

Review of Farm Animal Genomics in relation to BBSRC-Funded Research

**A report for BBSRC Council
July 2005**

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Foreword

Agriculture is changing fast under many influences that include social, political, economic, environmental and climatic factors. This is happening at a time of rapid advances in fundamental understanding of animal science, enabled by developments in molecular biology and increasing accessibility to genomic information. It is therefore timely for BBSRC to review its research in farm animal genomics; science that makes important contributions to our understanding of basic animal biology, informs human medicine and underpins developments in the animal breeding, production and health.

BBSRC Council established the farm animal genomics review panel in July 2004 to take a medium- to long-term view of future research in relation to current strengths and weaknesses and to recommend a strategy that would optimise the delivery of research priorities and remove any existing barriers. The strategy must take account of related programmes by other national and international funders in order to promote partnerships to ensure a coherent and productive framework for farm animal genomics research. The terms of reference and membership of the panel are given in Annex 1.

In preparing the report, the panel has sought views from academia, research institutes, industry, Government departments, NGOs and the public: a consultation document and questionnaire (Annex 2) was sent to over 300 potentially interested parties and publicised on the BBSRC website and by the Genesis Faraday Partnership. A list of all respondents can be found at <http://www.bbsrc.ac.uk/society/consult/farmgen/>. In addition, respondents to the written consultation were invited to a discussion forum held at the Smithfield Show and attended by members of the panel. The views expressed by consultees were used extensively in preparing this report, and the principal messages returned are summarised on the BBSRC website (previous link applies). We also took account of relevant international developments and drew on numerous recently-published reports that relate to farm animal genomics (referenced as footnotes).

Structure

We begin in Chapter 1 with an overview of the field of farm animal genomics that reflects its current context, the principal justifications for doing this research, and flag some of the societal and ethical issues that arise from research activities in this area. In Chapter 2 we review the current ‘state of play’, including an appraisal of the key international genetic resources currently available. We review the current national investment in farm animal genomics and identify current strengths and weaknesses in UK research in this area. In Chapter 3 we propose some priorities and challenges for future research and in Chapter 4 identify improvements in delivery mechanisms to assist the development of this field. We end by considering the level of funding that will be needed if the UK is to capitalise on current expertise and resources in farm animal genetics/genomics.

Acknowledgements

BBSRC and the review panel wish to thank those who responded to the consultation exercise for the many carefully considered and informative comments submitted, and the other research funding bodies who helpfully provided information for this review.

Executive Summary

1. For the purposes of this review we use the term Farm Animal Genomics to encompass a range of genomics and genetics approaches. It is defined as:
‘Science that promotes the understanding of genetics and gene function in livestock animals and the application of this knowledge to life sciences in general, in particular to farm animal health and welfare, product quality and efficiency, and human health’.
2. Genetics and genomics provide powerful approaches to address questions in basic animal biology and for strategic research to inform policy development (including public goods), sustainable land use applications, the animal breeding and animal health industries and ultimately the food industry.
3. The UK has research strengths in quantitative and molecular animal genetics and is well-placed to exploit this knowledge base as it is home to some of the world’s leading animal breeding companies. Whilst most farm animal genomics research is set in an agricultural context, farm animal species are also important model animals. The chicken, in particular, is widely used to study early vertebrate development and has made important contributions to our understanding of immunological mechanisms.
4. The selective breeding of farm animals has been based, for the past 50-100 years, on the discipline of quantitative genetics, but the genomics era has now changed the manner and the context in which biological research is conducted. There are now unprecedented opportunities to expand our basic knowledge of the genetic control of traits, including difficult to measure traits such as quality of produce or disease resistance, and to develop breeding strategies that encompass molecular and quantitative approaches to a wider range of breeding goals.

Recommendation 1. BBSRC should attach a very high priority to current and future research in farm animal genomics. It has great potential to generate basic knowledge and is of enormous strategic importance.

Current BBSRC research relevant to farm animal genomics and genetics

5. BBSRC currently invests ~£16 million pa in farm-animal related research. Of this, approximately £5.5M relates to research with a genetics component, and a further £5.3M relates to research with a genomics component (2003/2004 snapshot). This makes BBSRC the UK’s largest funder of basic research in this area. However, BBSRC’s overall investment in this area has been static in the period 2001-2004, decreasing in real terms and as a proportion of BBSRC’s research budget.
6. Defra and SEERAD have significant strategic investments of £6.1M and £4.8M pa in livestock genetics programmes, respectively, which are heavily reliant upon the basic science portfolio of BBSRC. In addition, the Wellcome Trust has investments in the complementary area of farm animal health, including a new £25M initiative in farm animal health in the developing world. BBSRC therefore has a particularly important role in funding the basic science that underpins both its own strategic research and that of other major funders.

Future priorities for research

7. The most important areas for future research fall under four broad headings. These are the areas where we see significant scientific opportunity and which received a high level of support both from industrial and non-industrial respondents to our consultation:
- **animal health:** understanding the susceptibility to endemic and exotic diseases and selection of genetic traits to improve resistance to disease and pests, and development of therapeutic agents, vaccines and diagnostic tools. From this and other consultation exercises, **animal health** emerged clearly as the top research priority. More broadly, the influence of genetic variation on morphological, behavioural and other factors influencing animal welfare was also viewed as an important research area.
 - **animal production:** identification and selection of genetic traits to improve the quality and efficiency of animal products. A high priority is identification of traits that support the economic and environmental **sustainability of livestock agriculture**. Research to improve farm **animal welfare** in the context of production systems was also a high priority.
 - **animal biology:** exploiting the opportunities created by the availability of genomics tools and information for the use of farm animal species, especially chickens, as experimental animal models; comparative genomics and genetic biodiversity management and conservation. The highest priority here is research to **benefit human health** through reduction of zoonoses, improved nutritional quality of animal produce, and a better understanding of human biology from translational research.
 - **enabling tools and resources:** essential to realisation of the priorities above, and including generic molecular and numerical tools and skills, including genomics technologies, GM technologies, bioinformatics and quantitative genetics.

Recommendation 2: Within farm animal genomics, animal health should be the leading priority. This will require a fully integrated ‘systems’ approach including pathogen and pest research. Farm animal sustainability, welfare and human health also form important priorities. BBSRC should engage with other funders to co-ordinate coverage of priority areas, and should particularly seek to develop both the environmental genomics interface with NERC and the human biology interface with MRC.

Prioritisation of research by farm animal species

8. Having identified the leading priority areas for future research, there is also merit in further prioritisation on the basis of farm animal species.

Recommendation 3. BBSRC should continue to focus support on genomic/genetic research in the species in which it has significant prior investment (chicken, cow and pig), whilst ensuring the flexibility to invest in other species as important opportunities emerge. In particular, thus there is a strong strategic case for supporting the upcoming genome sequencing project for the pig, and the UK has an opportunity to take a lead in genomics and genetics research for economically important fish species.

Delivery mechanisms

9. We make a number of recommendations that will improve the delivery of farm animal genomics research in the UK.

Improving coordination and communication between the main funders

10. The UK lacks a coherent national strategy for farm animal genomics research, and all of the main funders (principally BBSRC, Defra, SEERAD, Wellcome and industry) would benefit from more coordination of their activities, particularly in developing opportunities for joined-up strategies, joint funding and effective international engagement

Recommendation 4: BBSRC - as a major player in this area – should take the lead in seeking to bring together the other funders, including industry, in an appropriate way – for example a funders forum. Early aims should be to map how current strategies join up, seek opportunities for joint funding and effective international engagement and explore how SR2006 monies might be jointly leveraged for this area of research.

11. BBSRC has two main institutes that conduct research of relevance to farm animal genomics - Roslin Institute and the Institute for Animal Health, which together receive ~60% of BBSRC's funding in this area. RI and IAH provide a critical mass of complementary expertise and resources and as such have a major strategic role to play in delivering the research priorities. It is clear to us that these institutes should be working together more effectively than at present; particularly given that animal disease is the highest priority for future research.

Recommendation 5: In the light of the 2005 IAE and the new Institute Science Strategy, Council should work with the Institute Directors to ensure that CSG is deployed appropriately for collaborative research and to consider the need for a new cross-institute programme (CIP) focussed on genetics/genomics of animal disease and resistance.

12. We are also aware of the potential developments in the Edinburgh area, following the Sibbett report in 2004, involving the proposed creation of a new centre for animal bioscience. We consider that embedding farm animal genomics and genetics research at RI within such a larger structure is highly likely to bring significant benefits: We strongly encourage BBSRC to support timely implementation of this initiative.

Management of resources

13. Farm animal genomics is resource intensive e.g. requiring access to research farms, herds, challenge facilities, large-scale data handling capability and bioinformatics resources. With a few exceptions (see section 8) the UK is generally well-equipped, but further gains could be made by improved coordination and utilisation of existing resources. BBSRC should also ensure that grants in this area do not encourage unnecessary duplication of existing resources.

Recommendation 6: Council should invite the other main funders (as part of recommendation 4) to discuss how better coordination of collective resources can be achieved. The parties should consider the scope for consolidation of expensive research tools and resources, how best to secure their long-term viability and minimise duplication.

14. We propose that use of experimental herds should be complemented by more extensive use of normal commercial farm herds to test hypotheses built using experimental animal populations. This could potentially be achieved by drawing and building upon the networking experience of veterinary and industrial associations in this area. Commercial populations provide large numbers that are essential for fine-scale genetic mapping, and whilst logistically ambitious, such measures will contribute greatly towards meeting the challenges of our recommended priority areas, especially farm animal health.

Recommendation 7: BBSRC should seek ways to promote greater utilisation of commercial farm animal resources in academic farm animal genomics research. We encourage BBSRC to take an ambitious stance in this matter; to take the initiative and use financial leverage to work with other stakeholders (Defra, SEERAD, industry) towards the formation of a national network of commercial farms collaborating with academic researchers.

Communication between research communities

15. There is great potential for the outputs of farm animal genomics to inform the understanding of human systems and vice versa. Whilst there is evidence of joint activities there is scope to stimulate more interest in the value of farm animal genomics research for informing human systems, particularly in comparison to accepted experimental model species (e.g. mouse).

Recommendation 8: BBSRC should promote more interaction between the animal and human bioscience research communities. Options include joint workshops or networking activities, studentships and fellowships. We are of the opinion that a targeted initiative specifically aimed at translational studies would be a positive move by the Council to establish collaborative research.

Communication between public and private sector research

16. The UK has a strong animal breeding industry of global importance. However there is little concerted investment in research because, with a few notable exceptions, the sector is composed largely of SMEs operating on tight margins. Poor communication and flow of people between the public sector and industry is another issue of concern in farm animal genomics. The general situation is being improved by the Genesis Faraday Partnership (established in 2003, core funded by the Scottish Executive and Defra and supported in part by BBSRC), which received much praise in the consultation.

17. The consultation also highlighted a concern of the end-user community that there often remains a clear gap between research that falls under BBSRC's remit and the necessary level of development of a technology before it can be taken forward by industry and other funders.

Recommendation 9: The Bioscience for Industry Strategy Panel should be invited to review BBSRC's current KT/innovation activities in this sector and advise how best to engage and leverage more joint funding in the future. We further recommend:

- continuing support for the activities of Genesis-Faraday, or an organisation fulfilling its role, over the medium term period and beyond, subject to review;
- funding mechanisms need to take better account of strategic relevance
- the funding available through the follow-on-fund should be increased, or expedite the current application process.

Improving funding mechanisms

18. Basic and strategic research in farm animal genomics often involves commitment over a number of years, and therefore tends not to lend itself well to the 3-year quanta of funding prevalent in BBSRC project grants. There is a significant advantage of the CSG-funding work in institutes, where there is a level of continuity of longer-term strategic research. Whilst longer-term research proposals are not excluded from the responsive mode, there is a perception in the community that such applications are disadvantaged compared to shorter, less expensive project proposals. We are aware that the Tools and Resources Strategy Panel recognise the difficulties in funding tools and resources and will be reporting to Strategy Board on how to overcome them. We welcome and fully endorse this move.
19. BBSRC's Strategic Plan emphasises the importance of tools, resources and technologies in advancing bioscience and this is particularly true for the resource-intensive field of farm animal genomics. However, tools and resources are often not considered to be 'hypothesis driven' and consequently do not fare well in the responsive mode. Further, the longer-term funding commitment required for upkeep and development e.g. of databases or biological resources and access to high throughput technologies, is not best delivered via 3-year project grants.

Recommendation 10: We are aware that the Tools and Resources Strategy Panel will be reporting to Strategy Board on how to best fund and maintain tools and resources. The Panel should consider how best to support long-term resources on a more stable basis – such as decoupling funding from the model of 3-year responsive mode awards.

20. Some aspects of farm animal genomics and genetics research are best delivered through large national or international consortia, e.g. genome sequencing or annotation. Opportunities for the involvement of UK research teams can arise relatively quickly, and must be seized where the scientific and strategic case is strong. The involvement of UK researchers in international efforts brings many 'unquantifiable' benefits from having a seat at the table. A highly relevant example of an emerging opportunity is that of the international effort to sequence the pig genome, in which we urge BBSRC's participation.

Recommendation 11: BBSRC's funding mechanisms need to be sufficiently agile to allow involvement in national and international consortia at relatively short notice. We suggest that this could be achieved by utilising a small 'e-panel' of experts to peer review and support or reject a proposal to participate in a new initiative. Taking a proposal for such involvement through the normal peer review process at the next available grant round may miss the window of opportunity. The move to four grant rounds per year will increase the frequency of application points but will not reduce the time to reach a funding decision post closing date.

21. It is important that a proportion of BBSRC responsive mode research is aligned to the needs of its users, in this case a diverse farm animal industry and Defra as the principal policy department. BBSRC should ensure that its Technology Strategy takes due account of the underpinning needs of this sector.

Recommendation 12: BBSRC's Technology Strategy should take full account of the needs of the farm animal genomics sector. In the first instance we would recommend that enabling technology priorities include the development of informatics platforms, real-time diagnostics, SNP-typing at 0.1 cents per genotype, creation of embryonic stem cell lines and development of cryopreservation capabilities for farm animal germ lines.

Training

22. From the consultation exercise, academia and industry report shortages of researchers with skills in mathematical genetics, bioinformatics, biochemistry and whole animal pharmacology/physiology. Some of these skills shortages are impacting elsewhere in BBSRC's remit, and unless addressed will have consequences for the overall delivery of BBSRC's Vision and Strategic Plan.
23. There is an opportunity for the farm animal genetics industry to contribute to the funding of studentships in shortage areas to make them more attractive, following a similar scheme recently initiated to increase the level at which *in vivo* pharmacology and physiology studentships are funded. In addition, short-term visiting fellowships, industrial fellowships, more joint university/institute studentships which involve periods of research at both institutions and increased flexibility of student funding are all mechanisms by which training shortages could be met.

Recommendation 13: BBSRC should use the full spectrum of activities under studentships and fellowships, including bespoke fellowship calls and targeted incentives where necessary, to address:

- **skills shortages in the farm animal genomics area, in particular informatics and quantitative aspects;**
- **improve the flow and communication between industry and academia (see recommendation 9);**
- **improve the flow and communication between this area and research on human systems (see recommendation 8).**

BBSRC should also invite industry to jointly fund in key shortage areas using a similar model to that employed for integrative mammalian physiology and robustly support Genesis-Faraday CASE awards.

Ethics and public dialogue

24. Societal and ethical concerns related to farm animal genetics and genomics include concerns about the integrity, health and welfare of new genotypes, and the production of animals able to survive in poor and inappropriate environments. All BBSRC sponsored research in the area of farm animal genomics and genetics should be firmly embedded in a context of ethical awareness and public dialogue, and funders, institutions and researchers in the field share this burden of responsibility. However, it is our opinion that in most cases it is considerably more effective for individual PIs to contribute to established communication networks and programmes than to create their own.

Recommendation 14: All BBSRC research in this area should be embedded in a context of ethical awareness and public dialogue. Concerns about the health and welfare of animals used in and produced by farm animal genomic technologies can partly be addressed by the development of new welfare screening methods.

Future Funding

25. BBSRC is already the largest funder of basic research on farm animal genetic/genomics in the UK but its real-terms and proportional investment in this area has been steadily decreasing since 2001. Council may wish to consider in the light of this report whether the current level of investment is sufficient going forward? We are aware the BBSRC has earmarked £6M over the SR2004 period for research into animal health and welfare to seize opportunities presented by advances in genomics. This is to be welcomed but is not sufficient if the UK is really to capitalise on existing expertise, become a leading Nation - scientifically- in this field and retain its current strong economic position in animal breeding and animal health.

Recommendation 15: BBSRC's SR2004 investment should be seen as the vanguard for increased investment in farm animal genomics through into SR2006 and beyond. BBSRC should seek to ensure that the total new investment in this area is in the order of £25M over the next 5 years. Earlier in this report we propose several priorities for such funding and mechanisms to improve its deployment.

CHAPTER 1: FARM ANIMAL GENOMICS RESEARCH IN THE UK

- 1.1 In this chapter we introduce the field of farm animal genomics in the UK as it presently stands: its historical context, an evaluation of the merits of undertaking such research and societal and ethical issues that arise as a result.

Scope of the Review

- 1.2 For the purposes of this review we use the term Farm Animal Genomics to encompass a range of genomics and genetics approaches as follows:

‘Science that promotes the understanding of genetics and gene function in livestock animals and the application of this knowledge to life sciences in general, in particular to farm animal health and welfare, product quality and efficiency, and human health’

Historical Context and Background

- 1.3 Since early civilisation, humans have bred livestock animals to better fit various purposes including food, clothing and draught power. During the last few decades quantitative genetics has allowed more rapid breeding progress in easy to measure traits such as growth and fat levels. Most recently, we have been able to establish the genetic basis for some livestock characteristics. There are now unprecedented opportunities to expand our knowledge of the genetic control of traits, including difficult to measure traits such as meat quality or disease resistance, and to develop more advanced and sustainable breeding strategies that encompass molecular and quantitative approaches to a wider range of goals.

Contribution of farm animal genomics to basic science

- 1.4 UK genetic research in farm animals, whilst emerging largely from an agricultural context, has provided an important contribution to our understanding of fundamental biological processes in animals: farm animal species have emerged as important model or experimental animals. For example, chickens are widely used to study early vertebrate development as the embryo can be more readily accessed and studied than its mammalian counterparts. In addition, sheep are used as models to study respiration and reproduction and pigs for the study of obesity related traits or organ transplantation. Farm animal genomics research has led (and will increasingly do so) to an improved understanding of fundamental animal biology, and there are important gains to be made to human health from this knowledge

Sustainable livestock production

- 1.5 In the UK, where the demand for animal products is either stable or growing only slowly, the market is subject to other changes in demand, needing to respond to consumer concerns about animal health and welfare, product quality and product safety. There are also societal and Government policy drivers to develop more sustainable agricultural systems with reduced environmental footprints. The UK Government, through Defra and SEERAD, has stated a policy commitments to sustainable farming^{1,2},

¹ The strategy for sustainable farming and food - facing the future. (2002). Defra publications.

² A forward strategy for Scottish Agriculture (2001). Scottish Executive.

including animal health and welfare³, and has responsibility for conservation of biological resources⁴. Research in the area of farm animal genomics will contribute to this policy goal. Animal (product) quality, health and sustainability are determined by a combination of environmental and genetic factors. Modifying animal characteristics in response to changes in demand can be effected by changes in environmental inputs (e.g. feed, pathogens, vaccines, housing) or in genotypes, or both. Genetic improvements can be slower to implement but they are permanent, cumulative and have low maintenance costs; all features that are consistent with increased sustainability.

- 1.6 Improvements through selective animal breeding have had a major impact on animal productivity and performance, particularly over the past fifty years. However whilst these successes have been of considerable benefit, in other desired traits progress has been slower particularly in relation to fitness and disease resistance. Genome research in farm animals is already providing new understanding of the genetic control of complex traits and this new understanding is beginning to inform genetic improvement: there is clearly enormous scope for farm animal genomics to contribute to sustainability goals and public goods, and in doing so boost the favourable global position of UK animal biosciences.

Farm animal genomics and UK industry

- 1.7 UK research in the 20th century made substantial contributions to global knowledge on animal breeding and this can be linked directly to the presence within the UK of some of the leading global breeding companies. The world's first true livestock breeding companies were founded in the UK with advice from relevant academic groups. Global demand for animal products is predicted to increase by 50% by 2020 with most of the increase in demand arising in the developing world⁵. The UK livestock domestic market encompasses an estimated 200,000 livestock holdings and 500,000 related jobs (year 2000), and annual outputs of €13.5 billion (~£9.7b) (year 2002), of which €11.6b (£8.3b) related to livestock production⁶. It represents 60% of the UK's agricultural goods output of €22.6b (£16.2b; year 2002) and is therefore economically more important than crop production^{6,7}.
- 1.8 In addition, the UK farm animal health sector is worth an estimated £190 million per annum, excluding companion animals. The Global market for animal health products in 2002 was approximately \$14 billion, with animal products accounting for 62% of this market⁸. The world's largest animal health business is a British company and two of the top three companies have significant research operations in-house in the UK.

³ Animal health and welfare strategy for Great Britain. (2004). Defra publications.

⁴ UK Country report on farm animal genetic resources (2002). Defra publications.
<http://www.defra.gov.uk/farm/geneticresources/animalgenetics.pdf>

⁵ Livestock to 2020 - the next food revolution. Food, agriculture, and the environment Discussion Paper 28, Delgado, C. *et al.* (1999). International Food Policy Research Institute, Washington

⁶ Eurostat figures.

⁷ Review of the experience of implementation by UK stakeholders of access and benefit sharing arrangements under the convention on biological diversity (2005). Defra publications.

⁸ Immunodiagnosics and nucleic acid testing kits for the veterinary industry: current status and future prospects. Bogdanovic, S. and Langlands, B. (2003). PJB Publications Ltd (SR227).

- 1.9 A healthy research base in farm animal genomics in the UK is essential to nurture our industry. The increased understanding of complex traits offered by the genomic revolution will increase the vigour of the farm animal commercial sector. For example, UK companies are amongst the world leaders in breeding pigs, poultry, cattle and fish and disseminating this genetic improvement to global markets. These companies are well placed to exploit modern genetics and genomics approaches.

Farm Animal Genomics – Current State of Play

- 1.10 The selective breeding of farm animals has been based, for the past 50-100 years, on quantitative genetics. This is, in essence, conducted at the whole genome level. However, the models describing the genetic control of complex traits were essentially ‘black boxes’ in which the number of parts (genes), the size of their effects and the interactions between them were all unknown. We now have molecular tools that allow the expression of thousands of genes to be studied simultaneously. We have molecular and statistical tools to scan the genome of the major farm animal species as well as some wild and cultured fish species for the locations of genes controlling complex traits, so-called quantitative trait locus (QTL) mapping.
- 1.11 The shift towards genomic modes of investigation undoubtedly represents a paradigm shift as important as the advent of molecular genetics was in the late 1980’s to early 1990’s. Whilst bringing initial high expense and new logistical (curation) challenges, it is often forgotten that this is offset by the often quite startling savings made in molecular genetic reagents and research time: Southern analysis becomes redundant and paralogs can be identified in minutes. Entire new genome-wide approaches, such as genome wide RNAi knock-down or expression analysis not only become feasible, but often cost effective compared to more targeted molecular biology approaches. The genome revolution has already made an impact in farm animal research. It used to take an entire PhD project to find a farm animal ortholog of a human gene: something that can now be achieved with a quick database search. Our understanding of the genetic control of quantitative traits has been revised in the light of results from QTL mapping experiments⁹ and in a very few cases the single nucleotide mutations that explain a significant fraction of the variation in some quantitative traits have been identified¹⁰. With the advent of genomics, QTL mapping and population genetics are becoming much more integrated into basic biology.
- 1.12 **Current genome resources:** Draft genome sequences have been completed (chicken, 2004¹¹), are in progress (cattle, due to complete 2005¹²) or planned (pig). Clone-based physical maps (BAC contigs) have been completed or are in the final analysis phase for

⁹ Genetic mapping of quantitative trait loci for growth and fatness in pigs. Andersson, L., Haley, C.S., Ellegren, H., Knott, S.A., Johansson, M., Andersson, K., Andersson-Eklund, L., Edfors-Lilja, I., Fredholm, M., Hansson, I., Håkansson, J. and Lundström, K. (1994). *Science*, **263**, 1771-1774; Domestic animal genomics: deciphering the genetics of complex traits. Andersson, L. and Georges, M. (2004). *Nature Review Genetics* **5**, 202-212.

¹⁰ E.g. Positional identification of a regulatory mutation in *IGF2* causing a major QTL effect on muscle development in the pig. Van Laere, A-S., Nguyen, M., Braunschweig, M., Nezer, C., Collette, C., Moreau, L., Archibald, A.L., Haley, C.S., Andersson, G., Georges, M. and Andersson, L. (2003). *Nature* **425**, 832-836.

¹¹ Sequence and comparative analysis of the chicken genome provides unique perspectives on vertebrate evolution. Hillier *et al.*, International Chicken Genome Sequencing Consortium (2004). *Nature* **432**, 695-716.

¹² <http://www.hgsc.bcm.tmc.edu/projects/bovine/> http://pre.ensembl.org/Bos_taurus/

chickens, cattle and pigs¹³. Extensive libraries of large fragment genomic (e.g. BAC) and cDNA clones are available. From the latter, between 400,000 and 550,000 expressed sequence tags (ESTs) are in the public domain for cattle, chickens and pigs¹⁴. The cDNA clones or EST data have been used to develop microarrays (cDNA, oligo and Affymetrix GeneChips) with up to 20,000 independent probes per array for chickens, pigs and cattle. Many of these resources are available through the UK Centre for Functional Genomics in Farm Animals (*ARK-Genomics*)¹⁵. Genome wide linkage (chicken, cattle, pig, sheep) and radiation hybrid (cattle, pigs) maps with more than 2,000 mapped loci per map have been constructed. In addition to the 1,000 - >2,000 microsatellite markers available for each species, hundreds of thousands of single nucleotide polymorphisms (SNPs) are being identified as a by-product from the sequencing projects¹⁶. Bioinformatics resources include genome databases¹⁷, genome sequence databases¹⁸ and web resources¹⁹. Similar resources are being developed for some economically important fish species, e.g. salmonids, tilapia, sea bass. For sheep, other than linkage maps and a BAC library, most resources are held privately by groups in Australia and New Zealand, though there is now an international collaboration (part funded by BBSRC and SEERAD) to develop a clone based physical map of the sheep.

- 1.13 UK researchers have provided strong leadership in a number of high profile initiatives relating to farm animal genomics, including the chicken and bovine genome sequencing projects, ovine genomic resources and the European Animal Disease Genomics Network of Excellence for Animal Health and Food Safety (EADGENE). In addition, the UK benefits from strong international research leadership in the genetics of animal health, the management of farm animal genetic resources, and the genetics/genomics of farm animal pathogens. UK researchers have coordinated, and participated in, a number of significant EC projects that have been world firsts, relating to animal health, meat quality and description of genetic resources.
- 1.14 Farm animal genomics is clearly entering a new era of scientific opportunity. It is therefore timely for BBSRC to evaluate its current and future research commitments within the field.

Justification: why should BBSRC invest in farm animal genomics research?

- 1.15 BBSRC's mission directs the Council to:
 - i. promote and support, by any means, high-quality basic, strategic and applied research and post-graduate training relating to the understanding and exploitation of biological systems.

¹³ http://www.sanger.ac.uk/Projects/S_scrofa/ <http://www.bcgsc.ca/lab/mapping/bovine>

<http://www.genome.wustl.edu/projects/chicken/index.php?fpc=1>

¹⁴ http://www.ncbi.nlm.nih.gov/dbEST/dbEST_summary.html

¹⁵ <http://www.ark-genomics.org>

¹⁶ http://www.ncbi.nlm.nih.gov/SNP/snp_summary.cgi

¹⁷ <http://www.thearkdb.org>

¹⁸ e.g. <http://www.ensembl.org>

¹⁹ e.g. <http://www.chicken-genome.org>

ii. advance knowledge and technology (including the promotion and support of the exploitation of research outcomes), and provide trained scientists and engineers, which meet the needs of users and beneficiaries (including the agriculture, bioprocessing, chemical, food, healthcare, pharmaceutical and other biotechnological related industries), thereby contributing to the economic competitiveness of the United Kingdom and the quality of life.

1.16 **Following these principles, we consider that the field of farm animal genomics is a highly important area for strategic investment.** The following factors directly contribute to this judgement:

1. Benefits to the knowledge pool. Farm animals offer particular advantages for the study of fundamental biology that cannot easily be addressed using rodent and other model systems. For example, a large amount of current knowledge of vertebrate (including human) embryonic development can be attributed to work on chicken embryos, and this model system is likely to continue to be at the centre of vertebrate embryology. Other notable advantages of farm animals in basic research include:

- Livestock populations and breeds offer much greater within and between population genetic diversity than found in laboratory (inbred) mice. Experimental crosses between diverse breeds can be combined with analysis of segregating commercial populations for high-resolution linkage or recombination mapping, a combination not possible in human genetics. In this way, farm animal genomics has the potential to make prominent contributions to human biology and medicine, in addition to its direct applications for farm animals;
- Pigs and cattle are physiologically much more comparable to humans than rodents, and for this reason pigs are used, for example, in research related to human cardiovascular disease; pig tissues are also used in organ transplantation. Sheep are commonly used as a model species in human reproduction and fertility research, and provide models of other diseases such as Cystic Fibrosis or transmissible spongiform encephalopathies (TSEs);
- UK expertise in farm animal genomics has substantial potential for creating and strengthening the interface between functional genomics and developmental biology, which is a major strength of UK science;
- As many farm animals represent the ideal research platform for wild species of interest to environmental and other researchers, expertise in farm animal genomics has the potential to revolutionise the study of ungulate and avian wild populations. This is a major potential interface between BBSRC and NERC research areas.

2. Societal and policy benefits. Research in farm animal genomics provides new technologies such as marker assisted selection to improve the accuracy and pace of breeding programmes, and new diagnostic tools. This has the capacity to benefit society beyond direct contribution to a healthy UK economy, by contributing to, for example:

- The improved nutritional value of food;
- Improved models/tools for human biology and medicine;

- Reduction of infectious disease or reduced impacts of disease (e.g. via breeding for resistance or new/improved vaccines), resulting in return in improvements for animal welfare, food supply, food quality and nutrient capture (reduced pollution), and reduced zoonotic disease transfer and use of chemical intervention;
- Monitoring, management and conservation of genetic diversity within domestic animal populations, captive breeding programs and wild populations;
- Directly improved animal welfare (e.g. Reduction of piglet mortality, aggressive and injurious behaviour in pigs and poultry and improving cattle fertility and calf delivery);
- Better landscape management by grazing ruminants genetically selected for appropriate environmental impact.

In addition, research in this field informs Government policy development, including:

- Providing tools and expertise for surveillance and control measures for diseases and pests of farmed animals;
- Identifying and utilising genetic markers for food traceability, authenticity and security;
- Providing better technologies to address environmental and zoonotic challenges presented by the predicted major global growth in the human consumption of animal produce.

There may also be important benefits for health and welfare of developing world societies by promoting breeding strategies for sustainable pastoral agriculture, especially in challenging environments. This may lead to enhancement of livestock for:

- Reduced susceptibility to prevalent endemic diseases;
- Increased hardiness;
- Increased nutrient capture efficiency- maximising arable resources
- Improved nutritional value of animal products;
- Breeding livestock that are better suited to local environmental and management conditions.

Delivering such benefits could have tangible impacts on human and animal health and welfare in developing world environments.

3. Benefits to the UK economy.

It is a central tenet of BBSRC's mission to fund science that contributes to the continued fitness and future positioning of UK industry. Farm animal genomics exists largely in the context of the multi-billion pound agricultural and food industries. The UK currently has a strong livestock industry, but it is under great pressure due to many factors, including strong international competition, loss of subsidies, the socio-economic impacts of recent high-profile disease epidemics (e.g. BSE, FMD) and the financial and welfare impacts of lower profile endemic diseases (e.g. TB). Investment in genetics and genomics research in this area provides essential tools to promote innovation and problem-management within the industry and thereby support its long-term competitiveness. These include:

- Technology for improvement of rational breeding strategies in response to production, environmental, welfare and/or disease challenges;
- Technology for increased quality, safety and efficiency of animal produce;
- Technology for production of therapeutics and nutraceuticals ('pharming');
- Technology for selective breeding of livestock for performance whilst minimising inbreeding and loss of genetic diversity;
- Monitoring and management of genetic diversity within domestic animal populations;
- Pedigree control;
- Directly improved animal welfare (e.g. Reduction of piglet mortality and poultry aggression).

Some of these benefits overlap with benefits to society and policy.

1.17 The benefits arising from continued investment in farm animal genomics are compelling. The area is clearly of high importance both to the UK R&D agenda and the strategic priorities of BBSRC in its role as a funder of UK science, a message that was overwhelmingly returned by a diverse range of stakeholders in response to our consultation exercise.

Social and ethical issues arising from farm animal genomics research

1.18 Although farm animal genomics/genetics represents an important strategic area of research for BBSRC, this field also straddles some of the more prominent ethical and societal issues facing the biological sciences. The need to carefully consider the ethical and social implications of research in this field was a strong message returned in the consultation exercise. It is worthy of counter-note, however, that the ethical imperative in some aspects of this research is to press ahead especially where research could lead to the direct reduction in farm animal discomfort (e.g. combined farm animal and pest/pathogen genomics research for the better diagnosis and understanding of disease) and a better understanding of many wild species in need of conservation, both in the UK and abroad.

1.19 The critical potential social and ethical issues, as we see them, include:

- Public perception/acceptance of research and technologies, particularly in relation to areas that have already attracted controversy in other fields, such as stem cell research and genetic modification (GM) technologies. There is also, notably, resistance in some quarters to the use of any animals in research;
- Adverse welfare impacts in experimental animals or through inappropriate selective breeding decisions in commercial livestock;
- The utilisation of technology to support the promotion or continued use of poor husbandry practises and/or the use of livestock in entirely inappropriate environments;

- Loss of biodiversity through more effective and targeted breeding strategies, and potential short-term increases in inherited disease and disease susceptibility due to the predominance of a small number of individuals in breeding programs.

1.20 Recommendations as to how we address some of the leading social and ethical issues presented by the field are given in Chapter 4.

Conclusion

1.21 Farm animal genomics is of high strategic importance to the UK, and to BBSRC's remit in terms of high quality basic research. There is a wide range of benefits from such research, at the scientific, industrial/economic and societal levels. Integrating research in farm animal genomics and pest/pathogen genomics will be essential to understand host-pathogen interactions and tackle disease. The field presents a number of important ethical and social challenges which must be met, and in which BBSRC must play a part, as well as other public agencies and end users of the research.

Recommendation 1. BBSRC should attach a very high priority to current and future research in farm animal genomics. It has great potential to generate basic knowledge and is of enormous strategic importance.

CHAPTER 2: CURRENT BBSRC RESEARCH RELEVANT TO FARM ANIMAL GENOMICS

- 2.1 In this chapter we summarise the current funding landscape for farm animal genomics, including the level and distribution of current BBSRC investment and the major funding investments in the field by other bodies.

Funding arrangements for farm animal genomics research in the UK

Public Sector

- 2.2 UK academic research in farm animal genomics is funded currently through various mechanisms, including Research Council responsive mode, coordinated initiatives, core-funded programmes at research institutes, Government Departments' research programmes, industrial support through Levy Bodies, Government support for industrial research through LINK, regular workshops and central facilities.
- 2.3 The UK academic community in this field is spread mainly across University research groups and research programmes in Institutes. Significant concerted investment in farm animal research is currently directed through two BBSRC-sponsored institutes, Roslin Institute (RI) and the Institute for Animal Health (IAH). There are related research programmes at the SEERAD-funded Moredun Research Institute and Scottish Agricultural College.
- 2.4 Considerable expertise, particularly in the areas of animal disease and welfare, is located within the UK's Veterinary schools, the Animal Health Trust and the Defra-funded Veterinary Laboratories Agency (VLA). Ex-University research on aquatic species is centred upon two major research centres- the multi-site, Defra-funded, Centre for Environment, Fisheries and Aquaculture Science (CEFAS) and the SEERAD-funded Fisheries Research Services (FRS), which has freshwater and marine laboratories.

Private Sector

- 2.5 Of the Genesis-Faraday membership, at least 30 private companies are known to have R&D investments in this area. R&D investments of the private sector players range from in-kind contribution of resources worth a few thousand pounds to R&D programmes of a few million pounds per annum, for the larger breeding companies, to tens of millions (and even hundreds, when global spend is considered) for the animal health companies. An e-mail and telephone survey of the major commercial breeding organisations in the UK identified that the seven respondents to the survey had a total UK R&D spend of £13.6m PA on genetics and genomics (excluding the costs of on-going selection)²⁰. At least two farm animal breeding companies have in-house molecular genetic laboratories. In kind contributions by industry can also be very significant; e.g. large datasets or library/array resources.

²⁰ Survey undertaken by Genesis Faraday. Respondents provided information for use in an aggregate total figure, individual company figures are confidential. Most animal health companies declined to provide information on R&D spend.

- 2.6 Industry has an excellent track record of investment via LINK programmes in farm animal genomics and genetics research. In addition, eleven of Defra's industry-led Sustainable Livestock Production LINK projects have been in the area of farm animal genomics, with industrial investments of £442k in 2003-2004, and projected commitments of £689k for 2004-2005. Funding of individual projects is often by a relatively large number of relatively small stakeholders, possibly reflecting the high number of SMEs operating in this sector. Industry also invests in Knowledge Transfer activities, such as Levy Board pump-priming of the uptake of new selection technologies.
- 2.7 Overall, there is an enthusiastic 'route to market' for academic research throughout the spectrum of UK commercial stakeholders in the area, from SME's to multinationals.

BBSRC Funding

- 2.8 The term 'genomics' is used in this report to cover a broad spectrum of genetics and genomics approaches. However, for an analysis of BBSRC's funding this term is dissected to separate projects taking a predominantly 'genomics' approach from those that are predominantly 'genetics'. Figures presented must be considered to be approximations. Rigorous distinction between categories of research is difficult in many cases, and a broad definition of genetics was used in our database searches, e.g. including single gene studies where protein function was directly referenced to underlying gene sequence. A necessary, if somewhat arbitrary, line was drawn at protein-protein interaction studies. The inclusive definition of genetics will tend to overestimate the funding of 'genetics' in a narrowly defined classical sense but is consistent with the approach adopted throughout this report.
- 2.9 **Table 1** summarises BBSRC funding for research on farm animal species from 2001 until 2004. The proportion of funding allocated to genomics and genetics related projects (combined) has remained relatively constant, at 62-64% of all farm animal research. However, the level of funding for genomics has increased 33% in this period (mean) both in CSG and responsive mode. Over the same period, the funding for other genetics-related research has commensurately decreased by 21% (mostly in CSG). Funding for other (non-genetics based) farm animal research has remained relatively static, as has the overall spend on all farm-animal related research. That said, this static funding position represents both a 16% proportional decrease in farm animal research funding with respect to BBSRC's overall research commitments during this period and a 17% decrease in farm animal genomics and genetics funding.

Table 1: Summary of BBSRC funding for farm animal research

Funding category	Research funded per financial year (£k)		
	2001-2002	2002-2003	2003-2004
Genomics			
CSG	1,396	1,861	1,896
Responsive grants	2,622	2,241	3,460
Studentships	44	54	70
Total	4,062	4,156	5,426
Genetics			
CSG	3,775	3,651	2,679
Responsive grants	3,181	3,260	2,821
Studentships	100	105	98
Total	7,056	7,016	5,598
Non-genomics/genetics			
CSG	3,166	3,499	3,006
Responsive grants	2,535	2,735	2,852
Studentships	571	641	693
Total	6,272	6,875	6,551
Genomics + genetics combined total	11,118	11,172	11,024
Grand total	17,390	18,048	17,575
Total BBSRC research spend*	192,500	207,100	229,900
Genomics + genetics combined total as % of grand total	63.9%	61.9%	62.7%
Genomics + genetics combined total as % of total BBSRC spend	5.8%	5.4%	4.8%
Grand total as % of total BBSRC spend	9.0%	8.7%	7.6%

* Includes CSG, responsive research grants, initiatives, studentships and fellowships: figures from BBSRC annual reports.

2.10 **Table 2** summarises recent BBSRC funding in farm animal genomics, genetics and non-genetics research, and sub-divided by the primary subject animal. Avian species (primarily chicken) receive the largest research investment, which has been steadily maintained across the genetics and non-genetics categories; high but decreasing investments in avian genomic projects reflect high investment in the chicken genome project, which has tailed off over 2001-2004. Whilst bovine and ovine research commitments are relatively substantial in non-genetics and genetics research categories, investment in genomics in these species has been less. Funding for ovine research decreased significantly during 2001 to 2004 in all but genomics related projects the funding for which has risen steeply reflecting a transition from non-genomics research. However, the overall investment in ovine research is lower now that it was in 2001.

Table 2: BBSRC funding in farm animal research by species

Funding by species: combined CSG + grants + studentships	Research funded per financial year (£k)		
	2001-2002	2002-2003	2003-2004
Genomics			
Avian	2,034	1,632	1,309
Porcine	377	514	804
Bovine	133	399	585
Ovine	45	186	247
Fish	151	228	498
Farm animals (general)	1,235	1,131	1,898
General bioinformatics	87	67	85
Total	4,062	4,157	5,426
Genetics			
Avian	2,177	2,422	2,089
Porcine	659	646	641
Bovine	942	1,275	711
Ovine	1,620	967	643
Goats	26	15	67
Equine	71	0	0
Fish	460	397	266
Invertebrate (Shellfish)	15	92	92
Farm animals (general)	1,086	1,202	1,089
Total	7,056	7,016	5,598
Non-genetics			
Avian	1,442	1,792	1,591
Porcine	322	447	628
Bovine	1,056	1,690	1,889
Ovine	1,313	902	410
Equine	0	7	14
Deer	0	0	7
Fish	437	428	398
Farm animals (general)	1,756	1,609	1,614
Total	6,326	6,875	6,551
Grand Total	17,444	18,048	17,575

2.11 **Table 3** summarises the funding for farm animal research through CSG to sponsored Institutes. For genomics research, RI is the major recipient of CSG funding, which has remained relatively static between 2001 and 2004. The proportion of IAH-awarded CSG spent on genomics research projects increased 276% over this period, to 46% of the level of RI. For other genetics research, IAH was the institute receiving the most CSG funding, although this decreased steeply (35% reduction) between 2001 and 2004. RI also received over £1M pa for research in this category, the figure decreasing by 16% between 2001 and 2004. Overall, CSG spend on farm animal genomics projects has increased by 36% over the 2001-2004 period, whilst commensurately decreasing (29%) in other genetics-related projects.

Table 3: Core strategic grant funding distribution for farm animal research

CSG funding by Institute	Research funded per financial year (£k)		
	2001-2002	2002-2003	2003-2004
Genomics			
RI Total	1,204	1,298	1,152
IAH Total	192	563	530
IGER Total	0	0	214
Total	1,396	1,861	1,896
Genetics			
RI Total	1,221	1,051	1,030
IAH Total	2,455	2,508	1,572
BI Total	99	92	77
Total	3,775	3,651	2,679
Non-genetics			
RI Total	126	14	0
IAH Total	969	1,443	1,158
IGER Total	667	764	826
SRI Total	764	950	703
BI Total	419	111	6
IFR Total	221	217	313
Non-genetics total	3,166	3,499	3,006
Genomics + genetics total	5,171	5,512	4,575
Grand total	8,337	9,011	7,581

2.12 **Table 4** summarises recent responsive mode funding (mean annual funding, 2001-2004) for farm animal genomics and genetics projects by recipient institution. Non-genetics-related projects are excluded from this analysis.

Table 4: Responsive grant distribution for farm animal genomics & genetics research

Research provider	£k*	Research provider	£k*
Roslin Institute (RI)	1,747	Brunel University	73
Inst. for Animal Health (IAH)	702	Imperial College London	62
University of Nottingham	598	St Georges Hospital Medical School	62
University of Edinburgh	440	University of Dundee	58
University of Cambridge	245	University of Portsmouth	54
University of Aberdeen	186	King's College London	49
University of Glasgow	184	Queen Mary, University of London	48
University of St Andrews	154	University of Wales College of Medicine	48
Royal Veterinary College	148	University College London	46
University of Liverpool	140	University of East Anglia	35
University of Stirling	133	University of Wales at Cardiff	22
The Wellcome Trust Sanger Institute	124	University of Leicester	21
University of Manchester	119	University of Sheffield	18
University of Reading	114	University of Leeds	17
University of Bristol	90	University of Southampton	17
University of Exeter	88	Queen's University of Belfast	2
		Total	5,844

- 2.13 RI received by far the highest mean annual allocation of responsive mode funding, at £1.75M, followed and IAH at £0.70M. A further eleven HEIs received mean annual responsive funding of greater than £100k. Combining the CSG and Responsive mode funding as shown in tables 3 and 4 reveals that RI and IAH were allocated approximately 35% and 25%, respectively, of BBSRC's total spend for farm animal genomics and genetics research (2003-2004 CSG snapshot and mean annual responsive mode allocation over 2001-2004), demonstrating the critical strategic importance of the two institutes in delivering BBSRC's research portfolio in this area.
- 2.14 Whilst Tables 1 to 4 exclude research projects that are focused on animal disease agent and parasite species, BBSRC has a highly significant investment in this area. The overall investment in research relating to agents of animal disease is summarised in Table 5, which includes funding through CSG, responsive grants and studentships. The funding in table 5 is additional to the host-focused investments given in tables 1 to 4 (non-overlapping). Although these figures relate to all animal disease, the great majority of projects funded are directly related to, or indirectly impinge on, diseases/pests of farm animal species. BBSRC has funded the genome sequencing of *Eimeria*, *Neospora* and several bacterial pathogens.
- 2.15 The summary includes all categories of research (e.g. genomic, genetic, protein, therapeutics, modelling) but does not include research on foodborne TSEs. Whilst funding for farm animal species has remained static (decreasing in real terms), it is notable that investments in research for animal disease agents have increased by 25% between 2001 and 2004.

Table 5: BBSRC funding commitments in animal disease research

Research category	Research funded per financial year (£k)		
	2001/02	2002/03	2003/04
Endemic diseases (excluding parasites)	3,081	3,882	4,059
Exotic diseases	1,595	1,681	2,920
Other diseases	613	994	803
Parasites	1,790	1,748	1,819
TSEs	2,747	2,743	2,664
Total	9,826	11,048	12,265

Major programmes

- 2.16 There have been a number of recent BBSRC initiatives relating to genomics and genetics research, including Genomics in Animal Function (GAIN, - £7M investment), Investigating Gene Function (IGF- £18.9M investment), Exploiting Genomics (£25M investment) and Functional Genomics Technologies (3.1M). Investments in farm animal genomics arising within these initiatives are included in the funding figures presented in Tables 1 to 5, under the responsive grant category (where stated). The most significant resulting investment related to farm animal genomics research was the establishment of *ARK-Genomics* (RI) as one of seven consortia funded under the IGF initiative.

Other Funders

Defra

2.17 Defra is the major supporter of strategic and applied livestock genetics research in the UK. Recent investments under Defra's livestock genetics and genomics programme are summarised in Table 6. Defra funds in all of the major UK farm animal groups. In particular the Department has been a key funder of QTL mapping studies in pigs, cattle, sheep and chickens. The costs of establishing the necessary experimental animal populations and capturing the phenotypic data in such studies are substantial and Defra funding is critical in meeting these costs. Through the Sustainable Livestock Production LINK programme Defra has encouraged engagement with and participation by industry, typically in pre-competitive consortia of breeding companies. These LINK programmes could also be viewed as successes for the industrial partners in leveraging government funding to match their cash or in-kind contributions. Defra has also funded the development of genomics tools and resources, e.g. the pedigrees used for linkage mapping and part of the international programme to develop physical (BAC) maps of the pig genome. Over half of Defra's recent funding commitments in the area have been in the area of TSE research, highlighting the great prominence of TSE concerns on the agricultural R&D agenda.

Table 6: Defra funding commitments within the livestock genetics/genomics programme (£k)

Category	Research funded per financial year (£k)		
	2001-2002	2002-2003	2003-2004
Beef Cattle	142	151	172
Dairy Cattle	163	365	402
Sheep	395	398	414
Pigs	11	46	224
Poultry	291	463	479
Mice (transgenic)	544	728	734
TSE projects	3,751	3,425	3,629
Total	5,297	5,576	6,054

2.18 CEFAS receives £32M PA Government funding, £29M from Defra²¹. Fisheries biology and aquaculture and fish health research at CEFAS do not include significant genetics/genomics programmes, and take place as a subset of a wider remit including fisheries management, environmental management, environmental quality, food safety, information systems and commercial business development.

SEERAD

2.19 SEERAD's recent funding commitments in farm animal genomics research are summarised in Table 7. SEERAD funding of research in farm animals is focused largely on ruminants, historically sheep but increasingly also on cattle, and on fish. Two routes of funding support this work. A significant proportion of the SEERAD funding is committed to research programmes in the Scottish Agricultural and Biological Research

²¹ CEFAS Annual Report and Accounts 2003-2004, Defra.

Institutes (SABRIs)²². SEERADs programmes are complementary to those of BBSRC and Defra, focussing on quantitative genetics to improve product quality, animal health and welfare, and on the development of sustainable breeding strategies. Molecular genetics is used increasingly in these areas and investments have been made bioinformatics and importantly in proteomic facilities dedicated to strategic studies of ruminant endemic diseases. These laboratory and *in silico* based studies are complemented by large scale farm and housed animal facilities for the major species, and by laboratory and large animal experiment pathogen containment facilities. SEERAD is a contributor to genetics projects through the Sustainable Livestock LINK programme and has contributed to the RoBoGen bovine QTL programme and to the sheep ‘virtual’ genome project. Overall the programme is strategic to applied in nature, and with an emphasis on knowledge transfer and commercialisation, it demonstrates strong linkages to the livestock and related industries.

Table 7: SEERAD funding commitments relating to farm animal genomics, (£k)

Category	Research funded per financial year (£k)		
	2001-2002	2002-2003	2003-2004
Cattle	205	219	174
Sheep	1074	1335	1322
Fish	1411	1549	1554
Misc.	1247	1624	1741
TOTAL	3,937	4,727	4,791

2.20 The SEERAD’s agency, Fisheries Research Service (FRS), supports two principal laboratories (marine and freshwater) in Scotland. FRS spend on advisory, monitoring and laboratory services in support of SEERAD’s statutory obligations is ~£2.4M per annum, divided ~£2.1M/0.3M between fish health and aquaculture research. This spend is additional to the research expenditure provided in the above table.

Wellcome Trust

2.21 The Wellcome Trust invested ~£10.3M in farm animal-related research between 2001 and 2004. The most significant investment in this period was £5.3M invested research into the host tolerance and host-pathogen interactions in vector-borne parasitic diseases of cattle. In addition, the Wellcome Trust has invested ~£4.1M to date, through the Wellcome Trust Sanger Institute, into genomic resources for farm animal disease agents and parasites, most notably including £2.7M in *Trypanosome* species, £550K in *Salmonella* species and £535K in *Haemonchus contortus*- a major worldwide sheep pathogen, and closely related to the GI nematodes of cattle.

2.22 The Trust has recently finalised research awards of £13M as part of a £25M global funding initiative entitled ‘Animal Health in the Developing World’²³. The focus of this research programme will be livestock diseases in the developing world and their impact on human health and wellbeing, and amongst a spectrum of activities, this will include biomedical research into livestock diseases in developing countries.

²² SEERAD funding is currently in transition from provision of core grant-in-aid to SABRIs to grants for programmes of research, see Strategic Research for SEERAD, Environment, Biology and Agriculture, 2005-210.

²³ <http://www.wellcome.ac.uk/doc%5Fwtd004362.html>

DTI

2.23 The DTI is a minor funder of Genesis Faraday, and also funds business development and technology transfer through the Public Sector Research Exploitation (PSRE) initiative: recipients include RI, IAH and MRI through the £1.5M Genomia fund. The DTI funds little of direct relevance within LINK scheme, but funds some indirectly relevant research through this route.

Other Funders

2.24 Table 8 summarises the recent research investments of funders with a minor presence in the farm animal genomics/genetics research field. Organisations approached with little or no direct investment in the area included the Medical Research Council, Leverhulme Trust, Food Standards Agency and Gatsby Charitable Foundation.

Table 8: Other funders of farm animal genomics research; research investment (£k)

Funder	Area of investment	2001-2002	2002-2003	2003-2004
NERC	Avian plumage traits and cross-species proteomics.	0	288	303
DfID	Aquaculture and Fish Genetics Programme	324	292	256
	Animal Health Programme (<i>Theileria parva</i> genome resources)	1,151	1,617	1,521
Scottish Enterprise	Novel markers for meat quality	138 (timeframe not specified)		

Strengths and weaknesses of UK research on farm animal genomics

2.25 Based on the current funding landscape for farm animal genomics, and a historical perspective as provided in Chapter 1, a number of clear strengths and weaknesses of the UK farm animal genomics research portfolio can be identified. These are summarised in Table 9.

Table 9: Strengths and weaknesses of UK research in farm animal genomics

STRENGTHS	WEAKNESSES
Significant commitment by BBSRC, Defra, SEERAD, the Wellcome Trust and industry to fund genetics/genomics research in a range of species.	Co-ordination between different funders could be improved. Current arrangements leave gaps in the R&D pipeline.
Two BBSRC institutes, with dedicated research facilities, operate in this area.	Lack of stable funding for long-term projects, especially resources and databases (curation).
	Lack of large co-ordinated research programmes.
Critical mass of complementary expertise and resources at RI, IAH, the Sanger Institute, Veterinary Laboratories Agency, Veterinary Schools, Moredun Institute and SAC.	RI and IAH lack the necessary funding (scale and timescale) to support long-term more strategic research programmes – over reliance on research grants with short term goals.
Strong animal breeding industry. A MAJOR strength c.f. crop and plant science is that there is still a farm animal breeding industry in the UK, indeed one having a global impact! UK companies are the leading breeders of pigs, dairy cattle and broiler chickens (Anglo-American), so there is a clear route to market to capture the value from research.	Industry perceives the ‘innovation gap’ between what BBSRC will fund in responsive mode and the development necessary before they (or other funders) will take on development to be an important hurdle to better KT.
A strong animal health research base in industry.	Lack of new pharmaceuticals in animal health industry – an opportunity for genomics to provide innovative solutions.
Support for research from industry through in-house R&D and in-kind and cash contributions and through LINK and IPA schemes.	Insufficient sensitivity of BBSRC scientific committees to strategic value of industrial support.
Strong tradition in quantitative genetics in Edinburgh (University of Edinburgh, SAC, RI).	Difficulty attracting students into quantitative genetics and difficulty in recruiting post-docs and senior scientists in this field.
World-class genomics and bioinformatics research facilities, e.g. the Wellcome Trust Sanger Institute, European Bioinformatics Institute.	Lack of public sector funding in the UK and the EU to exploit the capabilities of these centres, e.g. UK / EU governmental support for genome sequencing has not matched the Wellcome Trust and NIH support and inhibits prioritisation of areas of interest to BBSRC.
Dedicated farm animal functional genomics facility with increasing international reputation (<i>ARK-Genomics</i>) and several major proteomics Centres well placed to exploit genome sequences in the context of ‘post genomics’.	Key resources, including <i>ARK-Genomics</i> and bioinformatics infrastructure are dependent upon short response mode grant funding, and there is a lack of policy to ensure optimal use of such investments.
World class pathogen research community	Farm animal and pathogen research is not as well integrated as is desirable.
UK scientists are recognised leaders in farm animal genetics and are currently major players in the application of genomics.	Over stretch. Leadership of UK farm animal genome research community lacks sufficient depth: it struggles to meet its international ambitions and manage national/local research programmes, although it never the less currently achieves such success.
Presence of an active aquaculture based fish farming industry.	Lack of investment in fish genetics and genomics research
Presence of a strong environmental research community in the UK.	Lack of coordination between farm animal genomics and environmental areas.

2.26 An analysis of the strengths and weaknesses of the UK farm animal genetics and genomics research programme and capabilities leads naturally to a consideration of opportunities and threats (Table 10). This analysis of the opportunities (and threats) for the UK, is also applicable, in many cases, more widely to the EU.

Table 10: Opportunities and threats to UK research in farm animal genomics

OPPORTUNITIES	THREATS
Real progress towards farm animal health and welfare goals.	Lack of serious investment by UK funders, stifling opportunities and putting UK researchers at a competitive disadvantage on a global stage.
Supporting the R&D pipeline for an area with a strong and diverse associated industries.	Loss of competitiveness of UK farm animal breeding and health industries due to poor conversion of technologies compared to global competitors.
Reinforcement of the important strategic roles of RI and IAH, and invigorating collaborations with HEIs and the SABRIs.	Failing to capitalise on critical mass and connectivity within the field.
Development of new research interfaces with other Councils, Government Departments and Charities.	Lack of coordination between funders, leaving important coverage gaps or leaky strategic pipelines.
	Lack of timely or correctly directed investment.

Conclusion

BBSRC is a major player in this area, but its investment has remained static and short term in recent years, decreasing in real terms and as a proportion of the total research spend. Defra, SEERAD and the Wellcome Trust have large related programs, most highly strategic. BBSRC has a particularly important role in funding the basic science that underpins both its own strategic research and that of other major funders.

CHAPTER 3: FUTURE PRIORITIES FOR RESEARCH

3.1 In this chapter we start by outlining some of the key drivers of research in farm animal genomics over the next 10 years and set out the future priorities for research in this area as we see them.

Drivers

3.2 The following drivers underline the need for continuing research in farm animal genomics and point to some of the most likely research needs in the future:

- There is a strong policy driver from Government Departments (particularly Defra) for more economic and environmental sustainability in UK land use; to minimise the ‘footprint’ of livestock production on the UK environment;
- There will therefore be continuing demand to reduce inputs and reduce waste in agriculture in order to reduce pollution and increase production efficiency;
- Global demand for farm animal produce is set to rise steeply, mostly in the developing world. There will be significant scientific opportunities and challenges relating to developing world pastoral agriculture;
- There will be increasing demand for animal produce that links food quality, diet and health, and improved mechanisms to promote food safety;
- There are increasingly strong social drivers for understanding and improving farm animal welfare in relation to experimental research, breeding and husbandry practises;
- The contribution of farm animal research to basic science, particularly using comparative genomics techniques, will make increasingly important contributions to human biology and medicine;
- UK PLC is in a strong position to develop and maintain a globally significant presence in livestock breeding, animal health and animal produce, and has a strong associated industry, but this is currently vulnerable to sustainability challenges, particularly relating to animal health;
- New diseases and pests are likely to arise, particularly as our climate in Northern Europe warms. More effective strategies for dealing with existing and emerging disease and pest problems will be required;
- A better understanding of zoonoses is required to inform strategies for detection, prevention and intervention;
- A better understanding of our livestock genetic resources is required, which will underpin biodiversity management strategies.

High priority research areas

- 3.3 BBSRC's first strategic objective is to deliver excellent science in the form of world-class basic and strategic research. The field of farm animal genomics/genetics offers many opportunities to fulfil this objective. We consider that the most important areas for research fall under four broad headings:
- Animal disease;
 - Animal Production;
 - Animal Biology;
 - Enabling tools and resources.

These are explained in a little more detail below before we consider prioritisation.

ANIMAL HEALTH

- 3.4 **Understanding susceptibility to disease, and identification and selection of genetic traits to improve resistance to disease and pests.** It is an important responsibility of society to maintain and nurture the health of the animal species that we rear for food. Genomics presents new opportunities to understand the genetic basis of the host immune system and disease susceptibility. There are significant scientific challenges, especially in the understanding and mapping of multifactorial traits responsible for resistance/susceptibility. It will be particularly important to adopt 'systems' based approaches to unravel host/pathogen interactions, and to integrate carefully genomics research in farm animals and pathogens. The rewards will include breeding strategies for increasing resistance to disease, and reducing the pathogen burden of animals entering the human food chain to lower the risk of zoonotic transfers. Breeding disease resistant animals may be a particular priority in the context of an expanding organic farming sector: there are significant challenges for the control of disease in the absence of chemotherapy, and important associated welfare implications.
- 3.5 **Development of therapeutic agents, vaccines and diagnostic tools.** The development of therapeutic agents and diagnostics may be considered a task for the private livestock industry sector. However, disease control is of such strategic importance that it is legitimate for public sector investment, at the level of basic research underpinning applications, and more applied research to seed industrial technology transfer and innovation. Private investment alone is not sufficient, and less profitable research can be neglected. It is a matter of concern that there are few, if any, major new pharmaceutical molecules entering the animal market and there is evidence that this area is unlikely to improve in the near future. BBSRC-funded basic research should focus on improving the integrative understanding of pathogenesis and natural variation in hosts and pathogens. This will provide leads for new therapeutic targets, vaccines and enable better diagnostic tools.

ANIMAL PRODUCTION

- 3.6 **Genetic traits to improve the quality and efficiency of animal products.** Sustainable agriculture requires that economic and environmental demands are both met. Improving production efficiency (more output for less input) addresses both of these needs, and can be very effective²⁴. The principle scientific challenges in this area relate to our understanding of metabolism; the processes that contribute to efficient nutrient capture and partitioning and the underlying genetics involved. In addition to the production of metabolically fit and efficient animals, there are a number of applications of genetic research to product quality. The genetic contribution to meat toughness and quality measures such as ‘boar taint’ of pork and the nutritional value of meat are subjects currently under investigation. With an increasing consumer demand for very high quality animal produce, the value of this type of research to UK industry is increasing.
- 3.7 **Product validation and pedigree control.** Comparative genomics tools offers new opportunities for the identification and utilisation of genetic markers that enable key genetic differences between species and, more challengingly, breeds within species, to be tagged. This provides exciting opportunities for genetic research on the underlying genetic differences of breed characteristics. This also has important applications for food traceability and security and for genotypic monitoring and control of pedigree lines.
- 3.8 **Research of benefit to developing countries.** Overlapping with the wider priorities of disease resistance and animal sustainability, there is much potential for applications aimed at addressing developing world needs. The over-arching strategic priority here is research aimed at improving resistance to locally endemic diseases and parasites, and breeding hardy animals to reduce reliance of developing world farmers on expensive chemicals. This area represents an interface with the activities of the Wellcome Trust and DfID.
- 3.9 **Production environments and animal welfare.** Welfare problems may arise as a result of mismatches between the animal’s genotype and its production environment, preventing the animal from functioning optimally. Research seeking to better match animal to environment would be beneficial. However, there is also concern that breeding should not aim to produce animals that can be reared in poorer conditions: we recognise the need for careful ethical monitoring of research outcomes in this area.
- 3.10 Genetic factors may directly influence welfare problems by affecting morphology (e.g. skeletal development and leg weakness in broiler chickens), behaviour (e.g. aggressive and other forms of damaging behaviour in pigs and chickens) and other factors (e.g. general fearfulness and stress susceptibility). A better understanding of such influences may lead to potential solutions, perhaps involving genetic manipulations.

²⁴ Applications of genomics to the pork industry. Van der Steen, H., Prall, G. and Plastow, G. (2005) *J. Anim. Sci.* 83 (E. Suppl.):E1-E8.

- 3.11 There are, therefore, important opportunities for research in farm animal genomics in relation to welfare issues. For example, QTLs influencing some behavioural traits of economic and welfare significance in chicken and quail have been identified (e.g. feather pecking in chickens). A more detailed understanding of the genetic bases of such behaviours is important, as is a general understanding of how behaviour in domestic animals (including companion animals) has been modified by selective breeding. Knowledge gained may be able to capitalise on new genetic technologies to provide solutions to behavioural problems with associated welfare issues.
- 3.12 Advances in the understanding of farm animal behaviour are also likely to have ramifications for human behavioural biology and medicine. Recent research has shown that traits such as pig aggression are heritable including the savaging of piglets by sows, and these behaviours may have features in common with some human behavioural disorders. It would be unwise to ignore both the fascinating biological questions and likely controversy bound up in researching potential links.

ANIMAL BIOLOGY

- 3.13 **Research into basic science promoting the understanding of the healthy human.** Farm animals can contribute to our understanding of basic human biology either through research which sets out with this aim, i.e. the use of chicken genetics and genomics to inform human developmental biology, or through research that has other prime objectives such as the identification of genes associated with fatness, which informs our understanding of human obesity²⁵. Also, we could well obtain valuable insights into the development of normal immune function in humans from model studies of the developing gut of the piglet. Knowledge gains for the benefit of human health from both routes are a valid and important use of BBSRC resources.
- 3.14 It is outside the remit of BBSRC to support advances in human medicine; this mainly falls under the remit of the MRC. However, BBSRC clearly has an important role in promoting the understanding of the healthy human and how these processes break down in disease. Genomic research in farm animals will increasingly make significant contributions to the area of human health including the health implications of diet.
- 3.15 **Comparative genomics.** Comparison of multiple genomes is an effective strategy for identifying genes and other functional elements of the genome that are conserved across evolution, and therefore likely to have highly important functions. The recently completed draft of the chicken genome is already making an important contribution to comparative genomics, and our understanding of the similarities and differences between mammalian and avian genomes. As other farm animal genomes are sequenced the power of comparative genomics will increase. Comparative genomics will also have a significant role in improving our understanding of how resistance and susceptibility of different species to pathogens occurs, and provide the basis for new strategies to combat disease.

²⁵ Domestic-animal genomics: deciphering the genetics of complex traits. Andersson, L. and Georges, M. (2004). *Nature Review Genetics* **5**, 202-212.

- 3.16 Although outside the scope of this review, we are not aware that any of the major UK funders of animal genomics have made significant research investments in canine or feline genomics resources, or plan to do so. It is our view that this is an important area of investment that should not be neglected in the UK simply by falling within the white space between funders. Both species offer great advantages for the study of heritable traits and breed differentiation, with detailed pedigree lines that could be readily resourced for comparative genomics studies (e.g. through blood samples donated for research from domestic populations, as opposed experimental populations). There is significant potential here to inform the study of diseases common to both companion animals and humans, such as arthritis.
- 3.17 **Ecosystem genomics, including biodiversity management/conservation.** Farm animals are the major large animals present in the UK countryside. Research on UK farm animals also provides a backbone for research on other animals across the planet, including domesticated, semi-domesticated and wild species and breeds. As an example, the elucidation of the bovine genome is already leading to interest in translational genetic research for buffalo, antelope and whale species. All fish species also exist as wild species, and aquaculture research heavily overlaps with research on the wild populations.
- 3.18 The increasingly sophisticated use of population genetics in domesticated and wild populations is an important mechanism underpinning better understanding of how genetic diversity contributes to infectious disease transmission, the impact of inbreeding in species (both in wild and domesticated) and the overall impact on the environment. This in turn informs decision about maintaining diversity in farm populations and also advice for conservation strategies in wild populations.
- 3.19 Animals utilised in developing world agriculture are often far more closely related to wild species than agricultural breeds in the developed world, or are interacting with wild populations. Research targeted at developing world agricultural issues (such as breeding for disease resistance) therefore relies on effective translation of backbone research on developed world livestock species to a greater diversity of animal populations.
- 3.20 Research into zoonoses is based on the host-pathogen interactions in semi-domesticated areas, which is likely to become an ‘ecosystem genomics’ study in the long run, with great potential for reducing the global incidence of serious infectious diseases. ‘Ecosystem genomics’ is an important potential interface between BBSRC and NERC research, an interface that BBSRC should seek to develop.
- 3.21 Genomics has great potential to inform the research of interactions between hosts and commensals and the complex and interesting ecosystems of the gut. The processes of the rumen are especially relevant to the environmental impact of cattle and sheep.

ENABLING TOOLS AND RESOURCES

- 3.22 It is essential that researchers in farm animal genomics/genetics have access to the necessary tools and resources to address complex biological questions. In many cases that will require development of the necessary tools (rather than acquiring off the shelf).

- 3.23 **Development of strategies to facilitate incorporation of desirable genetic traits in farm animals.** Much of past and current research in farm animal genetics has been undertaken with the strategic aim of genetic improvement. This can occur via selective breeding or genetic modification (GM), although commercial breeding is currently based entirely on selective breeding. The approaches have different results: selective breeding mixes up alleles within a population, whilst GM allows introduction of new alleles into a genetic background of choice, the over-expression of ‘native’ alleles and the use of antisense sequence to, for example, confer viral resistance. GM strategies offer advantages for research, and have been heavily used to improve our understanding of genetic interactions in transgenic plants.
- 3.24 Although through selective breeding it is increasingly easy to identify and eliminate some alleles associated with disease susceptibility, many traits of interest are controlled by the concerted action of many genes. There are significant scientific challenges associated with understanding such complex gene actions and developing new breeding strategies that can exploit improvements in our understanding of complex multifactorial traits. There is an associated need for more advanced modelling and molecular tools to inform selective breeding, and GM strategies may serve as important research tools to enable these considerable challenges to be met.
- 3.25 GM methods in farm animals are limited. Moderately sized transgenes can be integrated using lentiviral vectors in chickens. Microinjection/nuclear transfer enable cell-based gene transfer in other animals. There are, however, significant limitations in current capabilities, and there are associated welfare considerations. There is a need for improvement in GM technology as a research tool, to develop more efficient, more targeted and less invasive procedures for creating GM farm animals.
- 3.26 **Quantitative genetics, systems biology and predictive biology.** The tools and resources required for genetics and genomics research include not only biological and molecular resources, information, including sequence data, but also capabilities for analysis. There are opportunities to build upon and exploit UK strengths in this area, particularly in quantitative genetics.
- 3.27 In order to tackle the research challenges it will be necessary to integrate skills in quantitative genetics or numerical genomics, genomics technologies and information and experimentation in whole animal biology. New populations, phenotypic databases and computational methods will be required to dissect the interactions, including epistasis²⁶, in the genetic control of complex traits. Ultimately, the aim is to identify and characterise networks of genes and their effects. Whilst the foundations for such research are likely to be developed in simpler genetic systems – yeast, *C. elegans* and perhaps mice, research in outbred species such as farmed animals will not only be useful for applications in these target species but is likely to make a significant contribution to understanding the outbred species of greatest interest – *Homo sapiens*.

²⁶ Epistasis: too often neglected in complex trait studies? Carlborg, Ö. and Haley, C.S. (2004). *Nature Review Genetics* **5**, 628-625.

3.28 With the advance of transcriptomics, proteomics and metabolomics, a vast amount of novel phenotypic information can be generated, providing an amazing opportunity to supplement the traditional range of recorded phenotypes with thousands of measurements from different levels of cell biology. Studying the genetic regulation of these ‘omics’ phenotypes may facilitate the reconstruction of genetic pathways underlying phenotypes of interest.

The key scientific challenges in this area are:

- the computational logistics of analysing thousands of gene or protein levels in combination with hundreds (or even thousands) of genetic markers;
- the post-analyses inferences: how to use the data to generate putative genetic networks and improve understanding of systems biology in farm animal species.

3.29 **Long-term storage of genetic resources.** There are important fundamental research opportunities and challenges associated with the preservation of farm animal genetic resources. Long-term maintenance and propagation of genetic resources is currently difficult and expensive in farm animal genetic research because germplasm cannot be readily or inexpensively stored (unlike plant germplasm), and live animal populations must be maintained instead in most cases. Basic cell biology research could also provide strategic opportunities for reducing experimental reliance on whole animals: few cultured farm animal cell lines are currently available, limiting the experimental work that can currently be done outside of whole animal systems in genetically defined cells.

3.30 **Curation and archiving of data and libraries.** Access to biological resources, e.g. clones, libraries and microarrays, and the latest techniques, e.g. SNP genotyping, RNAi and proteomics, is critical to the future success of research in farmed animals in the UK. Centres such as ARK-Genomics with specialised resources and capabilities that are species-specific or at least optimised for research in the target farmed animal species are a cost effective manner of delivering access. The critical role of and value of Resource Centres to genome research are summarised in a recent review article in *Nature Reviews Genetics* in which ARK-Genomics is cited as an example. The current support for such underlying ‘infrastructural investments’ is too often short-term and reliant on response mode grant funding, which limits the effectiveness of key resources upon which future research will be built. As many of these resources are currently maintained across the research community, this is an issue that needs to be approached in a synergistic way by the major stakeholders (funders and users) in the field.

3.31 **Bioinformatics capability.** Scientists engaged in genome research programmes require unimpeded access to well-maintained database resources, together with the necessary analytical/display tools in order that increased knowledge and understanding can be developed from a synthesis of many individual experiments. Good bioinformatics is critical to deriving value from the funds invested in genome research. Some bioinformatics resources can be delivered effectively through national or international centres of excellence, e.g. EBI, but as the biology, drivers of research and the state of knowledge varies from species to species there is a requirement for bioinformatics capabilities to be located alongside groups active in farm animal genomics research.

Overarching prioritisation of research

3.32 We recognise that BBSRC does not have unlimited funds and whilst we consider all of the research areas (above) to be important it will nevertheless be necessary to prioritise. Prioritisation is based on a number of criteria including: main Drivers, scientific opportunities and knowledge generation; user need (including industrial and policy); and where there are particular opportunities for synergy with other funders. In prioritising we have also taken into account the Council's existing Strategic Plan and the many relevant replies received during the consultation.

1. Farm animal health.

3.33 From the consultation exercise, animal health emerged clearly as the top research priority, bringing the strategic aims of RI and IAH research programmes together. This is in agreement with a previous technology road mapping exercise undertaken by Genesis Faraday with their Partnership members in 2003, which showed animal health to be the top research priority of industry²⁷. Dissecting the genetic control of host responses to infectious disease perhaps represents both the greatest challenge and the greatest opportunity for farm animal genetics and genomics research. As with other complex traits it is likely that multiple genes are involved and that gene interactions are important. There is also an environmental component shaping the outcome for disease relating to the form of exposure to the pathogen. More broadly, the influence of genetic variation on morphological, behavioural and other factors influencing **animal welfare** was also viewed as an important research area. Again, the likelihood is that multiple genes and gene interactions are involved, and that interactions with the environment will also be important.

3.34 Sufficient long-term funding will be required on a long-term basis to allow existing animal facilities and resources to be maintained and detailed phenotypic recordings will be necessary to achieve this important research goal. These rely on the reagents and tools necessary to measure complex phenotypes such as immune responses. We acknowledge that BBSRC and SEERAD have provided support towards development of these reagents for farm animal species, in particular the cross-Institute Immunological Toolbox grant from the recent Controlling Viral Diseases of Livestock initiative, funding reagent development in five species (chicken, cow, pig, sheep and horse).

3.35 It is also important to stress the complementary role of pathogen/pest genomics projects in delivering strategic aims in farm animal health. Understanding and exploitation of host-pathogen interactions is required in order to dissect host genes of relevance to breeding strategies. An improved understanding of pathogen genomics will also assist in the development of new vaccines and novel approaches to control. Breeding for reduced susceptibility is important, but may not be the only answer. Particular alleles may reduce susceptibility to one disease whilst increasing susceptibility to another. We need to take a more integrated approach to the development of strategies for improving animal health as well as fully exploiting BBSRC investments. Likewise, expertise in the assessment of animal welfare, which is strong in the UK and has recently received

²⁷ http://www.genesis-faraday.org/downloadables/downloads/GF_Road-map_Update_November_2004.pdf

substantial BBSRC funding, should be integrated with expertise in genomics to drive forward animal welfare improvements through genetic routes.²⁸

3.36 The Wellcome Trust has a particular strategic interest in Animal Health in the Developing World, and it would be desirable for BBSRC to seek opportunities for synergy.

2. Farm animal sustainability.

3.37 Research which moves forward the ability of breeders to select for traits that support the economic and environmental sustainability of animals: - resource-efficient, healthy animals with low intrinsic welfare problems due to breeding strategies, and which supply high quality produce. This area has a strong policy pull from the strategic research priorities of Defra and SEERAD.

3.38 Productivity and efficiency remain important agronomic goals. The UK faces increasingly stiff competition from imported animal produce. Improvements to welfare through genomics/genetics-based research (e.g. minimising neonatal mortality in lambs and pigs, lowering levels of aggressive and injurious behaviour in pigs and chickens, improving leg conformation in chickens) are also likely to enhance productivity and hence offer economic as well as welfare advantages. There are associated ethical issues, for example the potential to produce animals that can survive in poor and inappropriate conditions, which will need to be considered very carefully.

3. Human health.

3.39 Benefits to human health through reduction of zoonosis incidence, improved nutritional quality of animal produce, a better understanding of mammalian diet/genotype interactions and a better understanding of human biology, which will underpin associated improvements to human medicine within the sphere of MRC and charity led research. The use of BBSRC resources in research to underpin improvements in developing world agriculture would also result in large-scale benefits to human health and welfare. This presents opportunities to interface with research supported by NERC, DfID and the Wellcome Trust.

Recommendation 2: Within farm animal genomics, animal health should be the leading priority. This will require a fully integrated ‘systems’ approach including pathogen and pest research. Farm animal sustainability, welfare and human health also form important priorities. BBSRC should engage with other funders to co-ordinate coverage of priority areas, and should particularly seek to develop both the environmental genomics interface with NERC and the human biology interface with MRC.

²⁸ Breeding and animal welfare: practical and theoretical advantages of multi-trait selection. Lawrence et al. (2004) *Animal Welfare* 13: S191-S196.

Prioritisation of research by farm animal species

- 3.40 Having identified the priority areas for future research, we need to consider the merits of further prioritisation on the basis of farm animal species. In many respects the choice of farm animal will be dictated by the nature of the research i.e. it is not very feasible to use pigs for fundamental studies on embryonic limb development, where chickens offer a much more suitable model. However there is an argument that BBSRC should focus investment in a small number of animal species where there is the opportunity to make the greatest impact (scientifically and economically) and to build on previous investment.
- 3.41 The UK is home to the world's largest pig, poultry and cattle breeding companies and sheep remain a critical contributor to sustainable agriculture in the UK. Thus, in order to support the UK's livestock sector and to access the latest farm animal research internationally, we need internationally competitive genome research in the major farmed animal species – pigs, poultry (principally chickens), cattle, sheep and aquacultural species. Moreover given the change in capabilities and tools generated by and subject to continuing development by the farm animal genome projects, the balance should switch from a need to justify the use of the target species to a need to justify the use of model species.
- 3.42 We consider that the following overarching principles are important when prioritising against farm animal species:
- focus resources on areas of scientific strength whilst maintaining the capacity to work on other species as important opportunities arise.
 - focus on species of major economic importance for the UK, as in the Terms of Reference (Annex 1).
 - focus on those species in which we have substantial prior investment and/or which are of obvious strategic importance to UK R&D
- 3.43 Against a background of these principles, Table 10 summarises the relative merits for the main farm animal species.

Recommendation 3. BBSRC should continue to focus support on genomic/genetic research in the species in which it has significant prior investment (chicken, cow and pig), whilst ensuring the flexibility to invest in other species as important opportunities emerge. In particular, thus there is a strong strategic case for supporting the upcoming genome sequencing project for the pig, and the UK has an opportunity to take a lead in genomics and genetics research for economically important fish species.

Table 10: farm animal species: Current resources and investments, strategic and scientific importance and priorities for BBSRC investment

Species	Current BBSRC and national investments	Strategic and scientific importance	Priority
Chicken	Draft genome sequence is complete, largely funded by USA investments. Significant BBSRC investments in chicken genomics include £1.4M in cDNA libraries and ESTs, and £0.65M in annotation of the chicken genome sequence.	The focus of genetic/genomic research on avian species, chicken is of high strategic importance; as one of the major UK and international food animals (broiler and layer hens), as an established model animal for fundamental biological studies (vertebrate embryology) and as a non-mammalian vertebrate for comparative genomics.	High.
Cow	Draft genome sequence due for completion in 2005 (largely through US funding and no UK public funding). BBSRC investments in cattle genome research include: the RoBoGen QTL mapping programme, radiation hybrid mapping, physical (BAC contig) mapping and annotation of the cattle genome sequence. (£0.5M)	The focus of genetic/genomic research on ruminant species, the cow is strategically important as a major large food animal, and the major ruminant food species in the UK, which provides information of relevance to other important ruminants (sheep and goats).	High.
Pig	BBSRC funded projects, ongoing for pig genomics since 1990, have included linkage and radiation hybrid map development and first farm animal genome database: PiGBASE. More recently, BBSRC is a major funder of the international programme to establish genome-wide clone-based (BAC contig) physical maps for the pig (£~0.5M). BBSRC <i>Exploiting Genomics</i> funding is supporting the generation of ESTs and SNPs (£0.25 M). BBSRC CSG funding to RI supports UK participation in the leadership of the Swine Genome Sequencing Consortium.	Economically important in the UK and globally, with a breeding industry that is well-primed to transfer technology arising from research. Physiologically similar to humans, and therefore an important species for research with medical implications.	High.
Sheep	There has been relatively low investment in sheep genetics to date in the UK, with Scrapie research forming the most significant draw for funding in sheep. Most of the information relating to sheep genomics is held by private companies in Australia and New Zealand.	Economically important, particularly in relation to rural landscape sustainability, but more extensively farmed. The sheep breeding industry is less primed to convert research outputs, although major breakthroughs (eg. Scrapie resistance) can be readily transferred. The cow genome will provide a source of ruminant-specific genomic information, and important advances in major disease issues may be readily transferable between cattle and sheep systems (e.g. TSE research). However, for some research the sheep is an excellent and cost effective ruminant model species, and sheep are a priority species for SEERAD investment. Sheep (and goats) are also of strategic importance in the developing world. It is anticipated that modest genomic resources will be developed for sheep in the short-term but, as one of the four main terrestrial farm animals, there will be a good medium term case for sequencing the complete sheep genome.	Low to moderate.
Fish	3.44 BBSRC has current commitments of ~£5M in fish research (~£1.5M PA), relating to basic and strategic research through the responsive mode in a number of species including salmon, trout, dogfish, plaice and flounder. CEFAS (Defra) and FRS (SEERAD) currently lead in strategic aquaculture research investments.	Aquaculture species are highly amenable to genetic approaches due to high fecundity and fast life-cycles. Tilapia and Fugu are important model species: genome sequence information from these species will inform aquaculture research. Aquaculture is becoming increasingly important, particularly as wild fish stock sustainability represents an ongoing problem. Fish are considered to be the animal food resource with the greatest inherent health benefits. Increasing efforts are being made to farm economically important marine species, and there is significant UK capacity for aquaculture volume increases. We propose that BBSRC has an important role in funding basic genomics research that underpins current and future aquaculture applications, prioritising the economically most important species currently under aquaculture (salmon) and species currently being domesticated and farmed (cod).	Currently low to moderate, but profile increasing rapidly.

CHAPTER 4: DELIVERY MECHANISMS

- 4.1 In this chapter we make a number of recommendations that should greatly improve delivery of the farm animal genomics research in the UK. In making these recommendations we realise that there are some actions that Council can take unilaterally – for example to change aspects of its own internal funding mechanisms. Other actions, however, lie outside the direct power of BBSRC to deliver alone, and for these Council should be seeking partnerships with others to help deliver.

Our recommendations to Council fall under four broad headings:

- **Improving coordination and communication;**
- **Funding mechanisms;**
- **Training;**
- **Ethics and public dialogue.**

In the final section of this chapter we consider future funding and indicate the likely level of support that will be necessary to properly develop and progress this field of research in the next 5-10 years.

Improving coordination and communication

- 4.2 As we show in Chapter 2, there are several major UK funders of farm animal genomics; principally BBSRC, Defra, SEERAD, Wellcome and industry. Together they cover the range from basic and strategic through to applied research. Given the strategic importance of farm animal genomics to the economy and society then we agree with a number of respondents to the consultation that there needs to be better national coordination of research effort in this area.
- 4.3 We are aware that all of the major funders (including BBSRC) have various degrees of office-level contact in the normal course of business. But we see little evidence that they are actively seeking to identify areas in which they have common research interests or synergies and where joint investment would pay dividends. Nor is there an obvious existing group or committee to which such a coordination role would naturally fall.
- 4.4 Faced with a similar situation in environmental science in 2003, NERC took the initiative and established the Environmental Research Funders Forum (ERFF). The ERFF meets only once or twice a year but brings the main funders together to discuss higher-level strategy and joint funding opportunities²⁹. Other models, which stop short of a formal funders forum, could be equally effective. The key criterion is to get the main players at a suitably senior level to meet as a group. For this to happen it requires one organisation to take the lead and invite the others participate.

Recommendation 4: BBSRC - as a major player in this area – should take the lead in seeking to bring together the other funders, including industry, in an appropriate way – for example a funders forum. Early aims should be to map how current strategies join up, seek opportunities for joint funding and effective international engagement and explore how SR2006 monies might be jointly leveraged for this area of research.

²⁹ <http://www.erff.org.uk>. Initial membership includes senior staff from UK public bodies that fund or use environmental research and trained scientists. Other organisations will be invited to participate in the Forum's activities.

- 4.5 We must also ask whether the UK and BBSRC can learn from the model of strategic co-ordination and funding of sheep and cattle genetics in Australia and New Zealand³⁰. These countries have a coherent overarching National strategy that has generated impressive gains in sheep and cattle genetics/genomics research (albeit coupled to high levels of investment [equivalent to ~£15 million pa]). The emphasis has been on the funding of co-ordinated programmes of research over longer timescales, rather than disconnected, short-term projects as predominate in the UK.
- 4.6 The UK has no equivalent national strategy for farm animal genomics and would no doubt benefit from developing one (we assume that it would be proper for Defra to take the lead as the principal Government Department). However, all of the major funders in the UK have reasonably well articulated individual strategies and the crucial lesson to be taken from the Antipodean experience is the benefit of coordination. Irrespective of whether the UK has a formal national strategy or not, the action associated with Recommendation 4 (above) will help significantly to increase the impact of our investments (which collectively are the order of that in Australia and New Zealand). The other important lesson to take is the value of programmes of research over longer timescales. We consider this in more deal in section 4.25.

Coordination and communication between BBSRC institutes.

- 4.7 BBSRC has two main institutes that conduct research of relevance to farm animal genomics – Roslin Institute and Institute for Animal Health. Further downstream, when one begins to consider the influence of genetics on meat quality and the impact on diet and health then the interests of a third BBSRC institute – Institute of Food Research – become relevant.
- 4.8 Of the two principal institutes, RI has the largest critical mass working on genomics and is the host of the *ARK-Genomics* centre (see section 3.30). RI and IAH received 35% and 25%, respectively, of BBSRC’s total funding for farm animal genomics research (2003-2004 CSG snapshot and mean annual responsive mode allocation over 2001-2004). RI and IAH therefore have critical roles in delivering the strategic priorities of BBSRC in this area.
- 4.9 As we indicate in Chapter 3, the over-riding strategic priority in farm animal genomics research is that of farm animal disease. It is clear to us that together the two institutes – RI and IAH - provide a critical mass of complementary expertise and resources, and should be working together more effectively than at present. It is therefore our view that, following the model of soil science, a new RI/IAH cross-institute programme (CIP) in the area of farm animal disease genetics/genomics would be highly desirable.

Recommendation 5: In the light of the 2005 IAE and the new Institute Science Strategy, Council should work with the Institute Directors to ensure that CSG is deployed appropriately for collaborative research and to consider the need for a new cross-institute programme (CIP) focussed on genetics/genomics of animal disease and resistance.

³⁰ Genetics and genomics of sheep and cattle in Australia and New Zealand. Global Watch Mission Report. Warkup, C. (2003) DTI.

Edinburgh Bioscience Research Centre (EBRC)

4.10 One of the drivers for recommending a new CIP is the benefit to research of drawing together complementary expertise and increasing critical mass. The review panel is aware of the potential developments in the Edinburgh area following the Scottish Science Advisory Committee's Report (the Sibbett report) in 2004. This would involve a new strategic alliance between Roslin Institute, Scottish Agricultural College, Moredun Research Institute, IAH Neuropathogenesis Unit and the Royal (Dick) School of Veterinary Studies, University of Edinburgh, to create a new centre for animal bioscience. Embedding the farm animal genomics research at RI within such a larger structure is likely to provide a net benefit by virtue of increased critical mass, centralised resources, rationalisation of animal resources, complementarity of expertise, and the mutual advantages of University and institute-led research. An example particularly relevant to this review is the experimental herds, long-term selection experiments and pathogen containment facilities, at RI, Scottish Agricultural College and Moredun. These are expensive to maintain and possibly under utilised, yet are an important resource. The opportunity to consolidate this resource in a framework of stable funding should not be missed; otherwise by early 2006 all RI's cattle and pig populations for genetic research will likely have gone. We consider that the likely synergy and savings of a 'regional hub' model, typified by the Edinburgh initiative, are likely to be positive and desirable.

Better coordination of existing resources and facilities

- 4.11 Farm animal genomics is resource intensive requiring access to, for example, research farms, herds, high throughput genomics technologies, challenge facilities, large-scale data handling/manipulation capability and bioinformatics resources. In section 3.22 we highlight some immediate and future requirements (an overview of the current UK resources and facilities is also provided on the BBSRC website at <http://www.bbsrc.ac.uk/society/consult/farmgen/>), but apart from these few exceptions the UK is generally well equipped. Nevertheless, further gains could be made by better coordination and utilisation of the existing resources. We provide examples below.
- 4.12 Single Nucleotide Polymorphism (SNP) resources are increasingly important but the hardware is expensive and dates/depreciates quickly. Much of the research community is unaware of current resource and/or feels that access is restrictive. Instead of duplicating platform technologies such as this in many BBSRC funded centres we propose that it would be a better use of funds to purchase capacity elsewhere- e.g. at The Wellcome Trust Sanger Institute, where there is the expertise, infrastructure and capacity to undertake such tasks.
- 4.13 The same principle applies to resources and expertise held by *ARK-Genomics*. *ARK-Genomics* was set up with a grant awarded from the BBSRC's IGF (Investigating Gene Function) initiative to provide a laboratory for automated analysis of gene expression using state-of-the-art robots and microarray scanners. *ARK-Genomics* received much praise during the consultation, and applicants for BBSRC funding in this area should be encouraged to use the existing resources rather than attempt to reinvent them.

Recommendation 6: Council should invite the other main funders (as part of recommendation 4) to discuss how better coordination of collective resources can be achieved. The parties should consider the scope for consolidation of expensive research tools and resources, how best to secure their long-term viability and minimise duplication.

- 4.14 The use of experimental herds could be complemented by more extensive use of normal commercial farm herds: the former are an invaluable tool upon which to build hypotheses, but the latter offer the particular advantages of greater diversity and larger herd size in order to test hypotheses: a great advantage to investigate some genetic phenomena. Commercial populations provide large numbers that are essential for fine-scale genetic mapping.
- 4.15 There are currently a few such communication networks for collaboration between researchers and farmers. Veterinary and industrial associations such as the National Beef Association (NBA) and Royal Association of British Dairy Farmers (RABDC) have experience of creating networks of ‘friendly farms’ between researchers and industry and believe that this model could be extended considerably. Sire referencing schemes also provide an excellent opportunity for academic research to utilise commercial resources. However, ‘difficult-to-measure’ or perhaps more accurately ‘expensive-to-measure’ trait data particularly relating to animal health, are not currently routinely captured in the commercial setting. This would need to be addressed in order to make the resource useful in the context of our recommended top priority research area. Some respondents to the consultation felt that it was important to recognise that farmers should be paid for services rendered, and we agree that it is an appropriate use of public money.

Recommendation 7: BBSRC should seek ways to promote greater utilisation of commercial farm animal resources in academic farm animal genomics research. We encourage BBSRC to take an ambitious stance in this matter; to take the initiative and use financial leverage to work with other stakeholders (Defra, SEERAD, industry) towards the formation of a national network of commercial farms collaborating with academic researchers.

Improving communication between the fields of farm animal genomics and human biology

- 4.16 We alluded earlier to the relevance of outputs from farm animal genomics to the understanding of human systems and vice versa. For example, researchers at RI have collaborative projects to map and identify genes for vision and eye defects in chickens, and comparisons with the human gene equivalents will illuminate human biology and health. However, it seems that much of the potential for developments in farm animal research to inform our understanding of human systems is currently under-realised. Leading figures in farm animal research have engaged with the field of human research through workshop and committee involvement but there is a perceived lack of reciprocation, inhibiting intellectual exchange and collaboration between the two fields.

- 4.17 BBSRC (alone or in partnership e.g. with MRC and/or Wellcome) should have a role in encouraging and facilitating contact between researchers with a view to generating more translational science. Mechanisms should be encouraged that promote direct communication and flow of knowledge/people, for example joint workshops, networks or targeted initiatives specifically with the purpose of encouraging joint research. There would also be value in using studentships and fellowships to bridge the gap between farm animal genomics and those working on human systems.

Recommendation 8: BBSRC should promote more interaction between the animal and human bioscience research communities. Options include joint workshops or networking activities, studentships and fellowships. A targeted initiative specifically aimed at promoting this interaction would be a positive move by the Council to establish collaborative research.

Improving the flow of knowledge and people between public and private sector research.

- 4.18 The Lambert report³¹ and the Government's ten-year science and innovation investment framework³² acknowledge that the UK has a poor record of translating knowledge and technical know-how into commercial products and services – the so-called 'innovation gap'. Sir Richard Lambert pointed primarily to improving the interchange between business and universities.
- 4.19 Many responses to the consultation were concerned about the poor communication and flow of people between public sector research and the livestock industries, and vice versa. A notable exception to this is the 'Edinburgh group' where there have been historically good links between the animal breeding industry and the University of Edinburgh, RI, SAC. Many of the geneticists that staff the breeding companies trained in Edinburgh, and industry staff and public sector funded research scientists participate in many of the same scientific meetings.
- 4.20 Improving communication, collaboration, training and technology transfer between academia and industry in farm animal genomics is the main aim of the Genesis Faraday Partnership, established in 2003. The Faraday partnerships, most of which operate in the physical sciences, were set up by DTI to help address the innovation gap. Genesis Faraday, which is funded in part by the BBSRC, received a great deal of support during our consultation, particularly from industry. Respondents repeatedly praised this model and urged BBSRC to continue to support it. We concur that the Genesis Faraday Partnership, or an organisation fulfilling this function, has a critical part to play in drawing the dispersed and diverse industry together in a more coordinated way.
- 4.21 BBSRC's Strategic Plan highlights the leading role that the Council has in promoting innovation and KT from BBSRC-funded science and training. As the UK biggest funder of basic and strategic research in farm animal genomics then BBSRC clearly has a dominant role in promoting KT and innovation in this area. The UK livestock industry is large (~£9 billion pa) and it is worth noting that it has not suffered steep decline in the

³¹ Lambert Review of Business-University Collaboration (2003). HMSO. ISBN: 0-947819-76-2. (http://www.hm-treasury.gov.uk/media/DDE/65/lambert_review_final_450.pdf)

³² Science and innovation: working towards a ten-year investment framework. (2004). HMSO. ISBN: 1-84532-002-6. (http://www.hm-treasury.gov.uk/media/F1761/science_406.pdf)

past 15 years unlike much of the agri-food sector. Despite the size of the industry it is composed, with a few notable exceptions, of many and diverse small breeders and SMEs that operate on tight margins. This creates difficulties in engaging the industry in a coordinated way, for example dissemination of information, KT and leveraging coordinated joint investment in research. The diversity of the industry is also problematic for farmers and other stakeholders who complain of feeling isolated from the latest technical developments. We are of the view that the Genesis Faraday has undoubtedly much improved the situation in recent times but would urge BBSRC to consider what more it can do – acknowledging the nature of the sector - to promote KT and innovation in farm animal genomics.

- 4.22 During the consultation, respondents flagged a number of KT/innovation issues that they considered needed to be improved. These included all of the difficulties that are commonly cited for other sectors - such as business does not understand academia (and vice versa), little funding for proof of concept, industry too secretive (more sharing of data), IP too restrictive, need more joint/collaborative research with industry, need more people trained in the skills required by industry. It seems to us that many of these issues would be improved by simply increasing the level of contact and exchange (joint meetings, networks, movement of people) between academia and industry. The small size of follow-on fund awards in relation to the effort required in applying for such awards was also felt to be unduly restrictive: researchers often instead target this effort to submitting a full grant proposal. To address this issue we propose that either the application process should be made much quicker, or that the size of follow-on fund awards should be increased from £50k to £100k to make the application time investment more worthwhile.

Recommendation 9: The Bioscience for Industry Strategy Panel should be invited to review BBSRC’s current KT/innovation activities in this sector and advise how best to engage and leverage more joint funding in the future. We further recommend:

- **continuing to support the activities of Genesis-Faraday, or an organisation fulfilling its role, over the medium term period and beyond, subject to review;**
- **funding mechanisms need to take better account of strategic relevance;**
- **the funding available through the follow-on-fund should be increased, or expedite the current application process.**

Harmonising data standards

- 4.23 Combined genomics research at the international level is creating an enormous wealth of data. This brings important logistical and infrastructural challenges if the power of the data is to be maximised and capitalised upon properly. Amongst the most prominent issues is the need for international common standards in experimental design, data quality and annotation, allowing linkage of datasets and synergy in data mining and analysis between laboratories and species. BBSRC should insist that researchers it supports follow agreed international standards (e.g. MIAME standards for describing array experiments) and make their data and resources available in compliance with international standards and protocols (e.g. timely release of sequence data).

Improving funding mechanisms

4.24 Council has three main routes by which farm animal genomics research is funded; responsive mode, targeted Initiatives and CSG to sponsored institutes. A number of improvements could be made to target funding better or to make funding more effective. We have already discussed (above) the benefits of better coordination of funding, but there are other changes to funding that would also be advantageous.

Longer larger grants

4.25 Basic and strategic research in farm animal genetics/genomics often involves commitment over a number of years - for example when pursuing the underlying function of traits with complex genetics, breeding programmes or long-term genome annotation studies. When the long breeding cycles of farm animals are also taken into account, it is clear that much of farm animal genomics does not lend itself to the three-year quanta of funding on project grants that are so common in the UK. This is a significant advantage of the CSG funding work in institutes, where there is a level of continuity of longer-term strategic research.

4.26 There is nothing to prevent grant applicants from applying for longer-term programmes of work where the science demands it; indeed BBSRC's website encourages such proposals. However, there is a perception in the community that the Research Committees do not receive such applications well and they are at a disadvantage compared to the shorter (and less expensive) project grants. We are aware that BBSRC's delivery plan signals Council's intention to establish a portfolio of large, multidisciplinary programs, and we strongly endorse this timely move.

Funding for tools and resources

4.27 BBSRC's Strategic Plan emphasises the importance of tools resources and technologies in advancing bioscience. As we have argued, tools and resources are extremely important in the area of farm animal genetics/genomics (see section 3.22) but we see two difficulties at present in the way that these are funded;

4.28 First, these types of tools and resources are often considered not to be 'hypothesis driven' and are consequently difficult to get funded through responsive mode. Second, resources often need longer-term commitment to funding for upkeep and development that is not best delivered via three-year projects grants. As a pertinent example in the farm animal genomics resource pool, we see strong strategic merit in placing the funding for *ARK-Genomics* on a more stable footing.

<p>Recommendation 10: We are aware that the Tools and Resources Strategy Panel will be reporting to Strategy Board on how to best fund and maintain tools and resources. The Panel should consider how best to support long-term resources on a more stable basis – such as decoupling funding from the model of 3-year responsive mode awards.</p>
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Agility of funding

4.29 Some aspects of farm animal genomics are best delivered through large national or international consortia – for example genome sequencing or large-scale genome annotation, which spread the effort and the cost. Opportunities for the involvement of UK research teams can arise relatively quickly and must be seized where the scientific

case and the needs are strong. That said, there is more than just the strength of the scientific case to consider as the involvement of UK researchers in international efforts brings many unquantifiable benefits from having a seat at the table (e.g. networking, immediacy of up-to-date data/information, reputational benefits, future partners of choice). A highly relevant and current example of an emerging opportunity is that of the international effort coming together to sequence of the pig genome, and in which we urge UK participation via BBSRC funding (see section 4.46 below).

Recommendation 11: BBSRC’s funding mechanisms need to be sufficiently agile to allow involvement in national and international consortia at relatively short notice. We suggest that this could be achieved by utilising a small 'e-panel' of experts to peer review and support or reject a proposal to participate in a new initiative. Taking a proposal for such involvement through the normal peer review process at the next available grant round may miss the window of opportunity. The move to four grant rounds per year will increase the frequency of application points but will not reduce the time to reach a funding decision post closing date.

Funding research of industrial and strategic relevance.

- 4.30 It is important that a proportion of BBSRC funded research is aligned to the needs of its users – in this case we are mainly referring to the diverse farm animal industry and Defra as the principal policy department.
- 4.31 BBSRC has introduced the Industrial Partnership Awards (IPAs) and Government Partnership Awards (GPAs) in which grant applications with industry or Defra³³ interest (15% cash or ‘in-kind’ contribution) are viewed more favourably in peer review providing they meet the overriding criterion of excellent science. Efforts to score industrial and strategic relevance, and to balance that against research excellence have not been particularly successful within the Research Committees. One solution would be to treat industrial and strategic relevance in the same way as the larger programme grants i.e. have a separate funding pot once the Committees have reached a view on the quality of the science.

Meeting the future needs of industry

- 4.32 BBSRC has developed a Technology Strategy that identifies areas of underpinning research and related technology necessary to meet industrial needs on a ten-year horizon. Leading priorities are: bioprocessing; *in vivo* physiology & pharmacology; biocatalysis and biotransformations; exploiting systems biology; intelligent storage, retrieval & analysis of large data sets; crop sciences and bionanotechnology. Clearly some of these, particularly, large data sets, will be of relevance to the farm animal genetics related industries. However, BBSRC should ensure that its Technology Strategy takes due account of the underpinning needs of this sector: *cf.* the inclusion of crop science in the Technology Strategy, there is a compelling strategic case that farm animal genomics should also be incorporated.

³³ GPAs apply to the Food Standards Agency as well as Defra

Recommendation 12: BBSRC's Technology Strategy should take full account of the needs of the farm animal genomics sector. In the first instance we would recommend that enabling technology priorities include the development of informatics platforms, real-time diagnostics, SNP-typing at 0.1 cents per genotype, creation of embryonic stem cell lines and development of cryopreservation capabilities for farm animal germ lines.

Training

- 4.33 High quality training and the supply of skilled researchers in the area of farm animal genetics/genomics are critical. BBSRC needs to ensure an adequate supply of appropriately trained researchers and that the overall training mechanisms are responsive to the skills needs of industry and other users.
- 4.34 From the consultation exercise, academia and industry report a shortage of researchers with skills in mathematical genetics, bioinformatics, biochemistry and whole animal physiology/pharmacology. Industry in particular requires more people with training in both molecular and quantitative genetics. The perception of the 'omics' as the more glamorous of the disciplines is contributing to an imbalance in skills. The limited availability/affordability of veterinarians in research was also highlighted as an important issue, a finding consistent with concerns raised in the Review of Pirbright in 2002³⁴, which recommended that IAH reinvigorate its interaction with the Veterinary schools over research training.
- 4.35 Many of the skills shortages, particularly in quantitative aspects, that are impacting on genetics/genomics are also pressures elsewhere in BBSRC's remit and unless addressed will have consequences for overall delivery of BBSRC's Vision. We recognise that Council cannot address these skills shortages alone but there are actions that could be taken now, such as enhanced stipends in areas of key skills shortages.
- 4.36 BBSRC has recently initiated a scheme to increase the level at which studentships in *in vivo* physiology and pharmacology are funded. The Pharmaceutical industry is contributing to this scheme that will make studentships more attractive (for students and University Departments) in this shortage area. We consider that there would be opportunity to develop such a scheme in partnership with the farm animal genetic/genomics industry if it helped the supply of quantitative bioscientists. Promotion of cross-talk between academia and industry would undoubtedly benefit from robust support of Genesis-Faraday CASE studentships and further incentivised industrial CASE awards (e.g. through competition).
- 4.37 Other actions concerning training that would be of value include:
- **Short-term visiting fellowships/ research development fellowships.** Allowing researchers to experience different research techniques or a different field of research;
 - **Industrial fellowships.** To reinforce end-user relevance in research training programmes;
 - **More joint university/institute studentships and doctoral training centres.** Stimulating collaboration and providing young researchers with experience of the

³⁴ Review of the Institute for Animal Health- Pirbright Laboratory. A report for BBSRC Council. July 2002.

different research environments early in their career, and exposure to a variety of research tools and project types;

- **Increased flexibility of studentship funding.** The requirement of UK citizenship to receive a full BBSRC studentship stipend is highly restrictive, particularly in priority skills-shortage areas such as quantitative genetics and informatics. We would like to see this requirement removed. We also believe that it is imperative that BBSRC should seek to fund studentships in genomics/informatics at the Wellcome Sanger Institute, either as full studentships at the Institute or CASE-style placements. This is an essential commitment to develop state-of-art skills in genomic/informatics amongst young BBSRC researchers;
- **Career-track Fellowships.** It is vital to develop and expand the next generation of research leaders to sustain the farm animal genomics sector, to take advantage of the increased scientific opportunities created by the availability of genomics information and tools and for succession planning; there are currently few opportunities to develop ‘new blood’ to replace the current cadre of ageing research leaders.

Recommendation 13: BBSRC should use the full spectrum of activities under studentships and fellowships, including bespoke fellowship calls and targeted incentives where necessary, to address:

- **skills shortages in the farm animal genomics area, in particular informatics and quantitative aspects;**
- **improve the flow and communication between industry and academia (see recommendation 9);**
- **improve the flow and communication between this area and research on human systems (see recommendation 8).**

BBSRC should also invite industry to jointly fund in key shortage areas using a similar model to that employed for integrative mammalian physiology and robustly support Genesis-Faraday CASE awards.

Ethics and public dialogue

4.38 BBSRC already has a strong commitment to public dialogue and addressing ethical concerns in research. It is a standard requirement for successful BBSRC research grant applicants to provide information on the context of the research, possible outcomes, regulatory issues (including the need to work on animals, under the Animals Scientific Procedures Act 1986) and the use of GM technology. BBSRC currently promotes public engagement by a variety of mechanisms including exhibitions, public events and workshops, discussion documents, consultations and a scientist-school link scheme³⁵.

4.39 There has been little research into public attitudes and values on genetics and genomics in the context of farm animals. However, the public concerns relating to GM crops signified a breakdown in communication and trust between government, scientists and the public that reinforces the importance of effective public dialogue in sensitive areas of research.

³⁵ See <http://www.bbsrc.ac.uk/society/Welcome.html> for further details.

- 4.40 As we indicated in chapter 1, and borne out by the consultation, farm animal genomics is a field of research where there seems to be a particular concentration of potential public and ethical concerns stemming from aspects of the research or its possible application. Concerns focus particularly on the integrity, health and welfare of new genotypes, the welfare implications of GM technologies used in research, and the production of animals able to survive in poor and inappropriate environments.
- 4.41 There are a number of programmes that are addressing the societal and ethical issues associated with genomics including - the Economic and Social Research Council (ESRC) Centre for Genomics in society “Egenis”³⁶, the Centre for Economic and Social Aspects of Genomics (CESAGen)³⁷, the Netherlands Genomics Initiative³⁸ and the “Centre for Society and Genomics”³⁹. At the trans-national level initiatives include the European Society for Agricultural and Food Ethics (EurSafe)⁴⁰, Sustainable European Farm Animal Breeding And Reproduction (SEFABAR)⁴¹. BBSRC-funded researchers are also involved with other EC projects, which have an ethical/social dimension, such as the European Animal Disease Genomics Network of Excellence for Animal Health and Food Safety (EADGENE).
- 4.42 RI, as the leading UK centre for farm animal genomics, has tended to engage with such existing programmes, rather than seeking to duplicate them. It has also been involved directly with groups such as Compassion in World Farming to stimulate discussion and debate, and to identify and refine concerns. This coordinated approach represents a model that could be extended to all institutions with significant research programmes in farm animal genomics.
- 4.43 All BBSRC sponsored research in farm animal genomics should be firmly embedded in a context of ethical awareness and public dialogue, and funders, institutions and researchers in the field share this responsibility. However, in most cases it is considerably more effective for individual PIs to contribute to established communication networks and programmes (such as those above) than to create their own.

Recommendation 14: All BBSRC research in this area should be embedded in a context of ethical awareness and public dialogue. Concerns about the health and welfare of animals used in and produced by farm animal genomic technologies can partly be addressed by the development of new welfare screening methods.

Future funding

- 4.44 We argue early in this report that farm animal genomics is an area of high strategic importance to BBSRC. Not only is there enormous potential for generating basic knowledge of biological systems but there is also a clear economic and social value. Unlike crop science, which is comparatively well-funded but with limited routes for uptake, there remains a strong and diverse livestock industry in the UK with good links

³⁶ <http://www.ex.ac.uk/egenis/about.htm>

³⁷ <http://www.cesagen.lancs.ac.uk/staff/twine.htm>

³⁸ <http://www.genomics.nl/data/international.htm>

³⁹ http://www.genomics.nl/data/pers/pers_230103_uk.htm

⁴⁰ <http://www.eursafe.org/>

⁴¹ www.sefabar.org

to the academic sector. It is our considered view that an appropriately high value should be accorded to basic and strategic research with application in the farm animal sector.

- 4.45 It is the view of the review panel that the current level of funding in farm animal genomics is not sufficient if the UK is really to capitalise on existing expertise, and become a leading nation, scientifically and economically, in this area. We acknowledge that BBSRC is already the UK's largest funder of basic research on farm animal genetic/genomics but Council's overall investment has decreased in real terms since 2001. We propose that £25M of new funding will be necessary over the next five years. We are aware the BBSRC has earmarked £6M over the SR2004 period for research into animal health and welfare to seize opportunities presented by advances in genomics. This is to be welcomed but should represent the vanguard of increased investment in the sector. To meet the desired level of commitment BBSRC should increase its own investment and work to leverage additional monies from other funders and industry. We propose a ramped delivery framework through SR2004 and SR2006 to allow for 'pump-priming' of a currently over-stretched field. This will allow it to develop the necessary infrastructure, skills and critical mass, within a realistic timeframe, to effectively respond to the new funding opportunities.
- 4.46 In addition to more funding we reiterate that there are certainly other further gains to be made in the better coordination of research and resources. There will also be gains from focussing more research effort on the leading priorities and species outlined in Chapter 3. But there is a clear case that ramped and sustained increases in funding are necessary in order to reinvigorate the sector and focus investment on the opportunities and challenges presented by the farm animal health agenda, as the leading research priority. We have proposed a number of measures in this report to improve farm animal genomics. If additional funding is to be provided then we recommend that it is deployed as set out below in loose priority order:
1. **Investment in the pig genome (Recommendation 3).** As a priority, we propose that the sequencing of the pig genome represents an ideal and timely opportunity for BBSRC to take a strategic lead in a large-scale genomics consortium and reap the intellectual and infrastructural benefits for genomics research that such a lead would bring: namely the associated training of UK researchers, collections of biological materials, and an early strategic lead for the conversion of academic outputs. The trans-Atlantic consortium planning to undertake the sequencing project is currently beginning financial negotiations, expected to be resolved in September 2005, and BBSRC will need to respond quickly to negotiate a leading involvement;
 2. **Targeted training of researchers (Recommendation 13).** We have set out a raft of measures that should be employed early to pump-prime the training and development of researchers and to address some of the current critical intellectual deficiencies. We recommend in the first instance that postgraduate training incentives should be targeted towards the quantitative genetics and informatics disciplines, and that career-track and research development fellowship awards be targeted towards researchers in farm animal genomics to augment priority areas and alleviate over-stretch;

3. **Curation of genomic databases (Recommendation 10).** We propose that new funding should be allocated to placing the support of ARKdb on a stable footing, as a UK genomic resource hub for farm animal research. The underpinning importance of well-resourced genomic database curation cannot be understated in an era when biological research is undergoing a paradigm shift as important as the advent of molecular genetics. Failure to allocate sufficient gravitas to the task of database curation will undermine downstream research programmes and lead to a poor-value return for investments;

4. **Farm Animal Health Initiative (Recommendations 2 and 5).** Farm animal health should be considered BBSRC's leading strategic priority for farm animal research. Acknowledging the funds earmarked for this purpose in BBSRC's SR2004 Delivery Plan, this should be a spring board for a period of sustained, robust investment in this priority area. Sustained funding should be allocated to develop infrastructure and foster the exploitation of genomic technologies in this area of research;

5. **Support of Academia-industry network facilitation (Recommendation 9).** We propose that ongoing role of Genesis Faraday, or another organisation fulfilling this role, is of sufficient strategic importance to warrant sustained investment by BBSRC in this activity, over the medium term period, including the continued provision of an allocation of BBSRC CASE awards;

6. **Creation of a 'Farmers and scientists' network for data collection from commercial herds/flocks (Recommendation 7).** This would represent an ambitious undertaking, requiring multilateral initiative and investment (ideally a model to be discussed and developed through a proposed 'funders forum') but this investment would provide a highly powerful new tool for academic researchers working in the medium term, particularly to address the considerable research challenges presented by the leading priority of farm animal health;

7. **Farm animal and human genomics initiative (Recommendation 8).** To promote awareness and realisation of the potential of farm animal research to inform research in human systems, and to foster communication and movement of researchers between the two fields.

4.47 We consider it vitally important that this investment in farm animal genomics research should be sustained over the medium to long term. Too often funding initiatives stimulate short-term activity that is not followed through with sustained momentum, and the initial investment is not capitalised upon. BBSRC should seek to avoid such pitfalls by creating an investment framework for farm animal genomics. We propose that this investment be reviewed after four years with a view to continuation.

Recommendation 15: BBSRC's SR2004 investment should be seen as the vanguard for increased investment in farm animal genomics through into SR2006 and beyond. BBSRC should seek to ensure that the total new investment in this area is in the order of £25M over the next 5 years. Earlier in this report we propose several priorities for such funding and mechanisms to improve its deployment.

4.48 The UK community in farm animal genomics and related areas are internationally renowned. However they are at a turning point. Robust strategic investment and innovative leadership by BBSRC would drive the UK farm animal genomics and related community to international excellence. With the right support we have a critical mass of scientists and mix of disciplines that would have few competitors internationally. Lack of investment or poor strategic decisions at this time will consign the UK to being an also-ran. The scientific challenges and economic rewards are attainable if the mechanisms and resources can be found.

Annex 1: Terms of Reference for the Review Group and Membership of the Review Panel

Terms of Reference

1. To review the BBSRC's current research through CSG, responsive mode and other funding relevant to farm animal genomics encompassing molecular and quantitative genetic approaches to selective breeding. To analyse research strengths and weaknesses in the context of a medium to long term (i.e. 10 - 20 year) strategy for work on U.K. farm animals (including fish but in particular relating to poultry, cattle, sheep and pig).

2. To consider how BBSRC's research priorities in this area relate to those of Government Departments, and in particular to DEFRA and SEERAD, and those of industry and other stakeholders, in the light of recently published aims and objectives, and other relevant reviews.

3. To advise on BBSRC's priorities for future research in farm animal genomics and how they should be developed, consideration to include:

- animal health and welfare (disease, reproductive fitness, development, growth and ageing),
- traits for quantity and quality of animal produce (meat, milk and hides) within a sustainable agricultural framework,
- translational research into basic science underpinning human health;

and to recommend a strategy:

a. that promotes synergistic structures and partnerships:

- within and between BBSRC Institutes
- between BBSRC Institutes and the Universities
- between BBSRC and other funders nationally and internationally;

b. that incorporates the most appropriate funding arrangements to support farm animal genomics research in Institutes and Universities, to ensure they retain the capability to deliver the research in the medium- to long-term, and take account of the various stakeholders' needs;

c. that optimises the transfer of the outputs of basic research (including that on model systems and species), funded through responsive mode or otherwise, into application in farm animals, and optimises knowledge transfer between farm animal research and human systems.

4. To report to Council by July 2005, with an interim report in February 2005.

Membership of the Review Panel

Name	Institution	Expertise
Prof. Cheryll Tickle (Chair)	Univ. of Dundee	Vertebrate limb development. BBSRC Council member and ARK-Genomics steering committee
Dr Nick Ambrose (Govt. Dept.)	SEERAD	Animal sciences/agriculture
Prof. Leif Andersson	Univ. Uppsala (Sweden)	Large animal and poultry genomics/genetics
Prof. Alan Archibald	Roslin Institute	Large animal genomics/genetics
Dr Ewan Birney Bioinformatics Institute	European	Genome annotation
Prof. Allan Bradley (Director)	Sanger Institute	Model animal genomics/genetics
Dr David Garwes	Defra (Govt. Dept.)	Animal sciences/agriculture
Dr Mike Mendl	Univ. of Bristol	Farm animal welfare
Dr Graham Plastow	Sygen International	Genomics research and commercial breeding (pigs and shrimp)
Prof. Martin Shirley (deputised by Dr Pete Kaiser)	Institute for Animal Health (Compton)	Farm animal disease
Prof. Andy Tait parasitology	Univ. of Glasgow	Veterinary & molecular
Marco Winters	Cogent	Commercial breeding (cattle)
Assessor to Panel Chris Warkup (industry- not for profit)	Genesis Faraday	Linking basic research in livestock genetics and industrial application
BBSRC Office Dr Paul Burrows	Head of Strategy Planning, BBSRC	
BBSRC Office- Secretary Dr Jef Grainger	Strategy Planning, BBSRC	

Annex 2: The consultation process

Written consultation

A consultation document was produced in October 2004, consisting of 34 questions set out amongst background information, divided into the four sections: *research and its implications; utilisation of research; resources and facilities; funding*. This document was sent to over 300 identified potentially interested parties, including academic researchers, Government Departments, industry, unions and societies, consumer groups and NGOs. It was also distributed to the Genesis Faraday membership and made available on the BBSRC website. It can be viewed at <http://www.bbsrc.ac.uk/society/consult/farmgen/Welcome.html>.

Whilst BBSRC has previously consulted largely with academic and major industrial stakeholders, this consultation document represented BBSRC's first attempt to address the challenge of exploring the wider issues of interest to a wide cross-section of stakeholders, whilst also addressing the specific interests and needs of the science base. We believe that attracting perspectives from a wide range of constituencies has helped us to challenge our own assumptions and identify the hopes and concerns that the science we fund triggers in other people.

Sixty three replies to the consultation document were received, from a balanced range of stakeholder groups. A list of all respondents can be viewed at <http://www.bbsrc.ac.uk/society/consult/farmgen/>. The consultation responses were considered by the Review Panel, and the key messages returning from the questions posed were extracted. In some cases, very clear majority views emerged (e.g. the importance of animal health and welfare as the leading research priority) whereas a wider range of opinion was expressed in other cases (e.g. advantages of institute versus university-led research), or a main message was complemented by a strong minority counter-view (e.g. should we be undertaking research in farm animals with the aim of improving human health).

The Panel firmly incorporated the messages emerging from the consultation process in the formulation of their arguments and conclusions: the key messages emerging from the consultation are referenced at the appropriate junctures within the main body of the report. All views represented were carefully considered by the Panel and although we might respectfully disagree with some views, our conclusions were based upon both the balance of opinions returned, and our own considerations of the issues and responses received. We would like to thank all who submitted questionnaires for providing high-quality responses and a strong depth of opinion on which the Panel could draw during its considerations.

Oral Consultation

Respondents to the written consultation exercise were invited to a discussion meeting, held at the Smithfield Show, Earl's Court, London, on December 4th, 2004. This discussion meeting was Chaired by Professor Tickle, and attended by Panel members Professor Archibald and Dr Plastow, representing academic and industrial expertise in the sector, respectively.

The meeting provided an opportunity to expand upon issues raised in the written consultation, and in particular, given the setting of the meeting, to address issues relating to animal breeding and agriculture. A small, mixed audience attended the meeting, including academics, industrialists and farmers.

Annex 3: Biological definitions

Allele: *One of the variant forms of a gene, differing from other forms in its nucleotide sequence.*

Gene: *A hereditary unit consisting of a sequence of DNA that occupies a specific location on a chromosome and determines a particular characteristic in an organism by directing the formation of a specific protein, and is capable of replicating itself at each cell division. Genes undergo mutation when their DNA sequence changes.*

Genetics: *The study of heredity and how traits are passed on through generations. A subdivision of the science of genetics is **molecular genetics:** the study of how genetic information is encoded within the DNA and how biochemical processes of the cell translate the genetic information into the phenotype.*

Genetic modification: *Stable and heritable artificial transfer of specific DNA sequences from one organism to the genome of another. Typically involves Integration of DNA sourced from one species into the genome of another species, allowing DNA transfer that could not occur through sexual processes.*

Genome: *All of the genetic information or hereditary material possessed by an organism; the entire genetic complement of an organism. Each cell in an organism contains a complete copy of the genome.*

Genomics: *The large-scale investigation of the structure and function of whole sets of genes and their interactions rather than single genes or proteins.*

Transgenic: *A genetically modified organism.*

Annex 4: Main abbreviations used in the report

BAC	Bacterial artificial chromosome
BBSRC	Biotechnology and Biological Sciences Research Council
BI	Babraham Institute (BBSRC-sponsored)
BSE	Bovine spongiform encephalopathy
CEFAS	Centre for Environment, Fisheries and Aquaculture Science (Defra-sponsored)
CSG	Core Strategic Grant (used to support long-term research in BBSRC institutes)
Defra	Department for Environment, Food and Rural Affairs
DfID	Department for International Development
DTI	Department of Trade and Industry
EBI	European Bioinformatics Institute
EMBL	European Molecular Biology Laboratory
ESRC	Economic and Social Research Council
EST	Expressed sequence tag
EU	European Union
FAWC	Farm Animal Welfare Council
FMD	Foot and mouth disease
FRS	Fisheries Research Services (SEERAD-sponsored)
FSA	Food Standards Agency
GM	Genetically modified (transgenic)
GPA	Government Partnership Award
HEI	Higher education institution
IAH	Institute for Animal Health (BBSRC-sponsored)
IGER	Institute for Grassland and Environmental Research (BBSRC-sponsored)
IGF	Investigating Gene Function (BBSRC funding initiative)
IPA	Industrial Partnership Award
MLC	Meat and Livestock Commission
MRC	Medical Research Council
MRI	Moredun Research Institute (SEERAD-sponsored)
NERC	Natural Environment Research Council
NGO	Non-government organisation
nvCJD	New variant Creutzfeldt-Jakob Disease
PA	Per annum
PI	Principal Investigator
RI	Roslin Institute (BBSRC-sponsored)
R&D	Research and development
SEERAD	Scottish Executive Environment and Rural Affairs Department
SME	Small to medium enterprise
SNP	Single nucleotide polymorphism
TB	Tuberculosis
TSE	Transmissible spongiform encephalopathy