to focus on viral pathogens, the Science Sub-Group supported continued research in bacteriology and parasitology, noting the need for flexibility in responding to emerging diseases and the small capital costs involved in additional facilities. The Science Sub-Group also supported continued research on both exotic and endemic pathogens but with an important caveat that funding for preparedness in disease emergencies is a Defra statutory responsibility. The provision and maintenance of SAPO4-level large animal containment facilities, while in the national interest, require Defra funding.

Recommendations

Recommendation 1

7. **Flexible, single site institute:** IAH should be set up as a flexible, single-site institute focused around core facilities and skills. There should be active strategic management of the research portfolio. The concept of a 'flexible institute' reflects the

long-term need for livestock disease research, coupled with uncertainty over the specific challenges that will be faced.

Recommendation 2

8. **Core Facilities¹**: In considering IAH's animal accommodation and laboratory requirements, a unified Institute on a single site should provide:
- Non-containment experimental facilities for (a) poultry and (b) large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
 - SAPO2/ACDP1- and SAPO3/ACDP2-level laboratory and animal accommodation facilities for poultry and large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
 - SAPO4-level laboratory space for poultry. Acknowledging the likelihood of evolving research priorities, level of provision should be based on affordability rather than current demand. An increase in provision above that already planned in the Pirbright Site Redevelopment Programme (PSRP) was not proposed;
 - SAPO4-level large animal containment facilities, continued provision of which is in the national interest. Where these facilities are required, Defra and BBSRC should develop a joint case for provision.

Recommendation 3

9. **Outsourcing**: In order to reduce the demand for animal accommodation, IAH should not continue to breed or house inbred pig lines, a dairy herd or flocks of sheep. Outsourcing of mouse lines should also be completed. External hosting or supply of animals is not without cost but significant savings (space and cost) could be made.

Recommendation 4

10. **Disease type (endemic / exotic)**: IAH should continue research on both endemic and exotic diseases, but a biosecurity risk analysis is urgently required to determine the feasibility of having the research co-located on a single site.

Recommendation 5

11. **Disease type (viruses / others)**: IAH should continue to work on viruses (as a priority) with research in bacteriology and parasitology as scientific demand requires and recurrent financial resources permit, noting that bacteriology and parasitology do not trigger any significant, additional facilities requirements.

Recommendation 6

12. **Scientific components**: The Science Sub-Group does not recommend transfer of any current research groups at IAH to other institutions either because this would lead to little cost-saving through expensive duplication of resources elsewhere or because the loss of capability would undermine the strategic mission of the Institute.

¹ SAPO and ACDP Regulations: for explanation and categorisations of the major pathogens used in IAH research, see Annex 6.

BACKGROUND

1. The BBSRC Institute for Animal Health (IAH) is an internationally competitive centre for research into exotic and endemic diseases of livestock. A prime feature of IAH is a range of facilities and unique resources, which underpin research on target host animals, including studies on active pathogens. The Institute also fulfils a vital public safety role in preparedness for disease emergencies.
2. The IAH is situated on two campuses (IAH-P at Pirbright, Surrey; IAH-C at Compton, Berkshire) and it is accepted that much of the physical infrastructure at both sites is in need of replacement. The Pirbright Site Redevelopment Programme (PSRP) had made good progress, but following the Foot and Mouth Disease (FMD) outbreak in Surrey in August 2007, major increases in cost (above the original estimate of £120M) are expected due to delays and anticipated changes in regulatory requirements². Furthermore, at the end of FY06/07 estates planning revealed IAH-C needed almost total redevelopment with an estimated cost of £276M capital and an annual running deficit, allowing for capital depreciation, of £6.5M³.
3. Since 2002, IAH has been the subject of many reviews. Several followed the Surrey FMD outbreak in August 2007 and, of these, two are particularly relevant to the current report:
 - Anderson Review (March 2008): The review examined the Government's reaction to the 2007 FMD outbreak and reported to Defra in March. The review included a personal recommendation from Dr Anderson to reposition IAH as a new 'National Institute of Infectious Diseases'. The PSRP was considered critical to bringing the facilities up to internationally recognised standards.
 - Beringer Review (April 2008): The review considered future funding, governance and risk management at IAH. Two key recommendations were the positioning of the Pirbright Laboratory as a new 'National Centre for Animal Viral Diseases' and completion of the PSRP without delay. The review recognised that the IAH-C laboratories require modernisation and recommended that, provided Council was persuaded by a scientific and strategic case, work should be relocated from Compton to join the new centre at Pirbright.
4. In February 2008, Professor Martin Shirley (Director, IAH) presented a paper to BBSRC Council on the redevelopment of IAH. The paper set out a research strategy for IAH science. It also drew on the findings of a report by consultants Davis Langdon and considered the benefits, opportunities and threats associated with consolidating all IAH science onto one of its two existing sites, and relocating some or all of IAH science to a number of alternative locations within the UK. On the basis that the PSRP goes ahead, the paper identified the preferred option that *'the science at IAH-C should be redeveloped on the Pirbright site, provided that all issues of governance, responsibility and secure funding streams for BBSRC-led science can be entirely resolved and that all biosecurity conditions can be met'*. Other recommendations were also proposed in the event of planning difficulties or if the PSRP were not to go ahead as planned.
5. BBSRC Council welcomed the IAH paper and, following the discussion of the Beringer Review, agreed that a Science Sub-Group be established to examine the research

² A Review of the Regulatory Framework for Handling Animal Pathogens (Callaghan Review)

³ Institute for Animal Health Part 2: Estates Strategy Second Stage Report (01/02/08) Submitted by IAH in partnership with Davis Langdon LLP

strategy and advise on the content of the institute, including whether components of IAH science should be relocated to IAH-P or elsewhere.

SCIENCE SUB-GROUP AND PROCESS

6. The Science Sub-Group was chaired by Professor Chris Gilligan (University of Cambridge and member of BBSRC Council) and included eminent scientists in animal disease research across a range of hosts and disease types. The terms of reference (ToR) for the Science Sub-Group are at **Annex 1**. The membership and declared interests are at **Annex 2**. The Science Sub-Group met twice (9 and 22 May 2008) and the information provided at each meeting is listed at **Annex 3**. Professor Fiona Tomley (IAH Acting Deputy Director) attended the first meeting and part of the second meeting as observer, where she was accompanied by Dr Peter Kaiser (Head, Division of Immunology, IAH), and Dr Geraldine Taylor (Group Leader, Vaccinology, IAH). Every effort was made to proceed as rapidly as possible with adequate examination of scenarios, so as to minimise periods of uncertainty for the Institute.

IAH IN CONTEXT

7. The Science Sub-Group recognised that livestock disease will continue to be a major and persistent problem that could cause serious economic loss and disruption of food supplies. This is set in a context where fuel costs and climate change-related drivers are likely to result in UK home food production assuming renewed economic importance in the future. Research on livestock disease requires strategic, long-term, multidisciplinary approaches together with access to specialised facilities for handling large animals at a range of containment levels. The Sub-Group agreed that there is a continuing national and international need for a BBSRC-funded Institute for Animal Health.
8. The IAH conducts high quality research which encompasses work ranging from molecular biology to whole animal and population studies. The 2006 Visiting Group (for the BBSRC Institute Assessment Exercise) commended the Institute for overall quality of the science: the BBSRC-funded research programmes were rated as high international (pathogen-host molecular interactions), international (arbovirology and mathematical modelling, food-borne zoonoses, mechanisms of host resistance) and high national (vaccinology). The externally funded foot-and-mouth disease programme was rated as outstanding. Research highlights of particular note included work on Rinderpest and *Eimeria*.
9. The Science Sub-Group considered IAH's international position and agreed that its scientific breadth and the high quality of its research placed it in a unique position. IAH covered the scope of Friedrich Loeffler Institute (Germany), WUR Central Veterinary Institute (Netherlands) and parts of INRA (France) combined. The Plum Island Animal Disease Center (USA) and the Friedrich Loeffler Institute are IAH's main competitors in exotic disease research. Recent trends among similar institutes overseas are towards a broadening of scientific scope.

FRAMEWORK FOR DISCUSSION

10. To establish the scope of the review, the Sub-Group agreed a framework for discussion. This provided an opportunity to set the context, highlight concerns and

comment on other on-going activities. Key components of the framework are set out below:

- **BBSRC/Defra remits:** As a BBSRC institute, IAH's mission is to undertake high quality basic, strategic and applied research. Preparedness for disease emergencies is a Defra statutory responsibility currently fulfilled in part via contracts to IAH. Work on exotic disease requires expensive containment facilities that are also essential for disease preparedness work. A partnership with Defra is essential to ensure continued provision of these facilities;
- **Single-site Institute:** The Science Sub-Group accepted the recommendations of the Beringer Review and IAH that a single-site institute should be established. They assumed that the location was likely to be Pirbright;
- **Realistic time-frame:** The Science Sub-Group recognised that the single-site institute would be 7-10 years in development and, as such, discussions focused on science strategy and related capacity needs over a 10-20 year timeframe. The Science Sub-Group were cognisant of the need for careful management of IAH-C in order to avoid planning blight during the transition period;
- **Uncertainties:** Due to a number of uncertainties (**Annex 4**) concerning co-location at Pirbright, when addressing the terms of reference the Science Sub-Group's proposals were not site-limited. In the event of the current Pirbright Site Redevelopment Programme not proceeding for strategic or financial reasons, the Sub-Group suggested that BBSRC Council may wish to reconsider the advantages and disadvantages of a single site close to a university;
- **Governance:** IAH governance issues fall outside the scope of this review and are being progressed through other routes.

11. The Science Sub-Group undertook a critical analysis of the revised IAH Research Strategy document and the Institute's potential future composition. Its starting point was a single-site institute, but not necessarily a single site for all on-going science activities.

TERM OF REFERENCE 1: TO CONSIDER AND COMMENT ON THE REVISED IAH STRATEGY PRESENTED TO COUNCIL IN FEBRUARY 2008

Strategy document

12. The Sub-Group recognised the difficulties inherent in determining long-term strategy at a time when there are many uncertainties (**Annex 4**) and where a generic ability to predict future research challenges is required. They were of the opinion that the IAH document struggles to liberate itself from the *status quo* and is framed around current scientific activity in a short to medium term context. Although some long term scientific goals are mentioned, it does not adequately capture requirements in the necessary 10-20 year timeframe. The Science Sub-Group provided comments on each section of the strategy - see **Annex 5**. The comments reflect some of the key points made in the remainder of this section.

Conclusion: The Science Sub-Group concluded that the IAH Research Strategy is framed around current scientific activity and planning in the short to medium term. Although some long term scientific goals are mentioned, it does not capture the change in capability and ethos that would be needed to establish a unified institute on a single site in the 10-20 year timeframe.

Facilities and skills

13. A clear institute strategy was considered essential to underpin long-term decision making. The Sub-Group recommended that IAH be set up as a flexible, single-site institute focused on core facilities and skills. This position reflects, in part, the uncertainty of the long-term research agenda. A flexible institute does not mean that IAH would cover 'everything, just in case', rather that the Director should be able to exercise flexibility in using the Institute's facilities and skills to respond to emerging research challenges and new strategic directions. Prioritisation will lead to some activities being initiated and others discontinued. The scientific programme should be informed by an analysis of potential emerging infectious diseases of livestock and justification as to why the activity should be placed in an institute setting.
14. BBSRC will need to agree what is affordable and key to this decision are the containment facilities and host animal accommodation, as they place the greatest demand on finances in establishing IAH on a single site. Full consideration should be given to capital and running costs from the outset. The latter are substantial and require sustained, reliable income streams. Funding partners must be prepared to make long-term commitments.
15. The Sub-Group identified a range of scientific expertise that is essential to the Institute. The expertise areas included: immunology, microbiology, vaccinology, mathematical modelling, molecular biology, entomology, imaging and genomics. The scientific expertise would need to operate flexibly in order to respond to new challenges in livestock disease. Under ToR 2 (paragraphs 34-36) the Sub-Group considered whether some of these scientific skill sets needed to be physically based at the Institute or whether they could be provided through other routes (e.g. via collaboration with universities).
16. A set of essential requirements for undertaking livestock research in containment facilities were also identified:
 - Statistics and experimental design expertise relevant to animal work;
 - Understanding of logistics and long-term planning of experimental work in containment settings;
 - Knowledge of the regulatory framework and associated training requirements;
 - Understanding of the agricultural context in which advances in animal disease control will be implemented.

Recommendation 1: IAH should be set up as a flexible, single-site institute focused around core facilities and skills. There should be active strategic management of the research portfolio. The concept of a 'flexible institute' reflects the long-term need for livestock disease research, coupled with uncertainty over the specific challenges that will be faced.

Containment facilities

17. An explanation of containment regulations and a list of pathogens currently handled by IAH are at **Annex 6**.
18. The Science Sub-Group considered the core containment facilities of a flexible, single-site institute based on likely disease type and associated containment level, animal host, and BBSRC / external funding. The Group concluded that the following were essential and must be provided on site:

- Non-containment experimental facilities for (a) poultry and (b) large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
 - SAPO2/ACDP1- and SAPO3/ACDP2-level laboratory and animal accommodation facilities for poultry and large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species.
19. The PSRP includes a plan to relocate virology work currently at the Veterinary Laboratories Agency's (VLA) site at Weybridge to the new facilities planned at Pirbright. SAPO4 poultry facilities are included in the PSRP, with laboratory space planned for 10 researchers. However, with the expansion of the VLA's work on avian influenza H5N1 (currently 35 researchers), the PSRP plans are now insufficient to meet current need. As such, VLA and IAH researchers would not be based together as originally planned and there would still be demand for VLA's existing SAPO4 facilities. In considering the need for long-term SAPO4 containment for poultry, the Sub-Group concluded that laboratory space should not be designed around current demand as priorities would change over time. An expansion of SAPO4 poultry provision, above that set out in the PSRP, was not recommended.
20. The Science Sub-Group considered that large animal SAPO4/ACDP3 laboratory and accommodation facilities should be contingent on joint support from Defra as they are used primarily for work on exotic viral diseases (e.g. FMD, African swine fever (ASF), Rinderpest). BBSRC's only obligation to research requiring SAPO4 containment stems from Defra contacts, but the current portfolio of BBSRC core support and grant funding is large (30 FTE) and it makes a major contribution to UK capability. The Sub-Group considered whether BBSRC should withdraw from large animal exotic virus work as there could be significant cost savings in not requiring SAPO4 and derogating the new ISO facilities to SAPO3 standard. The Sub-Group concluded that the provision of large animal SAPO4 facilities is in the national interest, but that Defra has a primary responsibility for such provision, working closely with BBSRC. The Group recommended that where these facilities are required the two organisations develop a joint case for provision with agreement on how they should be funded.

Recommendation 2: In considering IAH's animal accommodation and laboratory requirements, a unified Institute on a single site should provide:

- **Non-containment experimental facilities for (a) poultry and (b) large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;**
- **SAPO2/ACDP1- and SAPO3/ACDP2-level laboratory and animal accommodation facilities for poultry and large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;**
- **SAPO4-level laboratory space for poultry. Acknowledging the likelihood of evolving research priorities, level of provision should be based on affordability rather than current demand. An increase in provision above that already planned in the PSRP was not proposed;**
- **SAPO4-level large animal containment facilities, continued provision of which is in the national interest. Where these facilities are required, Defra and BBSRC should develop a joint case for provision.**

Host species: resources

21. The Science Sub-Group considered the range of animal host species for IAH research. They concluded that cattle and poultry should remain the Institute's priority over the medium term, whilst maintaining flexibility to work with other species (pigs, sheep) as priorities evolve.
22. **Cattle:** IAH currently houses MHC defined cattle (4 families, 20-30 animals) on the farm at IAH-C. They are central to several IAH research programmes including bovine immune mechanisms, immunology of exotic virus infection and vaccinology. It is not feasible to move the MHC defined cattle to IAH-P because of the requirement to maintain them as part of a dairy herd. The Science Sub-Group noted that the VLA has appropriate facilities (4 farms) and may have space to house them. The Sub-Group recommended that the MHC cattle be outsourced and IAH explore relocating them to VLA.
23. **Poultry:** The Institute currently houses numerous inbred poultry lines in a poultry production facility. The lines have been characterised for particular immunological responses to a wide range of strategically important pathogens. The Science Sub-Group recognised the importance of inbred poultry to IAH's research and noted that no suitable technological alternative existed for preserving the lines. To date, work on embryo storage had not been successful and further effort is needed to achieve this. In light of the above, and the fact that no other UK organisation had facilities to house the lines, the Science Sub-Group recommended that the inbred poultry lines should continue to be accommodated in a poultry production facility. Additional accommodation may be required if the Institute is to house transgenic chicken lines in the future.
24. **Pigs:** Research on pigs was reduced in 2004/05 with the removal of programmes such as African swine fever (ASF) cell biology and porcine immunology. Pigs have not been accommodated as a primary animal in the PSRP specification, but they may become important in the long term with the increasing threat of classic swine fever (CSF) and ASF and increased understanding of zoonoses. Currently, IAH houses a fully inbred line of Large White pigs (the Babraham line) and two MHC-inbred lines of mini-pigs originally imported from the USA. Although these lines are not widely used by the Institute, they are important in porcine immunology work particularly in relation to ASF. The Science Sub-Group considered that, while IAH needed to retain experimental capacity to work on pigs, the Institute itself did not need to breed and maintain the inbred lines. This would reduce the demand for large animal accommodation and may provide an opportunity to reduce costs, although cost implications would also be associated with outsourcing to an alternative site. Lack of access to breeding pigs on site would partially compromise the gnotobiosis work (see also paragraph 35), but this was considered to be a single, isolated area. The University of Bristol or the VLA may provide an appropriate alternative home, with VLA preferred in order to meet regulations for transporting pregnant sows to IAH.
25. **Sheep:** With the transfer of work on transmissible spongiform encephalopathies (TSEs) to EBRC, IAH's use of sheep has reduced in recent years and the requirement for experimental animals relates largely to work on bluetongue, FMD and *peste des petit ruminants* viruses. A breeding programme involving Dorset sheep (which have the capacity to breed more than once a year) is in operation, with lambing three times per annum, providing a more or less continuous supply of young animals for studies of bluetongue. The Science Sub-Group concluded that, while IAH needed to retain the experimental capacity to work on sheep, it did not need to maintain breeding flocks and animals could be purchased from commercial breeders.

26. **Mice:** The Sub-Group noted that IAH currently holds numerous mouse lines, but has planned to relocate most of these to an external provider. Coupled with the relocation of most of the Jenner Institute from Compton and transfer of work on TSEs to EBRC, this will substantially reduce the scale of small animal facilities (housing and experimental) that will be required.
27. Outsourcing of animal accommodation together with a single-site location could generate some small savings in personnel required in animal husbandry and engineering maintenance.

Recommendation 3: In order to reduce the demand for animal accommodation, IAH should not continue to breed or house inbred pig lines, a dairy herd or flocks of sheep. Outsourcing of mouse lines should also be completed. External hosting or supply of animals is not without cost but significant savings (space and cost) could be made.

Disease type

28. The Science Sub-Group accepted that IAH should cover both endemic and exotic infectious animal diseases as invasions mediated by global change are making the distinction somewhat arbitrary (e.g. 2007 bluetongue outbreak). However, concerns were raised over the co-location of exotic and endemic disease research on a single site and an urgent biosecurity risk analysis was recommended. Decisions concerning the scale of research effort on exotics will need to be informed by the cost implications of facilities and Defra's position (paragraph 31). The Sub-Group noted with concern the decline in Defra's funding of endemic disease research. The importance of endemic diseases has not decreased and real problems exist, notably in anti-microbial resistance, the impact of disease on animal welfare and sustainability of food supply. This is particularly relevant in the context of a likely renewed focus on UK animal production in the future, responding to economic and climate-change drivers. The Sub-Group supported BBSRC's commitment to fund basic, strategic and applied research on endemic diseases and considered it essential that Defra maintain a strong position in this area in the long-term.
29. The largest part of IAH's research is directed toward virology and it has made valuable contributions to global food security (e.g. Rinderpest, bluetongue) and economic impact (e.g. Marek's disease). The Science Sub-Group considered that virology should remain central to IAH and a critical mass of expertise is required to meet long-term research challenges. Reducing the number of viruses studied would not affect the capital costs of IAH re-development and, while running costs could be reduced, overall unit cost would increase. That said, work on a virus type should not continue if its strategic relevance declines. The Director will need to be proactive in managing a dynamic portfolio of virus types.
30. The Institute also undertakes smaller scale, high quality research in bacteriology (e.g. bovine TB and food-borne bacterial pathogens) and parasitology (e.g. *Eimeria*). The Sub-Group agreed that there is a strong economic argument for retaining research on both these groups of diseases as they do not trigger additional facilities requirements, other than ammonia fumigation for *Eimeria* work. Relocation risked the costly duplication of facilities elsewhere.

Recommendation 4: IAH should continue research on both endemic and exotic diseases, but a biosecurity risk analysis is urgently required to determine the feasibility of having the research co-located on a single site.

Recommendation 5: IAH should continue to work on viruses (as a priority) with research in bacteriology and parasitology as scientific demand requires and recurrent financial resources permit, noting that bacteriology and parasitology do not trigger any significant, additional facilities requirements.

Defra

31. The Science Sub-Group expressed concern about Defra's position on several issues:
 - A single-site institute housing both BBSRC and Defra funded activities could raise ownership issues that influence the mission and direction of the research;
 - Declining support from Defra for endemic disease research (paragraph 28);
 - Uncertainty over financial commitment to the re-costed PSRP. Defra has agreed to the revised capital investment but the department's position on recurrent costs is not resolved.
 - Tensions between the recommendations of the Beringer Review (research focused) and the Anderson Review (disease outbreak focused);
 - Whether Defra will continue its commitment to exotic disease research and provision of high containment facilities in the UK.
32. While these issues are outside the ToR of this Review, the Sub-Group recognised the substantial added value obtained from bringing together basic, strategic and applied research with the surveillance laboratories and international reference collections. They noted that in other parts of the world surveillance and control of exotic animal disease were co-located with research programmes and, as a part of this review, IAH provided a summary of the benefits of this interaction (**Annex 7**). Separation of these functions implied duplication of expensive facilities. Any decline in Defra's support for exotic disease research would make BBSRC's related research prohibitively expensive. It would also compromise the ability of the UK to manage future disease outbreaks and so would not be in the national interest.

Capacity for scale-down

33. The Sub-Group considered whether IAH science could be reduced in breadth or depth, since the scale of institute activities will depend on affordability to BBSRC and other funders. A key issue here, however, is the cost of core facilities (capital / recurrent) and, if they have been provided, there is an argument that they should be used to optimal capacity. Scaling down the science at IAH did not necessarily make an economically sensible argument. If the facilities were under-utilised then the cost of each 'unit of science' would increase.

TERM OF REFERENCE 2: TO IDENTIFY WHICH COMPONENTS OF IAH-C AND IAH-P SCIENCE MUST BE RETAINED IN A NEW IAH BASED AT THE PIRBRIGHT SITE AND IDENTIFY THOSE ACTIVITIES THAT COULD OR SHOULD BE RELOCATED ELSEWHERE. ACCOUNT SHOULD BE TAKEN OF DEFRA'S PLAN TO LARGELY WITHDRAW FUNDING FORM ENDEMIC RESEARCH

34. Based on the previous section, the Science Sub-Group considered that the following components of IAH-C and IAH-P must be retained at a single-site institute:
 - **Facilities** for exotic and endemic disease research:

- Non-containment experimental facilities for (a) poultry and (b) large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
 - SAPO2/ACDP1- and SAPO3/ACDP2-level laboratory and animal accommodation facilities for poultry and large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
 - SAPO4-level laboratory space for poultry. Acknowledging the likelihood of evolving research priorities, level of provision should be based on affordability rather than current demand. An increase in provision above that already planned in the PSRP was not proposed;
 - SAPO4-level large animal containment facilities, continued provision of which is in the national interest. Where these facilities are required, Defra and BBSRC should develop a joint case for provision;
 - Poultry Production Facility.
- **Scientific expertise:** immunology, entomology, microbiology, vaccinology, mathematical modelling, molecular biology, imaging and genomics;
 - **Other essential skill sets:**
 - Expertise on the practicalities and limitations in bridging the gap between laboratory, large animal and poultry experimentation under containment;
 - Statistics and experimental design expertise relevant to animal work;
 - Understanding of logistics and long-term planning of experimental work in containment settings;
 - Knowledge of the regulatory framework and associated training requirements;
 - Understanding of the agricultural context in which advances in animal disease control will need to be put into effect.

35. The Science Sub-Group considered whether areas of IAH activity could or should be relocated elsewhere. It focused on areas perceived as not central to the Institute's mission and core technologies where there may be scope for outsourcing or scaling down.

- **Food borne zoonoses (FBZ):** The Science Sub-Group agreed that the FBZ work, while world-class, is not central to the IAH's mission. It occupied a unique niche, using the IAH facilities to undertake specialist work on the interactions with carrier species. The studies complement work at Edinburgh and the Institute of Food Research, but relocation would not be practicable without access to specialist facilities (ACPD2/3 lab and animal facilities, inbred poultry, surgery). Thus, it was concluded that IAH should have an on-going role in FBZ work, but that this should not extend beyond interaction with the host/carrier. **Outcome: Retain**
- **Immunology:** The Science Sub-Group considered that IAH's immunology research is set in the context of the infectious diseases being studied. The Institute should continue host-response work when studying pathogenesis, but avoid extending this into a large fundamental research programme. The current capacity and focus (cattle, poultry) in immunology was considered appropriate and recent work on the systems biology of enteric immunology is an interesting new development. **Outcome: Retain**
- **Mathematical modelling (including bioinformatics):** The Science Sub-Group considered that, while modelling had potential for relocation, it must be integrated with IAH experimental studies in order to have an effective influence on IAH research. This reflected BBSRC's Review of Mathematical Biology in BBSRC

sponsored Institutes, which recognised the need to build critical mass and develop a more quantitative bioscience in the Institutes. IAH currently has 12 researchers involved in mathematical modelling and work with the Met Office on epidemiology of bluetongue has been particularly effective. **Outcome: Retain**

- **Gnotobiosis:** Work should continue, providing that pregnant sows could be purchased from relatively local suppliers. **Outcome: Retain**

36. IAH's current scientific expertise constitutes a solid base capable of adapting and responding to the research challenges over a 10-20 year timeframe. No significant gaps or unnecessary activities were identified. This latter point may reflect, in part, the restructuring that took place in 2005.

Recommendation 6: The Science Sub-Group does not recommend transfer of any current research groups at IAH to other institutions either because this would lead to little cost-saving through expensive duplication of resources elsewhere or the loss of capability would undermine the strategic mission of the Institute.

TERM OF REFERENCE 3: TO IDENTIFY POSSIBLE RESEARCH ORGANISATIONS TO WHICH IAH SCIENCE COULD RELOCATE (ESPECIALLY VETERINARY SCHOOLS) IF THESE ARE WILLING TO ACCOMMODATE THE RESEARCH

37. The Science Sub-Group considered the scientific scope and facilities provision at the following research organisations:
- UK Veterinary Schools: Cambridge, Glasgow, Royal (Dick) Edinburgh, Royal Veterinary College (London), Bristol, Liverpool, Nottingham;
 - Institute of Food Research;
 - Veterinary Laboratories Agency (VLA);
 - Moredun Research Institute (MRI);
 - Other departments: Liverpool School of Tropical Medicine; London School of Hygiene and Tropical Medicine
38. The VLA and MRI had strong synergy with some IAH facilities and skills, and this is detailed at **Annex 8**.
39. While, arguably, the work on food-borne zoonoses could be re-located, potential moves either failed to offer any clear benefits or would detrimentally affect access to important animal facilities for retained research. Thus, the Science Sub-Group did not identify any science areas as candidates for relocation.

TERM OF REFERENCE 4: TO IDENTIFY ANY FACILITIES THAT MAY BE REQUIRED IN RELOCATING SCIENTIFIC GROUPS

40. This term of reference is no longer applicable as no scientific groups were identified as suitable for relocation.

CONCLUSIONS AND RECOMMENDATIONS

41. **Response to IAH Research Strategy** The Science Sub-Group concluded that the IAH Research Strategy was framed around current scientific activity and planning in the short to medium term. Although some long-term scientific goals were mentioned, it did not capture the change in capability and ethos that would be needed to establish a unified institute on a single site in the 10-20 year timeframe.
42. **Scientific strategy: Host capabilities** Recommendations from the Science Sub-Group are focused on the creation of a flexible, single-site, institute that is built around core facilities, capabilities and skills for research on livestock disease that should initially be focused on poultry and cattle with potential to change to other large animals (pigs or sheep) as new challenges emerge. A flexible institute does not mean that IAH would cover 'everything, just in case', rather that the Director should be able to exercise flexibility in using the Institute's facilities and skills to respond to emerging research challenges and new strategic directions.
43. **Scientific strategy: Pathogen capabilities** While recognising the imperative for IAH to focus on viral pathogens, the Science Sub-Group supported continued research in bacteriology and parasitology, noting the need for flexibility in responding to emerging diseases and the small capital costs involved in additional facilities. The Science Sub-Group also supported continued research on both exotic and endemic pathogens but with an important caveat that funding for preparedness for animal disease emergencies is a Defra statutory responsibility. The provision and maintenance of SAPO4-level large animal containment facilities, while in the national interest, require Defra funding.
44. The Sub-Group's recommendations are set out in the box below.

Flexible, single site institute: IAH should be set up as a flexible, single-site institute focused around core facilities and skills. There should be active strategic management of the research portfolio. The concept of a 'flexible institute' reflects the long-term need for livestock disease research, coupled with uncertainty over the specific challenges that will be faced.

Core facilities: In considering IAH's animal accommodation and laboratory requirements, a unified Institute on a single site should provide:

- Non-containment experimental facilities for (a) poultry and (b) large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
- SAPO2/ACDP1- and SAPO3/ACDP2-level laboratory and animal accommodation facilities for poultry and large animals. The large animal facilities should be sufficiently flexible to accommodate a range of host species;
- SAPO4-level laboratory space for poultry. Acknowledging the likelihood of evolving research priorities, level of provision should be based on affordability rather than current demand. An increase in provision above that already planned in the PSRP was not proposed;
- SAPO4-level large animal containment facilities, continued provision of which is in the national interest. Where these facilities are required, Defra and BBSRC should develop a joint case for provision.

Outsourcing: In order to reduce the demand for animal accommodation, IAH should not continue to breed or house inbred pig lines, a dairy herd or flocks of sheep. Outsourcing of mouse lines should also be completed. External hosting or supply of animals is not without cost but significant savings (space and cost) could be made.

Disease type (endemic / exotic): IAH should continue research on both endemic and exotic diseases, but a biosecurity risk analysis is urgently required to determine the feasibility of having the research co-located on a single site.

Disease type (viruses / others): IAH should continue to work on viruses (as a priority) with research in bacteriology and parasitology as scientific demand requires and recurrent financial resources permit, noting that bacteriology and parasitology do not trigger significant, additional facilities requirements.

Scientific components: The Science Sub-Group does not recommend transfer of any current research groups at IAH to other institutions either because this would lead to little cost-saving through expensive duplication of resources elsewhere or because the loss of capability would undermine the strategic mission of the Institute.

**BBSRC
June 2008**

**INSTITUTE FOR ANIMAL HEALTH
SCIENCE SUB-GROUP**

TERMS OF REFERENCE

1. To consider and comment on the revised IAH research strategy presented to Council in 2008
2. To identify which components of Compton and Pirbright science must be retained in a new IAH based at the Pirbright site and identify those activities that could or should relocate elsewhere. Account should be taken of Defra's plan to largely withdraw funding for endemic research.
3. To identify possible research organisations to which IAH science could relocate (particularly veterinary schools) if these were willing to accommodate the research.
4. To identify any facilities which may be required in relocating scientific groups.
5. To report to Council Sub-Groups as appropriate.
6. The Science Sub-Group is time-limited.

Approved: BBSRC Council, 9 April 2008

**INSTITUTE FOR ANIMAL HEALTH
SCIENCE SUB-GROUP MEMBERSHIP**

Name	Affiliation	Conflicts declared
Sub-Group Membership		
Professor Chris Gilligan (Chair)	University of Cambridge	Previous collaboration and ongoing interactions with Simon Gubbins, IAH
Dr Malcolm Weir (did not attend either meeting)	Heptares Therapeutics Ltd	
Professor Tony Minson	University of Cambridge	Number of friends and colleagues at IAH. Trustee of the Animal Health Trust.
Professor Charles Penn	University of Birmingham	Member of IFR governing body. Currently preparing a BBSRC grant application with Mark Stevens, IAH. Member of FSA review panel for programme B14 'Foodborne Diseases', June 2008. Member of DEFRA-funded SGM review of research into bovine and badger tuberculosis, to report summer 2008.
Dr Tony Holder	The National Institute for Medical Research	None to declare
Professor Ivan Morrison	University of Edinburgh	Formal collaborations with two groups at IAH. Member of review board for Jenner Institute. Member of Defra-funded Independent Scientific Group on Cattle TB
IAH representatives		
Professor Fiona Tomley (Observer)	IAH	N/A
Dr Peter Kaiser (meeting 2 only)	IAH	N/A
Dr Geraldine Taylor (meeting 2 only).	IAH	N/A
BBSRC Office		
Professor Nigel Brown	BBSRC Office	Taking up a position at the University of Edinburgh from September 2008
Dr Paul Burrows (meeting 1 only)	BBSRC Office	None to declare
Dr Amanda Collis (review secretary)	BBSRC Office	None to declare
Dr Jef Grainger	BBSRC Office	None to declare
Miss Laura Notton (meeting 1 only)	BBSRC Office	None to declare

INFORMATION PROVIDED TO THE IAH SCIENCE SUB-GROUP

1	Structure of IAH
2	IAH Navigation Table: Provided information on divisions and groups, group leaders, site, Visiting Group 2006 research programme affiliation, disease type and key facilities / resources.
3	IAH Science Strategy (2005-2015)
4	IAH Visiting Group 2006 Report
5	Paper from IAH to BBSRC Council (Feb 2008): 'The Redevelopment of the Institute for Animal Health.'
6	Davis Langdon (report 1/2/08): Site Assessment extract for IAH-Pirbright only (with or without PSRP going ahead).
7	Paper from IAH to BBSRC entitled 'Redevelopment of the Institute for Animal Health': Focuses on the scientific and strategic need to maintain the activities currently at IAH Compton in moving to the new Centre at Pirbright.
8	Paper from IAH entitled 'Redevelopment of the Institute for Animal Health: Paper form IAH to the IAH Science Sub-Group. The paper contained input from research leaders, particularly those in the Division of Immunology.
9	BBSRC research spend in animal disease research and at IAH.
10	Overview of the animal infectious disease research interests of other UK research organisations.

DEFINED UNCERTAINTIES IN ADDRESSING THE TERMS OF REFERENCE

Planning permission

1. Planning permission for movement of IAH-C to Pirbright (including housing for support staff) is not yet assured (noted in discussion of this issue by the Davis-Langdon report).

Potential for infrastructural expansion at Pirbright

2. Infill around the planned (PSRP) rebuild at IAH-P appeared cramped with little scope for significant further expansion (e.g. business accommodation) or provision for on-site housing for essential staff groups. Furthermore, site constraints risked relative inefficiencies in the location and management of low-containment facilities.
3. Flexibility for future infrastructural developments is dependent to a large extent on the future availability/usage of the part of the Pirbright site currently occupied by Merial Animal Health Ltd. Lease renewal for this site is due in 2015 and, therefore, this remains a significant uncertainty within the likely 7-10 years time-scale for completion of a move of IAH-C activities to Pirbright.

Biosecurity arrangements at Pirbright/PSRP

4. The implications for biosecurity arrangements/authorisations in bringing together IAH-C and IAH-P activities on the Pirbright site are currently not fully resolved. There may be as yet unidentified regulatory obstacles preventing effective redistribution of IAH-C research activities and allied animal resources within the PSRP facilities as currently specified.

Funding partners and Institute governance

5. The future commitment of Defra to the funding of animal disease research and surveillance activities at IAH remains uncertain, with significant implications for the feasibility of a sustained, co-ordinated programme of research between BBSRC and Defra.
6. There are potential conflicts in the recommendations of the reports by Anderson (envisaging a Defra-led institute) and the Beringer report (envisaging a research/BBSRC-led institute) reports. These conflicts affect considerations of the balance between:
 - underpinning, long-term research that couples basic and strategic with applied research appropriate to the mission of a research council;
 - often short-term, empirical research with heavy emphasis on detection and statutory surveillance appropriate to a Defra agency, such as VLA.

RESPONSE OF THE SCIENCE SUB-GROUP TO THE REVISED IAH RESEARCH STRATEGY PRESENTED TO BBSRC COUNCIL IN FEBRUARY 2008

1. The Science Sub-Group's responses are arranged under the headings used in the revised IAH research strategy document.

There is a continuing need for the Institute for Animal Health

2. The Sub-Group accepted this conclusion and the reasoning as summarised in paragraphs 1-6 of the revised IAH research strategy, with the caveat that the Institute's mission remains to undertake basic, strategic and applied research under the governance of BBSRC.

The IAH will address global as well as national animal health problems

3. Accepted. The Sub-Group was of the opinion that IAH should increase its efforts to maximise synergies with leading international efforts on emerging animal diseases in Asia and Africa, seeking to attract funding from DfID.

The IAH will provide a strong research base across livestock species

4. The Sub-Group accepted (a) that generic capability in terms of facilities and skills is important; and (b) the proposed focus on cattle and poultry, whilst maintaining flexibility to work on other species.

IAH will respond to challenges from changing domestic agriculture

5. The Sub-Group accepted that this is necessary positioning for a BBSRC institute but considered that routes to achieving this objective are unclear, beyond aiming to construct facilities that are flexible and responsive to change.

IAH will place more emphasis on research into zoonotic infectious diseases

6. The Sub-Group accepted this position but only in so far as research should focus on the infectious agent and animal host/carrier, in line with the Institute's mission.

The IAH will contribute to the 'one medicine' agenda

7. The Sub-Group accepted that there are considerable synergistic benefits to be realised between animal- and human-disease research areas, focused on pathogens that can infect both livestock and humans. This extends to wider cross-fertilisation of research strategies between human and veterinary research areas. The Sub-Group considered, however, that within the context of IAH's mission, such studies must be confined to studies on animal systems. The Sub-Group also maintained reservations as to whether this agenda could be effectively developed in the absence of close collaborative partnership with an appropriate HEI(s).

The IAH will work more closely with stakeholders

8. This was accepted as being an important principle, but noting the ongoing decline and future uncertainty in Defra's funding of the institute's activities, it was far from clear to the Sub-Group how this can be achieved. In particular the Sub-Group saw a need to clarify, across BBSRC, Defra and the devolved agencies, where responsibilities lie with respect to:
 - Reference laboratories;
 - Surveillance and detection activities;
 - Provision of facilities and trained personnel for preparedness for national emergencies relating to animal disease.

Evolution of IAH science over the next 20 years

9. The Sub-Group accepted some aspects of the generalised framework presented in paragraphs 25-26 of the revised IAH research strategy but did not accept it in its entirety. The Sub-Group considered that long-term strategy should be framed around the core facilities and skills that would be needed to respond to emerging research challenges and new strategic directions, and be informed by cost implications. This should include a more direct consideration of prioritisation and the identification of activities that may be foreseeably phased out.

Requirements for delivery of IAH Science

Physical requirements

10. The Sub-Group accepted the requirement for a poultry production unit but considered that savings in animal accommodation could be made by outsourcing the breeding and housing of MHC cattle, genetically-defined pigs, sheep and rodents.
11. The Sub-Group noted that staff housing is considered essential for animal and maintenance staff, but provision is not evident in current PSRP development plans.

Clear governance, responsibilities and funding streams

12. The Sub-Group accepted the case for a single governance and management arrangement. It considered that, in the context of a decline and ongoing uncertainties in Defra's funding of IAH activities, the feasibility of close strategic and managerial partnership with Defra with respect to reference collections and VLA-led virology is unclear, other than for statutory work.

Key partnerships for the future

13. The Sub-Group accepted that the proposed research partners listed in paragraphs 35-39 of the revised research strategy represented a logical collection, but considered that the document lacked sufficient detail to allow unreserved endorsement.

Options for location of a redeveloped IAH

14. The Sub-Group accepted the conclusion that:
"If PSRP goes ahead: IAH-C should be redeveloped on the Pirbright site provided that all issues of governance, responsibility and secure funding streams for BBSRC-led science can be entirely resolved and that all biosecurity conditions can be met".
 The Sub-Group strongly endorsed and reiterated the listed provisos to this outcome, and would also add the additional condition that satisfactory design of the site is adequately resolved.

Sustainability

15. The Sub-Group noted that there appeared to be significant running costs and running deficits associated with all scenarios but the details of the costings were not entirely clear in the Davis-Langdon document. The Sub-Group recommended that further work be undertaken urgently to more confidently resolve the financial projections

SAPO AND ACDP REGULATIONS: EXPLANATION AND CATEGORISATIONS OF THE MAJOR PATHOGENS USED IN IAH RESEARCH

Specified Animal Pathogens Order (1998) (SAPO)

1. SAPO, currently administered by Defra, covers a list of specified animal pathogens, irrespective of pathogenicity to humans. The main purpose of SAPO is to prevent the release of dangerous animal pathogens into the environment, as opposed to maintaining the safety of laboratory workers. It places restrictions on how specified animal pathogens can be held or worked with. Handling of specified pathogens is authorised under licence from Defra, usually on a five-year basis.
2. There are three levels of containment, licensed by SAPO: Categories 2 to 4, in order of increasingly stringent containment and disposal conditions. 'Category 1' reflects 'non-containment' level, non-specified organisms. The most dangerous pathogens (Category 4) include those which are either exotic or produce notifiable disease and, if released, have a high risk of spread from the laboratory. They have potential to cause serious human/animal disease, in many cases also causing economic loss to the British livestock industry. FMD virus is in this category. IAH and Merial Animal Health Ltd are the only facilities in the UK licensed to work with FMD virus.

Advisory Committee on Dangerous Pathogens (ACDP)

3. The Advisory Committee on Dangerous Pathogens (ACDP) is a non-statutory advisory non-Departmental Public Body which advises Government on all aspects of hazards and risks to workers and others from exposure to pathogens. ACDP therefore regulates work involving human pathogens. This includes, in the context of IAH research, zoonotic organisms. The ACDP Approved List of Biological Agents is implemented under section 15 of the Health and Safety at Work etc. Act (1974).
4. Biological agents appearing in the ACDP Approved List are classified on the basis of their ability to cause disease by infection. As with SAPO, only agents in Groups 2, 3 and 4 are listed (in order of increasingly stringent containment and disposal conditions). However, those not listed in these groups are not implicitly classified in Group 1; for example any virus isolated from a human source must be handled as for Group 2.
5. A single organism can have a SAPO hazard group but not a ACDP group (and vice versa), or can be placed in different SAPO/ACDP groups. For example, avian influenza is categorised as SAPO4 purely on the basis of its infectivity for poultry. It is also categorised as ACDP3 (or occasionally 2, depending on subtype), on the basis of its infectivity, or potential infectivity, for humans.

Table 1: Pathogens handled at IAH-C

Pathogen	Hosts used	ACDP Group	Defra Hazard Group
<u>Bacteria</u>			
<i>Mycobacterium tuberculosis</i>	Cattle	3	2 (not SAPO)
<i>Mycobacterium bovis</i>	Cattle	2	2 (not SAPO)
<i>Mycobacterium bovis</i> (BCG)	Cattle	2	
<i>Mycobacterium avium</i>	Cattle	2	
<i>Burkholderia Pseudomallei</i>	Lab only	3	
<i>Campylobacter</i> spp	Poultry/pigs	2	
<i>Escherichia coli</i>	Poultry/cattle	2	
<i>Escherichia coli</i> , (verocytotoxigenic)	Cattle	3	
<i>Salmonella enteritidis</i>	Poultry/pigs/cattle	2	
<i>Salmonella typhimurium</i>	Poultry/pigs/cattle	2	
<i>Salmonella</i> (other serovars)	Poultry/pigs/cattle	2	
<i>Streptococcus</i> spp	Cattle	2	
<u>Parasites</u>			
<i>Eimeria</i> spp	Poultry/rodents	1	
<i>Cryptosporidium parva</i>	Lab only	2	
<i>Neospora caninum</i>	Lab only	1	
<i>Theileria parva</i>	Lab only	1	SAPO2
<i>Histomonas</i>	Lab only	1	
<u>Viruses</u>			
Avian Influenza, high pathogenicity	Poultry	2/3	SAPO4
Avian Influenza, low pathogenicity	Poultry	2	
Other influenza A viruses	Poultry	2/3	
Avian infectious bronchitis virus	Poultry	1	
Avian infectious bursal disease virus	Poultry	1	
Avian leukosis viruses	Poultry	1	
Marek's disease virus	Poultry	1	
Turkey rhinotracheitis virus	Poultry	1	
Herpes virus of turkey's	Poultry	1	
Bovine viral diarrhoea virus	Cattle	1	
Respiratory syncytial virus	Cattle/rodents	2	
Vaccinia virus	Cattle/rodents	2	
Fowlpoxvirus	Poultry/rodents	1	
Sendai virus	Rodents/cattle	1	
<u>Unconventional agents</u>			
BSE and other related animal TSEs	sheep	3	

Table 2: Major viral pathogens handled at IAH-P⁴

Pathogen	Hosts used	ACDP Group	Defra Hazard Group
Foot-and mouth-disease virus	Cattle, sheep, pigs & guinea pigs		SAPO4
Swine Vesicular Disease	Pigs		SAPO4
African swine fever virus	Pigs		SAPO4
Rinderpest virus	Cattle		SAPO4
Peste de petit ruminants virus	Goats		SAPO4
Bluetongue virus	Sheep & cattle		SAPO3
African Horse Sickness	Horses		SAPO3
Sheep Pox, Lumpy Skin Disease, ORF			SAPO3
Classical Swine Fever	Pigs		SAPO3

⁴ Non-exhaustive. Some stocks held of viruses having ACDP categorisation (e.g. measles virus) but these are used infrequently, and are not used in animal work.

RELATIONSHIP BETWEEN SURVEILLANCE AND RESEARCH ACTIVITIES WITHIN THE IAH - EVIDENCE FOR HOW THESE TWO ACTIVITIES PROVIDE SYNERGY

[Document supplied by IAH]

- Reference laboratories have large and unique collections of viruses and antisera that have been collected over many years from all corners of the world. These enable rapid development of new diagnostics and validation of new tests;
- Controlled animal experiments and field studies undertaken for research purposes can provide clinical samples for the evaluation and validation of diagnostic tests;
- Genome sequences of viruses held in the collections are used to design pan-reactive and type-specific molecular diagnostic probes and assays. Virus collections in reference laboratories and from animal experiments enable sequencing studies with a wide range of applications to disease control and understanding viral evolution;
- Parameters of infectiousness and transmission and factors affecting this are used to model epidemics and test different disease control measures *in silico*;
- Immunological assays that are developed in the research labs are utilised for both vaccine development and for serological diagnosis of disease;
- Having banks of virus stocks in the reference labs means that we can carry out detailed vaccine matching for FMDV.

Some specific examples:

- When Bluetongue struck Northern Europe in 2007, IAH was able to rapidly serotype the virus as BTV-8 and carry out detailed molecular PCR diagnostics using tests that were only possible to develop because of the collections we house. We were also able to identify the likely geographical origin of the virus because we could rapidly compare the sequence of the outbreak strain with others in the collection;
- When the current African swine fever outbreak started in Georgia, it was IAH that was able to give a definitive molecular identification of the virus strain and likely geographical origin;
- The ASFV strains in the reference laboratories are used by the research groups for much of the vaccine studies, pathogenesis and molecular epidemiological work that is ongoing at IAH;
- The rinderpest eradication campaign in the mid 1980's was dependent upon diagnostic tests that used monoclonal antibodies developed at IAH from fundamental work to understand virus replication. Rapid and accurate ELISAs, first indirect and then cELISA to monitor vaccination, were major assets to the eradication campaigns and this latter test is still being used for sero-surveillance to confirm eradication of this disease;

- Fundamental work on rinderpest virus pathogenesis and replication led to development of molecular probes that dispensed with the need to carry out animal testing to confirm whether disease was caused by rinderpest or *peste des petit ruminants* virus. Reverse-transcriptase PCR tests were used for genetic typing and accurate tracing of virus movements in endemic areas. This led to complete refocusing of the rinderpest eradication campaign in the mid-1990's when IAH showed there were two distinct rinderpest strains circulating in Africa. The epidemiological situation would have been very blurred without this knowledge and it made a major contribution to eradication;
- In 1988 when marine morbilliviruses dramatically emerged, it was the IAH molecular probes which showed that phocine distemper virus was distinct from canine distemper virus. Since then IAH has continued to make major contributions to the epidemiology of morbilliviruses in wildlife, work that has gone on side by side with basic research to develop reverse genetics systems and with continued modernisation of diagnostic tests, currently a new real time assay for *peste des petits ruminants*;
- Without the collections of morbilliviruses, the initial research work on pathogenesis and host range, which in turn fed back to the reference labs, would not have been possible;
- Virus receptors identified in basic research have proven to be useful ligands in a range of diagnostic assays for virus detection and serology for FMDV and are now also being explored as immunopotentiating ligands for targeting antigens to dendritic cells and as antiviral agents to block attachment;
- Understanding the structure of the virus capsid has allowed stabilising mutations to be introduced by design with application in manufacture of more stable and effective vaccines and diagnostic reagents;
- Modelling work is fully integrated with the research and reference laboratory activities, focused on bluetongue and foot-and-mouth disease and with close collaborative and productive links with the Met Office;
- During the 2007 FMD outbreak new tests developed by IAH research were applied, including a lateral flow device for rapid detection of virus particles, whole genome sequencing to promptly and definitively identify the order in which premises were infected, and PCR tests to detect infection prior to onset of clinical symptoms.

SUMMARY OF FACILITIES AT IAH, VETERINARY LABORATORIES AGENCY (VLA) AND MOREDUN RESEARCH INSTITUTE (MRI)

Facility type	IAH-C	IAH-P	VLA	MRI
Large animal SAPO4	No	ISO10 - 25 adult cow equivalents; ISO11 - 39 adult cow equivalents	No. But ACDP3 facility (below) could be used with appropriate licence	No
Large animal ACDP3	69 adult cow equivalents;	ISO11 - 39 adult cow equivalents	24 adult cow equivalents (or 30 young cows)	27 sheep equivalents. Calves, sheep or pigs
Large animal SAPO3	No	Currently use the SAPO4 facilities	No	As above
Large animal ACDP2	52 adult cow equivalents; 30 small cow equivalents; 70 pigs; 1800 sheep	Currently use the SAPO4 facilities	Large amount in different configurations - but naturally ventilated	1040 sheep equivalents. Cattle, sheep, pigs. 20 deer
Large animal conventional	26 adult cow equivalents; 80 small cow equivalents; 60 calf equivalents	ISO9, if it comes back into use can hold up to 48 clean cattle	Large amount in different configurations ⁵ .	2240 sheep equivalents. Cattle, sheep, pigs.
MHC defined cattle	Yes	No	no, but capacity to house IAH-C herd	Cattle and sheep
Small animal SAPO4	No	BSU - breeding plus 2 experimental rooms	No	No
Small animal ACDP3	2800 mice in 224 cages	No	No	3000 mice in 600 boxes
Small animal ACDP2	2800 mice in 224 cages	Currently use the SAPO4 facilities	General small animal hose and SPF mouse house	10000 mice in 2000 boxes
Small animal conventional	224 cages; 6 isolators	Currently use the SAPO4 facilities	General small animal hose and SPF mouse house	30000 mice in 6000 boxes; 3 isolators
Poultry SAPO4	48-480 in 8 isolators (in progress)	No	490 in 7 rooms	No
Poultry ACDP3	48-480 in 8 isolators (in progress)	No	490 in 7 rooms	No
Poultry ACDP2/conventional	6000 in 61 rooms	No	Small amount of experimental accommodation	No
Poultry Production Unit	~3000 birds at different stages of SPF production	No	Small conventional production unit	No
Inbred poultry	Yes	No	No	No
Insectary	No	Yes	No	No
Gnotobiotic facilities	7 calf isolators; 12 pig isolators; 5 chicken isolators; theatre	No	No	3 large animal isolators for pigs, calves or lambs
Large animal theatre/surgery	Yes - conventional/gnotobiotic and ACDP 2/3	No	?	Yes
Bioimaging	Yes	Yes	Yes	Yes
Modelling	Yes	Yes	Yes	No
Bioinformatics	Yes	Yes	Yes	Yes
Mass spectrometry/ proteomics	Yes	No	Yes	Yes
Microarray suite	Yes	Yes	Yes	Yes
High throughput sequencing	No	Yes	Yes	No (but can do sequence analysis)
Robotics	?	Yes	Yes	Yes

⁵ Could house IAH-C MHC herd, sheep flock and, possibly, inbred pig lines