BACKGROUND STUDY PAPER NO. 18

منظمة الأغذية والزراعة للأمم المتحدة

联合国粮食及农业组织

Food and Agriculture Organization of the United Nations

Organisation des Nations Unies pour l'alimentation et l'agriculture

Organización de las Naciones Unidas para la Agricultura y la Alimentación

E

COMMISSION ON GENETIC RESOURCES FOR FOOD AND AGRICULTURE

OPPORTUNITIES FOR INCORPORATING GENETIC ELEMENTS INTO THE MANAGEMENT OF FARM ANIMAL DISEASES: POLICY ISSUES

by

Stephen Bishop [1], Mart de Jong[2], Douglas Gray [3]

1. Principal Investigator, Roslin Institute, specialising in disease genetics, epidemiology and animal breeding.
2. Professor of Quantitative Veterinary Epidemiology at the Universities of Wageningen and Utrecht.
3. Regional Coordinator for the International Livestock Research Institute in South East Asia.

This study is put at the disposition of the Commission by the Animal Production and Health Division (AGA), for its possible use in the further development of the *Global Strategy for the Conservation of Farm Animal Genetic Resources*, and the development of the first *State of the World's Animal Genetic Resources for Food and Agriculture*.

This study is the responsibility of its authors, and does not necessarily represent the views of the FAO, or its Members.

Index

Page

Summary 1

1. Introduction 3

2. Background 5

3. Opportunities 9

3.1 Nature of opportunities 9
3.2 Understanding how to respond to opportunities 10
3.3 Current possibilities for action 12

4. Benefits13

4.1 General nature of benefits 13
4.2 SWOT analysis of genetic strategies for disease management 14
4.3 Economic benefits 16

5. Critical factors for success 17

5.1 Appraisal of current situation 17
5.2 Desired situation 17
5.3 Pathways to success 18

6. For consideration 21

7. Bibliography 22

Appendix 1: Factors influencing the possible rate of parasite evolution, in response to genetic changes in the host 26

Appendix 2: The persistence of genetic variation in host resistance to disease 27

Appendix 3: Genetic factors underlying resistance and tolerance 27

Appendix 4: Principles of genetic markers 28

Appendix 5: Cost benefit analyses of incorporating genetic elements in disease management strategies for four diseases 28

Appendix 6: The terms of reference 31

Appendix 7: The Authors 32

SUMMARY

1. This Background Study identifies the need for enhanced investment in the genetic element of disease management. This can best be integrated within the overall livestock development strategy for breeds, the development of which is supported by genetic improvement guidelines being detailed by FAO within the Global Strategy for the Management of Farm Animal Genetic Resources.

2. All livestock production systems are influenced substantially by both genetic and environmental factors and their interaction. Systems commonly involve diverse production goals and diverse resources. Many of the genetic and environmental factors are under the control of, and continually modified by, livestock keepers and other stakeholders. Disease contributes an important set of problems within these systems, including production losses, uncertain family food security, loss of income, and some diseases and the strategies used to manage them directly impact upon human health. Partial costing estimates of the impact of animal disease are 17 percent of turnover within the livestock sector of the developed world and 35-50 percent in the developing world. There are a number of disease management options, including vaccination, chemotherapy, improved husbandry and genetic change. Each of these options can partly manage disease problems, and use of any one of these options has consequences for the production system as a whole. Management options may interact; the use of one option may enhance or diminish the effectiveness of another. The development of capacity and systems to address one disease will enable other disease problems to be addressed more effectively.

3. The specific advantages of incorporating genetic elements into the management of farm animal diseases include low input and maintenance costs once the strategy is established, and permanence and consistency of effect. Together these attributes result in genetic approaches contributing to sustainable disease management. Genetic improvement of disease resistance can be an element of overall genetic improvement, which in turn is a component of sustainable livestock production system development.

4. There are a number of important diseases in livestock production systems where genetic approaches have been shown to be effective in providing benefits for livestock keepers and the wider community. These are in developed and developing countries; in intensive and extensive systems; and in subsistence and market-oriented enterprises. Successfully managed diseases have included tick infestations, helminth infections and Marek's disease. Additional diseases where genetics is currently being used as a component in disease management include trypanosomosis, mastitis, scrapie and *E. coli* diarrhoea in pigs.

5. Options for incorporating genetics into disease management strategies include choice of breed; crossbreeding to take genes from one breed to another; selection by measurement of outcome of disease challenge, genetic markers or a combination of both. Benefits depend upon specific diseases and which options are used. These include reduced reliance on chemicals, increased production, increased food security, more efficient use of inputs, reduced disease risks to humans and livestock, and enhanced international trade.

6. Whilst there is still much to be learned, there is sufficient current information to make immediate policy decisions on the use of existing animal genetic resources for disease management. Additionally, there is sufficient genetic variation between breeds in resistance to a wide range of diseases in most livestock species to justify decisions on the management of animal genetic resources that combine breed conservation and utilisation.

7. To reap the benefits of genetic elements in disease management there are several broad requirements. (Specific technical recommendations are made within the report.)

- There needs to be recognition that genetic resistance to disease can be of major significance to livestock development. Additionally, there is the need for those responsible for animal disease management to recognise that genetic approaches have a role to play in integrated disease management. *This requires investment in multidisciplinary teams to develop the capacity to undertake appropriate research and scoping studies and plan development interventions.*

- There is a need for countries to further analyse disease problems to establish opportunities where genetic elements may effectively contribute to sustainable management and define the process by which these options can be integrated into management programmes. *This requires investment in collaborative development activity amongst technicians of different backgrounds and skills.*
- There is a need to develop specific genetic options for disease management and integrate these into whole-system solutions. Stakeholder and community participation is an essential part of this process. *This requires investment in implementation of genetic elements into integrated disease management strategies in communities which depend on livestock.*

8.The key policy items for consideration are presented in Section VII.

1. INTRODUCTION

9. The Global Strategy for the Management of Farm Animal Genetic Resources is an intergovernmental initiative being detailed for country use, by the Food and Agriculture Organization of the United Nations. Genetic resources are the building blocks of sustainable agriculture. Genetic diversity has enabled farmers and breeders to develop and use domestic animals that are suited to a wide-range of production environments from frozen tundra and temperate regions to hot deserts and moist tropical conditions. The Global Strategy consists of several inter-related components and elements, which provide nations with a comprehensive framework to characterise and plan the use, development and conservation of their livestock breeds.

10. Disease management is a critical component of livestock production and therefore, this Background Study will contribute primarily to the sustainable intensification element of the Global Strategy, with potential implications for the conservation and characterization elements. The Study identifies the need for enhanced investment in the genetic element of disease management, which can be integrated within the overall genetic improvement strategy for breeds or populations.

11. All livestock production systems are influenced substantially by both genetic and environmental factors, and their interaction. Systems commonly involve diverse production goals and diverse resources. Many of the genetic and environmental factors are under the control of, and continually modified by, livestock keepers and other stakeholders. The variable resources available to livestock keepers include animal genetic resources, and keepers have different capacities to work with and modify these resources. Appropriate genetic improvement of animal genetic resources is one of the major modifications that can be made by livestock keepers and others contributing to the sustainable development of these production systems. Genetic improvement may focus on production traits and also on disease resistance. Disease contributes an important set of problems within livestock production systems, including production losses, uncertain family food security, loss of income, and some diseases and the strategies used to manage them directly impact human health.

12. Infectious disease[1] has major adverse effects on livestock production and animal welfare, worldwide. In market-oriented terms, the costs of disease are estimated as 17% of turnover within the livestock sector in the developed world (£1.7 billion in the UK) and 35-50% in the developing world. All animal production systems are subjected to challenges by infectious disease and all animal production systems are liable to large production losses from disease. Disease also poses threats across species barriers. Firstly, several animal infections pose zoonotic threats to human health. Secondly, diseases in one species may act as reservoirs for infections in other species. Uncertainties in terms of threats to food security and instability of livestock production systems are a further impact of animal disease.

13. Options for the management of infectious disease include vaccination, chemotherapy, improved management, diagnosis and removal of infected animals, and genetic change. Each of these options can contribute to solving the problems caused by disease. Use of any one of these options has consequences for the production system as a whole. Management options may interact; the use of one option may enhance or diminish the effectiveness of another. However, disease management can break down. Strategies based on a single approach are the most vulnerable to breaking down. Those based on multiple approaches are inherently more resilient and stable. For example, integrated pest management (IPM), a strategy combining several approaches, is well established in the management of plant diseases. Additionally, integrated strategies including the control of the movement of livestock and livestock products, strategic vaccination and targeted disinfections are widely used for many livestock diseases.

---

[1] For the purposes of this paper, infectious disease is defined as covering diseases caused by organisms that colonise a host, such as viruses, bacteria, protozoa, helminths, ectoparasites, etc. These organisms are referred to generally as parasites.

14. Sustainable long-term management of animal disease is a major priority for many governments. Massive research and development effort continues to be expended on research and application of non-genetic control measures aiming to ameliorate or manage the major diseases impacting livestock. Success is mixed, depending upon the disease. A critical issue is the long-term sustainability of currently used strategies. The evolution of pathogens or parasites resistant to currently used therapies, e.g. antibiotics, anthelmintics or vaccines is a major global concern.

15. There is predicted to be a large increase in demand for animal products, primarily in developing countries. This is largely a result of increased population and affluence in these countries, consequences of which include increased urbanisation and intensification of livestock production. This will make the management of animal diseases even more important. The relative importance of different diseases is also likely to change as livestock production systems evolve. Hence the capacity required for managing animal disease will increase.

16. There are now major developments in basic tools such as genomics for use in research, in the development and use of technologies for disease management and in the application of genetics to disease management. Massive complementary work of relevance is also underway for human disease. Together, these new tools will provide unparalleled opportunities for disease management. Of specific relevance to this document is the fact that these technologies will all facilitate the use of genetics to assist in the management of disease.

17. Against this background it is timely to consider opportunities for utilizing genetics as an additional tool in the strategies aimed at achieving sustainable disease management. This document covers technical, policy and operational issues relating to the topic. The use of genetics to assist in disease management is a relatively new field, and crosses the disciplines of veterinary, animal and social sciences. There is a dearth of information giving complete overviews of the topic and many misconceptions exist. In this document policy recommendations are drawn from a consideration of available knowledge.

18. This document contains the following:

- Background – a summary of information necessary to understand the potential of genetic elements in the management of disease
- Opportunities – a summary of the technical opportunities to address and realise the potential of genetic elements in the management of disease
- Benefits – a summary of benefits that will arise from the successful implementation of genetic elements in the management of disease
- Requirements – a summary of where countries, livestock sectors and industries currently are in terms of genetic management of disease; and the requirements for them to move to a position where genetic elements constitute an integral component of effective disease management strategies
- Policy Issues – a summary of policy issues to be considered by countries and other stakeholders.

2. BACKGROUND

What is the distinction between infection and disease, and between tolerance and resistance?

19. Disease is often used to cover two distinct concepts: infection and disease. Infection is the colonization of a host animal by a parasite. In some but not all diseases, multiplication of the parasite within the host is part of the infection process. Parasite is a general term describing an organism with a dependence upon a host. Parasites include many organisms, including viruses, bacteria, protozoa, helminths, flies and ticks. Disease describes the side effects of infection by a parasite. Disease may take several forms including acute, sub-acute, chronic and sub-clinical, which may or may not be debilitating.

20. An important point to note is that an individual host may be infected by a parasite, but show little or no measurable detriment. This is known as tolerance. In contrast, resistance is the ability of the individual host to resist infection or control the parasite lifecycle.

Is there a difference between managing resistance and managing tolerance?

21. Disease management also covers two distinct concepts: the management of infection, i.e. resistance, and the management of tolerance. The management of infection aims to reduce or eliminate the transmission of infection through a population of host animals. An outcome of successful infection management will be a subsequent reduction in the incidence or severity of disease in the host population and also in other populations in contact with the host population. At best, genetic improvement of a population in terms of its resistance to a disease may lead to eradication of that disease. This is currently being attempted with breeding programmes for scrapie resistance in sheep.

22. The management of tolerance, i.e. managing the symptoms or effects of disease, will alleviate suffering in infected individuals. However, if the transmission of infection is not simultaneously reduced, it will not reduce the incidence or severity of disease in other populations in contact. In some circumstances the management of tolerance is an effective means of managing a disease problem, especially when there is no means of reducing the infection pressure faced by the population. However, it may not be appropriate when a requirement is to manage transmission of infection in addition to alleviating animal suffering. At worst, management of the symptoms of disease alone, rather than the underlying cause of disease, may mask problems and lead to greater future disease problems.

How are disease and infection currently managed in farm animals?

23. A wide variety of strategies are currently used in the management of farm animal diseases. Such strategies have been the focus of many years of intensive research and international collaboration. Chemical intervention strategies have been used to control many diseases, notable examples being anthelmintics for nematode parasite control, acaricides for tick control and antibiotics for the control of many bacterial diseases. However, in addition to the problems noted below, access to these control measures is likely to be beyond the financial means of most smallholder farmers.

24. Vaccines have been used to successfully manage numerous diseases. For those diseases caused by microbiological agents the examples are plenty and well known but irradiated larval vaccines have also been used successfully for the control of lung worm diseases of cattle (*Dictyocaulus* viviparus) and sheep (*Dicytocaulus filaria*) in some countries – notably Britain and Yugoslavia respectively. However, there has been a failure to develop and bring into general use effective vaccines for a number of important diseases, notably other nematode infections and East Coast fever. Even for foot-and-mouth disease, many governments do not consider the available vaccines adequate to be used as an element in disease management.

25. Often there is no practical and affordable disease management strategy available to farmers and this leads to the large losses observed for many diseases. The farmer is then left to suffer losses, or treat

individual animals as best he can. A well-known example is the treatment of cattle affected with foot-and-mouth disease by the Maasai peoples of Kenya. In many circumstances, local animal genetic resources may have evolved that tolerate endemic diseases, however this is often threatened by the importation of exotic breeds with poor adaptation to these diseases. Therefore, situations in which disease management options were minimal may have been worsened with inappropriate importations.

How does the management of livestock disease impact upon realising sustainable livelihoods?

26. Sustainable livestock production systems contribute to sustainable livelihoods. Sustainable livelihoods are defined by being resilient to external shocks and stresses, not dependent upon external support, they maintain the long-term productivity of natural resources and, lastly, they do not undermine or compromise the livelihoods of others. Sustainable livestock production systems are those which are socially, biologically, environmentally and economically viable over a foreseeable period of time, and thereby contribute to the wellbeing of all stakeholders.

27. The vulnerability context frames the external environment in which people and livestock production systems exist. Sustainable livelihoods are fundamentally affected by critical trends, shocks and seasonality, over which people often have little control. Livestock disease is one of the critical shocks affecting sustainable livelihoods, particularly in terms of the effects it has on peoples' assets and natural capital and, as a consequence, their financial capital. Livestock disease reduces the productivity of animal resources and, in many circumstances, leads to considerable mortality. This will often lead to poverty. At critical times it can threaten food security of communities. Thus, disease management is central to poverty alleviation and, in some circumstances, food security.

28. In market-oriented terms the cost of disease to world animal production is estimated to be 17% of turnover within the livestock sector in the developed world (£1.7 billion in the UK) and 35-50% in the developing world. Economies within the developing world are particularly vulnerable and disease epidemics threaten communities and their infrastructure. Therefore, sustainable provision of animal-derived food and products to societies in the 21st century will rely upon the management of animal disease.

29. An important sociological aspect of the sustainability of a livestock production system is the extent to which it depends on external inputs, for example chemicals, feedstuffs, breeding material, etc. Another sociological aspect is the recognition and enhancement of the value of the indigenous animal genetic resources, when they contribute to disease management. Such recognition further empowers local communities. Therefore, genetic management strategies that utilise indigenous animal genetic resources and reduce the reliance on external chemical inputs are those most likely to be successful and sustainable.

What aspects of the sustainability of livestock production systems are important when considering disease management?

30. Many current disease management strategies are not biologically sustainable. In most circumstances this occurs when disease management is dependent upon external support, especially the provision of chemicals or vaccines. Firstly, environmental constraints may preclude the use of currently available chemicals. Secondly, financial constraints may preclude the use of many chemicals. This is especially evident when government support for disease management strategies is withdrawn and control is left to the individual stakeholders. Thirdly, parasites have and will continue to evolve a response to many disease management strategies. Important examples include:

- the evolution of resistance to anthelmintics by nematodes in all major sheep producing countries. This threatens sustainable sheep production throughout the world. Resistance has developed to all classes of anthelmintic, and no new classes are being produced by pharmaceutical companies.
- the evolution of resistance to antibiotics by bacteria. This threatens the efficacy of antibiotics in many production systems. This is especially problematic in intensive production systems where antibiotics are used to control unknown and sometimes sub-clinical disease problems.

- the evolution of resistance to anti-protozoals. For example, there is widespread resistance to drugs used to control animal trypanosomosis.
- the evolution of resistance to vaccines by viruses. The best-known example is the evolution of resistance of viruses to Marek's disease vaccines. Following each new generation of Marek's disease vaccine, a new and more virulent strain of the virus has arisen.
- The evolution of resistance to acaricides by ticks.

What are the wider impacts of livestock disease upon human health?

31. Livestock disease can impact upon human health in ways that are wider than the consideration of sustainable livelihoods at the community level. For example, one impact is due to the evolution of antibiotic resistance. Such evolution in animal populations threatens the sustainable use of the antibiotic usage in human populations. This has serious long-term consequences for human health.

32. A second impact of animal infections is in zoonoses and food-borne diseases. Zoonotic infections are those that cause disease in humans but are transmitted from animals. Often zoonotic infections are not pathogenic to the animal host and may not be recognized as a disease in animal populations. For zoonotic diseases it is the transmission of infection that must be managed, rather than the disease.

33. Food safety concerns overlap with zoonoses. An arguable difference is that the major proliferation is often in the product rather than the individual animal. There is a need for a precise definition of the zoonotic agent. This is required to ensure that correct target organism is identified and also that the target for control is not too broad so as to preclude successful eradication. An example is *E. coli* bacteria, in which some strains cause often-fatal food poisoning (e.g. *E. coli* 0:157), whereas other strains are harmless to humans. Once again, it is the transmission of infection that must be managed, rather than the disease.

Can genetics contribute to the sustainable management of disease?

34. For almost every disease that has been intensively and carefully investigated, evidence for host genetic variation has been found. Almost certainly, there will be genetic variation in resistance or tolerance for a wide variety of additional diseases. Genetics offers an effective and sustainable means of assisting in the management of infection and disease in many situations. Some of the many diseases for which there is known genetic variation between individual hosts within a population or between populations of hosts for either susceptibility to infection or tolerance of infection are listed in Table 1. In many situations it is not known whether the observed genetic variation is for resistance or tolerance, and often there will be an overlap between these processes. An important question to be addressed for each disease is: Does it matter whether the disease management strategy is based on resistance or tolerance?

35. Using genetics to assist in the management of the symptoms of disease, i.e. genetically increasing the tolerance of a population to infection, will be effective in reducing the incidence or the effect of disease in the target population. However, it may not decrease the prevalence of the parasite. Hence, the disease incidence in other populations in the same environment will not be affected. In worst-case scenarios, the presence of infection in the environment may be masked. For example, in the case of zoonoses, using genetics to manage tolerance of infection would be unwise as it may lead to human disease threats being unrecognised.

36. Using genetics to help manage the transmission of infection has the benefits of reducing the incidence of infection in the target population. This reduces the effects of disease and reduces transmission of infection to other populations, e.g. to humans or to populations that are susceptible to infection. This is a beneficial disease management strategy.

If genetics is used to help manage resistance, will the parasites evolve in response to changes in the host?

37. All control measures that aim to reduce numbers of parasites can lead to genetic change in the parasite population to evade the control strategy. This is best documented in the case of control by chemicals and antibiotics. This could also happen as the result of using genetics to manage parasite populations. However, although this has been documented in plants, there are currently no recorded examples of this occurring in domestic animal populations. Detailed consideration of factors that might influence parasite evolution is given in Appendix 1.

Why do domestic livestock not develop complete genetic resistance to disease?

38. There are evolutionary and epidemiological reasons to expect genetic variation between animals within a population for disease resistance and these are outlined in Appendix 2. Therefore, the existence of genetic variation in disease resistance is not a surprise. When there is genetic variation between animals within a population for tolerance, natural selection will push populations towards enhanced tolerance. This explains the presence of breeds with disease tolerance in areas where there is consistent and predictable exposure to infection. In such stable endemic situations, host and parasite tend to evolve together to a situation of balance between host survival and parasite replication. The end result is a relatively resistant and tolerant host and a relatively mild pathogen. Both tolerance and resistance are involved in the host evolution. This phenomenon is particularly common in tropical animal production systems. It has been well described for tolerance to trypanosomosis in African cattle. Rinderpest in the grey steppe cattle of Europe and Indian plains zebu were both good examples of host tolerance developing to the pathogen. Other good examples of the tolerance of different breeds of particular livestock to pathogens include sheep to bluetongue virus and horses to African Horse Sickness.

What is the relationship between disease resistance and immunity?

39. Immunity is the ability of the individual host to combat infection or disease due to the presence of antibodies or activated cells. It may be divided into various types: (a) acquired immunity which is conferred on an individual after recovery from a disease, (b) natural or innate immunity which is inherited from parents, or in some cases antibodies may be passed across the placenta or in the first milk (colostrums) and therefore be present in the blood at birth or immediately afterwards, (c) lactogenic immunity which provides protection to young animals from gut pathogenic microbes from antibodies present in the milk while they continue to suckle, (d) artificial immunity which may be induced by the injection of a vaccine, denatured antigens of a parasite, or antiserum which contains antibodies and thus may be used when the individual host is already infected. Immunity is often not complete and may vary between individual animals within a population. As described in Appendix 3 one of the mechanisms underlying genetic differences in resistance or tolerance is an appropriately targeted immune response: genetic differences in immune response and hence the degree of immunity developed by an individual may be associated with genetic differences in disease resistance or tolerance.

40. Herd immunity describes the immunological status of a population of hosts with respect to a given parasite. The level of herd immunity is determined by the net rates at which individual animals acquire and lose their immunity. A feature of herd immunity is that it is not necessary for all animals in the population to be completely immune for the population as a whole to exclude introduction and transmission of infection. In the same manner, it is sometimes not necessary for all the animals in a population to be genetically resistant for the population as a whole to be free of infection and disease.

Can genetics contribute solutions to future uncertainties caused by global change?

41. The current diversity in animal genetic resources is a consequence of past and continuous changes in environmental circumstances. This diversity also acts as a buffer against current uncertainties. Therefore, it is essential to maintain current genetic diversity to allow us to address future challenges caused by factors such as population growth, increasing urbanization and climate change. The maintenance of animal genetic resources is usually best achieved through their appropriate utilisation.

3. OPPORTUNITIES

3.1 Nature of the Opportunities

42. There are many diseases for which genetic variation between hosts within a population or between populations has been demonstrated for resistance to infection or tolerance of infection. Some of these diseases are listed in Table 1. Many of these diseases are extremely important at regional and global level. Perry *et al.* (2002) ranked livestock diseases for their impact on poverty, in terms of direct effects on production and indirect effects on international trade and marketing. Many of the diseases for which host genetic variation in resistance has been demonstrated appear on their list of important diseases. For example, helminthosis (predominantly infection by nematode parasites) was ranked the most important livestock disease globally, with ectoparasites, liver fluke and Newcastle disease ranked at 4, 5 and 7, respectively. These are all diseases for which genetic elements may be incorporated into the disease management strategies. Other diseases with global impact for which genetic management opportunities currently exist include haemonchosis (a subset of helminthosis), trypanosomosis, mastitis, coccidiosis, theileriosis (caused by *Theileria annulata*), dermatophilosis and East Coast fever (caused by *Theileria parva*).

43. Resistance and tolerance may be controlled by different physiological mechanisms. Moreover, genetic differences between animals may be due to the effects of one, a few or many genes. In situations where livestock production systems are constrained by more than one major disease, it is important to ensure that a genetic management strategy for one disease does not lead to increased susceptibility to another disease. An outline summary of these concepts is given in Appendix 3. These factors will impact upon the disease management strategies described below.

44. Genetic management strategies may be defined as the utilisation of genetic differences between individual animals or between populations of animals to assist in combating transmission of infection or the effects of disease. These strategies may be simple, however they become more complex as (i) the structure of a genetic improvement programme in livestock development and the analysis of the data become more sophisticated, (ii) artificial breeding technologies are used to accelerate genetic improvement, or (iii) molecular tools are used to more accurately identify better breeding animals.

45. Starting from the most straightforward, genetic management strategies for disease include:

- Choice of appropriate breeds for the production environment. In tropical environments where there are severe endemic diseases that exotic breeds are not adapted to, then locally adapted breeds are likely to be superior to imported exotic breeds. In extreme form, this may mean reinforcing decisions made by local producers and rejecting exotic genotypes. An example is the superiority of Red Maasai to Dorper sheep in areas of Kenya that are heavily infested with nematode parasites.
- Crossbreeding to introduce genes for tolerance or resistance into breeds that are appropriate in every other respect.
- Selection of individual animals for breeding on the basis of their resistance or tolerance (i) using a measurement of animals' resistance or tolerance of infection, (ii) using genetic markers or gene tests to assist the selection, or (iii) a combination of both. The use of genetic markers can potentially allow the selection of animals in the absence of infection challenge. An example is genetic markers for trypanotolerance that have been identified in African cattle.

Technologies such as artificial breeding and information technology can enhance these strategies but do not replace the need to set realistic and achievable production and breeding goals.

46. Programmes for genetic change require systems for recording animal pedigrees and performance in relation to the diseases of interest. At the simplest level this is observation by the farmer and choice of best breeding stock. At its most sophisticated it requires national and international databases. However the principles remain the same.

47. For all genetic management strategies there is either explicit or implicit knowledge required of:

- The major disease problems in different environments or production systems.

- The animal genetic resources available in each environment, as well as other animal genetic resources that might be appropriate to the environment of concern.
- The relative resistance or tolerance of infection of each of the types of animals (individual or population) in that environment.

This information enables matching of genetic resource to environmental conditions.

48. As genetic management strategies become more sophisticated, and overall disease management strategies become more complex, additional technology and expertise is required.

- Technology is required to store and process information and to predict the consequences of different genetic and non-genetic management strategies. At its most complex, this can include epidemiological prediction. For example, predicting the consequence of matching different genotypes to the environment in terms of disease incidence and severity.
- Expertise is needed to implement sophisticated genetic management strategies. For example, this can include implementing selection programmes for enhanced resistance.
- Technology and expertise is required to diagnose the presence of infection, the effects of disease and to measure the response of animals to infection.
- Technology is required for developing molecular tools, e.g. genetic markers (see Appendix 4).

49. Animal identification, data collection, data analysis and operational use for the management and breeding of livestock for productivity and product quality has commonly been developed and undertaken separately from the equivalent tasks for animal health monitoring and disease management. There is strong potential for reduction in costs as well as substantial added value through the integration of animal data recording systems and operations.

50. Many of the technologies required for genetic management are generic and the incentive for developing technologies is often from human health. Major opportunities exist for cross fostering information between animal and human studies. For example, animal models allow studies that are not possible with human studies. Conversely, results from human disease studies may give greater understanding of related animal diseases.

3.2 Understanding How to Respond to Opportunities

51. The decision-making process is important in the development of cost-effective policies for establishing the disease management strategy. These decisions need to be made at several levels by appropriate groups of people, with accurate information:

- Strategic decisions on the utilisation of animal genetic resources, which need to be made jointly by stakeholders, governments and the private sector, in consultation with farmers, NGOs, and technicians. For such advances to take place in developing countries, governments need to take the lead and provide an enabling environment.
- Decisions on livestock development objectives, which need to be made by farmers and their advisors.
- Identification of disease constraints, which need to be made by farmers, veterinary services and (inter)national disease control agencies.
- Identification of genetic opportunities for disease management, which need to be made by animal breeding specialists in conjunction with stakeholders.
- Operational breeding decisions, including how to measure performance, record pedigrees, source animals and reproductive techniques. These need to be made by farmers, farmer organisations and private sector interests, supported by governments and animal breeding specialists.

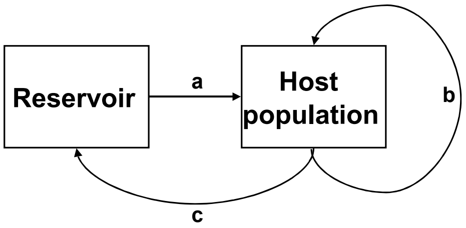
52. Decision-making is central to correctly matching (a) tools and technologies with (b) disease and environmental scenarios with (c) animal genetic resources. Initially, a series of primary questions must be answered:

- Are there major diseases of importance needing to be addressed in relation to the development objective?

- Are current management strategies adequate, sustainable, and cost-effective?
- Do current animal genetic resources cope with these disease challenges?

53. If the answer is "yes" to the first question and "no" to either of the other questions, then genetic management strategies may have an important role to play in dealing with the infection and the subsequent disease. It is then necessary to match the available tools to the disease being addressed. A series of secondary questions must now be asked. Firstly, what is the nature of the infection challenge and transmission of infection? Consider the simplified pathways of transmission shown in figure 1.

Figure 1. *Summary of pathways of infection for diseases in domestic livestock.*



54. A critical first question is whether transmission of infection from the reservoir to the host population along pathway **a** is sporadic or predictable. This will often determine whether or not field data describing individual animal response to the infectious challenge is adequate, or whether deliberate challenge experiments need to be set up.

55. If there is some degree of continuous or predictable challenge, i.e. animals in the field are challenged by the parasite at specific predictable times, then phenotype measurement is a possibility. In that case the next questions to be addressed are whether or not there are measurements that show (i) if the individual animal has been challenged, (ii) the degree to which it has been challenged, (iii) the response of the animal to the challenge, and (iv) the degree of disease suffered by the animal? Such measurements should also be informative about the state of the infection, e.g. is the infection latent or is the individual animal fully infectious? Additionally, carrier state animals should also be identifiable.

56. It is easiest to evaluate genetic variation in host resistance, and opportunities for including genetic elements in disease management strategies, when (i) there is predictable challenge from an endemic disease and (ii) phenotypic or observable indicator traits are available which allow discrimination between levels of resistance. When these requirements are not met, molecular genetic markers may offer powerful tools for use in enabling the breeder to determine the underlying genetic resistance of individual animals. This may require specific disease challenge tests from which genetic markers of resistance are developed, either at the research stage of verifying the value of the markers, or as a continuing operation; the latter approach being difficult particularly for diseases of high cost. The basic principles of molecular genetic markers are outlined in Appendix 4.

57. The management of infection and the management of tolerance have generally been discussed under the single heading of disease management within this section. In practical terms, the distinction between tolerance and resistance may not always be necessary. Additionally, the principles of integrating genetic and non-genetic management strategies will be valid, irrespective of whether it is resistance or tolerance that is being managed. However, in the situations where transmission of infection must be managed, it must be ensured that the genetic element of the management strategy will indeed reduce the transmission of infection, rather than favour individual animals or populations better able to cope with infection.

3.3 Current Possibilities for Action

58. Potentially each of the diseases listed in Table 1 represents an opportunity for incorporating genetic elements in disease management. However, in most situations considerable work will be required to evaluate, plan and realise these opportunities. It is likely that the diseases in Table 1 are only a subset of all possible diseases for which genetic management strategies are a possibility. Three scenarios are presented in Box 1, 2 and 3 as examples describing situations where:

- Genetic management strategies have been implemented (Box 1: the eradication of scrapie)
- Genetic management strategies have been initiated, but technical improvements are needed (Box 2: breeding for resistance to intestinal helminths in small ruminants)
- Substantial opportunities exist for incorporating genetic elements into disease management strategies (Box 3: poultry diseases)

59. There are a small number of diseases for which molecular genetic markers for resistance already exist. These markers enable selection of individual animals with enhanced resistance to infection. These diseases include Marek's disease, scrapie, and neonatal and post-weaning *E. coli* diarrhoea in pigs. These are all disease conditions considered problematic in developed country agricultural systems. As such, they have been able to attract greater research funding.

60. For diseases of importance in developing countries, molecular genetic markers are likely to be available soon for helminth resistance in sheep and trypanotolerance in cattle, although further development work may be necessary to implement breeding programmes of value to smallholders. For trypanosomosis in cattle, the markers are largely for tolerance to this disease; therefore genetic management strategies that employ these markers will not influence disease transmission.

61. Implementation of genetic management strategies will generally use technology somewhat simpler than genetic markers. More frequently, selection of individual animals or breeds with enhanced resistance will rely on phenotypic assessments of resistance in animals that are challenged by the target infection. There are a number of diseases, especially those affecting extensively managed ruminants, where sufficient knowledge exists to commence selection of individual animals or breeds for resistance (or enhanced tolerance) immediately in many circumstances. In sheep, these diseases include nematode infections (helminthosis), mastitis, footrot and flystrike. In cattle, amenable diseases include tick infestations, nematode infections, theileria, East Coast fever and mastitis.

62. As described in Box 3, smallholder poultry production systems represent a situation where the benefits of incorporating genetic elements into disease management are potentially enormous. However, realising these benefits will require additional research. This research should be given a high priority. Critical factors for success are described in section 6. These include recognition of the role of genetics in disease management, identification of opportunities for the utilisation of genetics and implementation underpinned by sound technical knowledge.

4. BENEFITS

4.1 General Nature of Benefits

63. The benefits of including genetic elements in animal disease management strategies may be grouped into several broad categories.

Sustainability

64. The major general benefit from the incorporation of genetic elements into disease management strategies is that of the sustainability of livestock production systems. Enhanced disease resistance or tolerance will lead to reduced requirements for inputs, greater outputs and greater reliability of outputs. This is especially beneficial in low input agricultural systems, particularly in agricultural systems in developing countries. Genetic change is permanent, and it is consistent in its effect across time. For large-scale production systems within market-oriented enterprises, genetic management strategies can lead directly to enhanced profit and enhanced product quality. For smallholder systems, the added benefit of security of production is critical to the sustainability of the enterprise. Once the required level of genetic management is established, little further resource input is needed. This is critical when disease management relies upon chemicals that have to be imported and are expensive to the smallholder.

65. Effective disease management strategies seek to integrate genetic and non-genetic approaches to health management. Used effectively, the components can complement each other and reduce the risks of any one component breaking down. For example, reduced reliance on chemical control prolongs the effective life of those chemicals before resistance develops. This is because selection pressure on the parasite population and the number of selection events is decreased. This diversity of approaches within a single management programme contributes to the sustainability seen in, e.g., IPM programmes.

Added Value

66. Enhanced genetic resistance to one disease may also increase the resistance of individual animals or populations to other related diseases. For example, increased resistance to one species of gastrointestinal nematode will provide increased resistance to other species. This represents added value when compared to the initial justification of the disease management strategy.

67. Moreover, the tools and technologies required for genetic management of different diseases are often similar. Therefore, developing capabilities for one disease will result in enhanced capabilities to deal with other diseases.

68. The most efficient genetic management strategies for both disease and production performance are achieved when animal identification, performance recording, herd health monitoring, and disease surveillance are integrated. This leads to added benefits, as production performance recording is also important for monitoring and improving livestock management. The importance of this integration will further increase with the development and use of molecular genetic and information tools. Therefore, it is essential that production performance recording and herd health monitoring development be undertaken as an integrated activity.

Community Level Benefits

69. An opportunity arising from identifying and developing animal genetic resources with enhanced resistance is that the owners of these resistant stock may benefit by being able to sell animals, semen or embryos to other potential users. This facilitates sovereignty and ownership of animal genetic resources to remain with the communities owning these resources.

70. The community also benefits from the implementation of genetic improvement programmes. For example, implementation of the programme will develop infrastructure for the exchange of information. This can be used to improve skills in livestock and farm management, possible sharing of market opportunities and creating a community sense that helps pursue common interests.

71. Disease management, itself, has wider benefits. Security of production through having individual animals or populations better adapted to the environmental constraints, i.e. disease, leads to benefits beyond that of enhanced and more reliable production. These benefits will commonly be realised by the broader community in agricultural sectors of developing countries. They lead to greater opportunities for women to participate in rural development. Additionally, this security of production may help halt the decline of rural populations in these areas, maintaining the integrity of the rural societies. This will also improve food security in situations where the production systems are vulnerable and improve nutrition for children. Reducing the vulnerability of livestock production to unpredictable disease events has proved in practice to provide confidence for farmers to invest in livestock production as a means of enhancing livelihoods.

Society Level Benefits

72. The development of sustainable disease management strategies may also reduce many disease risks to man. This is a direct effect when the disease being addressed is zoonotic. Reduction of the transmission of zoonotic infections will directly enhance the health of human populations. Important indirect benefits will arise through the reduced requirement for chemical control measures, especially through the reduced requirements for antibiotics. Antibiotic resistance is a major current threat to the effective control of some human diseases, notably tuberculosis and MRSA. In general, antibiotic resistance problems could be worsened by indiscriminate use of antibiotics in animal production. Reduced and more effective antibiotic usage will lead to reduced evolution of antibiotic resistance, with long-term benefits to mankind.

National Benefits

73. Management of infection may lead to benefits at the national level, by enabling international trade in animals and animal products. Much of this trade is conditional upon the animals or the animal products being free of contamination by specific pathogenic organisms. As a consequence, many potential trading opportunities are currently closed due to infection risks when animals or their products come from certain countries. This can have a large economic cost to many countries, especially developing countries. Genetic management of infection can help to reduce (sometimes to zero) the risks of contamination by specific parasites. In situations where no other diseases block exports, this can re-open specific markets to many countries or regions, with large trading and economic benefits to these countries.

74. Additionally, eradication of specific diseases, e.g. FMD, may allow countries or areas to use FMD freedom as a legal trade barrier to prevent the introduction of alternative cheap products from neighbouring infected countries that saturate the local market. Commercial producers in Southern and Central Philippines, where FMD has been eradicated by non-genetic means, have identified this as the most significant economic advantage.

4.2 SWOT Analysis of Genetic Strategies for Disease Management

75. The results of a SWOT analysis of benefits of incorporating genetic elements into disease management strategies, at the level of the livestock production system and the community, are summarised in Table 2. Most of the benefits highlighted pertain to the sustainability of disease management and the inherent low cost of genetic elements, once they are established. These are discussed above. Some other issues need further elaboration.

Table 2. *A SWOT analysis of benefits of genetic improvement as a disease control strategy*

STRENGTHS	WEAKNESSES
• Genetic change is permanent • Consistency of effect: “just keeps working” • No cash input when established • Prolong/protect the effectiveness of other methods (life-time) • Broad spectrum effects, i.e. increased resistance to one disease can increase resistance to others • Low evolutionary change in macro-parasites, e.g. helminths • Adds to diversity of management strategies	• Goals of production system may change more quickly than genetic change can be implemented • Uncertainty of genetic outcomes in different environments and production systems • Need for some level of controlled breeding • Cost of measurements and analysis • Evolution of micro-parasites, e.g. viruses and bacteria, is possible • Adds to technologies to be understood and implemented
OPPORTUNITIES	THREATS
• Marketing of disease resistant stock • Infrastructure which can be used for the other purposes, e.g. performance recording • Mobilise communities for related activities: including training and acquiring skills for farm and community management, marketing, politics	• Inappropriate stock may become cheap and/or widely available • Genetic material may not be owned by local stakeholders • Opposition/competition from existing investors in other control options, e.g. chemical suppliers

76. Factors influencing parasite evolution in response to genetic change in the host are outlined in Appendix 1. Parasite evolution is potentially both a strength and a weakness of using genetic elements within disease management strategies. For macro-parasitic diseases such as gastrointestinal parasites, genetic improvement of resistance will lead to only weak pressure on the parasite to evolve. This is in contrast to chemical control measures that impose strong selection pressure. Therefore, in parasite evolution terms, genetic strategies are expected to be more sustainable than many other intervention strategies for macro-parasitic infections. However, this may not be true for bacteria and viruses, where evolutionary change in the parasite population may eventually occur. In this situation, genetic strategies may perhaps be as prone to long-term failure as chemical or vaccine control measures.

77. Investigating and implementing genetic elements into disease management strategies will often require considerable input and may take considerable time in some circumstances. The expense is incurred through acquiring the technology, the costs of measurement and analysis, and the need for controlled breeding. Often these processes may require international collaboration. For example, this collaboration may be between countries which have ownership of the animal genetic resources and countries which are able to input technology. However, once established, these inputs should be of direct benefit to the livestock production system. Moreover, the development of international collaboration should have large direct and indirect (spin-off) benefits to all participating countries in the short and long term. The time required to develop and implement technologies becomes a weakness in the face of changing environmental or political circumstances, or the emergence of new diseases.

78. Opportunities arising from marketing of animals, improved infrastructure and community activities have been discussed. Accompanying threats arise from the inappropriate ownership of resources, lack of appreciation of the value of the animals with disease resistance attributes, or opposition from sectors with vested interests in management options that are perceived as competing. These threats can undermine the benefits of utilising genetically improved animals, swamp the market with animals that do not have these attributes, or make the livestock keepers dependent upon the external supply of animals – outcomes that make the keepers vulnerable once again to the consequences of disease.

4.3 Economic Benefits from Incorporating Genetic Elements into Disease Management Strategies.

79. Examples of economic benefits, in market-oriented terms, are presented for several important diseases where genetic elements can be incorporated in disease management strategies with immediate effect. Summary results are presented here and the details of the calculations and the assumptions made are given in Appendix 5. For diseases not evaluated here, the economic benefits may be equally large but higher initial costs may be required for research and technology interaction.

Ticks and Tick-Borne Diseases

80. **Selection of individual animals with enhanced tick resistance, based simply on tick counts, can quickly lead to reduced tick infestation.** The potential economic impact of such a strategy is:

- Annual cumulative benefits of $US2.1m in Australia, $2.4m in Zimbabwe, $5.8m in South Africa and $13.3m in Kenya.

Helminth Infections

81. **Major benefits can be achieved through breed substitution or selection of individual animals using faecal egg count and indicators of anaemia.** Potential economic impacts are:

- Annual cumulative benefits of £4.1m in the UK (a high-cost economy) once selection is as widespread as selection for performance traits.
- Annual benefits of $1.8m in Australia, $0.2m in Indonesia, $1.2m in India and $0.06m in Nepal, similar to the benefits from implemented non-genetic endoparasite control.
- Large returns on current research investment. The net benefits of current research in developing countries, over a 30-year time horizon are:
    - $387m, IRR = 78.9%, benefits:costs = 180:1 for a phenotypic measurement project
    - $160m, IRR = 40.7%, benefits:costs = 70:1 for a genetic marker project

Trypanosomosis

82. **Trypanotolerance can be genetically improved by a combination of breed substitution, within-breed selection and, in the near future, molecular genetic markers.** Economic benefits across affected areas of Africa include:

- Large returns on research investments, from both field observation-based and genetic marker-based approaches. The net benefits of current research over a 50-year time horizon are:
    - Field observation approach, benefits = $32m, benefits:costs = 5.1:1, IRR = 32%
    - Genetic-marker approach, benefits = $281m, benefits:costs = 5.2:1, IRR = 12%

Mastitis

83. **Selection can help reduce clinical mastitis incidence and by using somatic cell counts also reduce subclinical mastitis.** Potential economic benefits include:

- Annual cumulative benefits to the UK dairy industry of £1.5m/year.

84. There are also disease situations where genetic management strategies may be required to protect the very existence of an industry or a livestock production system. This occurs with Marek's disease in intensive poultry production systems where vaccine control has apparently worsened virus virulence and breeding stock with enhanced resistance are necessary to ensure the viability of such production systems. This situation can also occur with zoonoses and potential zoonoses, and it is the rationale for the selection of sheep for resistance to scrapie and BSE in the sheep industries of Western Europe.

5. CRITICAL FACTORS FOR SUCCESS

85. To achieve success in incorporating genetic elements into disease management strategies, it is necessary to (i) appraise the current situation vis-à-vis genetics and disease management, (ii) determine the desired situation, (iii) specify possible strategies for reaching this desired situation, and (iv) plan, fund, implement and maintain the programme for the preferred strategy.

5.1 Appraisal of Current Situation

86. There are substantial opportunities and benefits from the use of genetic elements in disease management. The nature of these opportunities, and appropriate responses, are described in section 4. For opportunities that can be immediately exploited costed examples of the benefits are presented in section 5.

87. Despite these opportunities being compelling, at the present time they are largely unexploited. This is equally true in developed and developing countries. The reasons for the lack of implementation of opportunities include:

- A belief by many sectors: governments, scientists, farmers and animal producers in the adequacy of existing disease management strategies, even when these are failing.
- The lack of awareness of the opportunities. This is partly a function of the interdisciplinary nature of the skills required to exploit these opportunities. For example, veterinarians often have a poor appreciation of genetic opportunities, whereas geneticists often have a poor understanding of diseases and are not able to prioritise diseases or predict the consequences of genetic management. This lack of awareness is apparent at many levels: at the government level, within the scientific community, and amongst farmers and animal producers.
- The lack of relevant and effective infrastructure to exploit the genetic opportunities. Exploitation often requires considerable information, infrastructure, cooperation and will. At times it also requires additional technology. This infrastructure must extend across scientific and animal production sectors, often with government underpinning.
- The lack of specialists and multidisciplinary teams to enable delivery of relevant technology to end-users.
- The lack of framework (i) for decision-making, i.e. the prioritising of diseases for which genetic elements can contribute, (ii) for the use and delivery of new technologies and (iii) for novel approaches to existing technologies, especially in developing countries.

88. Sometimes the technologies required to implement genetic elements into disease management strategies are minimal, yet can deliver considerable benefits. The comparison of the productivity of indigenous acclimatised livestock with exotic breeds when faced with disease challenge provides an example of this. In this case, the most important decision to be made may be the rejection of the exotic genotypes.

5.2 Desired Situation

89. To achieve adequate and sustainable food supply throughout the world, it is paramount that integrated disease management programmes are developed and implemented. This requires the optimal use of all components in an integrated programme, including the use of genetics. Adding an additional component to disease management strategies makes them more sustainable and robust. However, genetic approaches bring the additional benefit that once established they are inherently long lasting and reliable. This situation will sometimes be realised by inputs from the private sector. In other situations public investment will be necessary and debate will be required to prioritise these investments.

5.3 Pathways to Success

(I) Recognition of role of genetics in disease management at the policy level

90. It is now timely to exploit the opportunities for the use of genetic elements in disease management described in section 4. Efforts and recognition must first be made at the government level:

- Countries must recognise that there is now important potential for expanding the understanding and use of genetic elements in disease management. For diseases such as helminth infections, tick infestations and trypanosomosis, amongst others, the appreciation and use of existing technologies is the major requirement. For other important diseases, e.g. African swine fever, Newcastle disease or foot-and-mouth disease, new technology will be required.
- Countries must recognise the potential for international collaboration in this area. Such collaborations will lead to additional benefits and opportunities. Additionally, when strategies require a high level of technology, collaboration may be essential to achieve end goals as few countries will have the capacity to supply all necessary technologies. Typically, one country might supply the animal genetic resources, the second might supply the genetic technology and the third might supply the operational expertise.

91. Recognition by countries of opportunities for utilising genetic elements in disease management strategies must be followed by commitments. In the first instance, each country should develop the capacity to recognise and respond appropriately to opportunities as they arise. This will take investment in expertise. Once opportunities are recognised, they must be assessed as to their feasibility and potential payback. This in turn requires investment. Finally, for the most promising opportunities, commitment must be made such that these opportunities can be realized.

(II) Identification of opportunities for incorporating genetics into sustainable disease management programmes

92. Guidance is now given on the detailed requirements for ensuring that genetic opportunities for assisting in the management of disease are recognised and acted upon. The first level of responsibility often lies with government, however this may depend upon the disease and the complexity of the required management strategy. Responsibilities for developing management strategies will be taken at either the international, national or farm level. Irrespective of where responsibilities lie, there are a series of steps to be taken to identify the problem. These initial steps are listed, although in many livestock production systems some of these steps have already been taken. These steps are derived from the decision-making steps listed in section 4.

Assessment of livestock production systems

93. The first step is for countries to document the livestock production systems it has and the available animal genetic resources. This information is invaluable for planning in the general sense, and for initiating studies into opportunities for using genetic elements in disease management.

Assessment of prevalent diseases within these production systems

94. Secondly, countries must document the major diseases afflicting its animal genetic resources. This also includes an assessment of the nature of each major disease, the degree of challenge posed by these diseases, their epidemiology and their economic consequences.

Assessment of current disease management strategies

95. Countries must make an assessment of the adequacy and sustainability of currently advocated or implemented disease management strategies. If such strategies are adequate, sustainable and cost-effective, then the case for additional genetic management strategies might not be sufficiently strong to justify investment. This step has the added benefit of highlighting problems with current non-genetic management strategies and identifying improvements that can be made in these strategies.

Assessment of how genetic resources and diseases co-exist, and assessment of genetic opportunities

96. The initial assessment of opportunities for genetic disease management will arise from consideration of co-existence of animal genetic resources and diseases, along with an appraisal of the

literature on genetic aspects of disease resistance. Countries must document all cases where animal genetic resources apparently exist and produce satisfactorily despite the presence of an economically important disease. Equally importantly, cases where animal genetic resources fail to co-exist with a disease must also be documented.

97. After the data collection phase, a decision-making phase is entered. Here, using the data collected, decisions are made as to the requirements for genetic elements in disease management strategies and the steps required for implementing such strategies. Potential opportunities for using genetics to assist in disease management will need to be assessed for the economically important diseases that require additional control strategies. Information to assess will opportunities will arise from two sources:
(i) Information (often anecdotal) collected by countries on how animal genetic resources and diseases co-exist. Often this will indicate breeds or genotypes that appear to be more resistant to, or tolerant of, infection.
(ii) Information collected elsewhere, e.g. scientific papers, on genetic variability between individual animals or between populations for host resistance or tolerance.
In some circumstances, there may be no direct evidence of genetic variability in host resistance but inferences made from epidemiological data, or knowledge of closely related diseases, might indicate that host genetic variability is likely.

98. The assessment of the opportunities includes assessment of the nature of each opportunity and the appropriate response. For example, using the response framework developed in section 4, questions will need to be answered as to:

- The most appropriate genetic management strategy; e.g. breed choice, crossbreeding or selection of individual animals for breeding. Additionally, an assessment must be made of whether it is resistance or tolerance that requires management.
- The nature of the information or technology still to be acquired; e.g. will field studies of affected animals or populations suffice, will deliberate challenge experiments be required, will development of molecular markers be required?
- The level of technology required to implement management strategies incorporating genetics; e.g. breeding plan design, veterinary expertise, information technology, molecular expertise, etc.

International collaboration may be required to identify these opportunities and develop the required capacity for planning and implementing action.

(III) Developing the capacity to implement genetic elements into disease management strategies

99. Implementation will be at several levels. These include researching opportunities, developing technical and operational capacity, and building the multidisciplinary groups required for successful implementation. Benefits arise from the recognition of opportunities, as well as the actual implementation strategies.

100. There needs to be recognition that genetic resistance to disease can be of major significance to livestock development. Additionally, there is the need for those responsible for animal disease management to recognise that genetic approaches have a role to play in integrated disease management. ***This requires investment in multidisciplinary teams to develop the capacity to undertake appropriate research and scoping studies, and in planning development interventions.*** Small groups such as these have been established in different parts of the world. Sharing of their experience and expertise may provide significant new insights into integration of genetics and disease management. Also required is an active programme to alert national and international disease management authorities to the opportunities associated with genetics. Recognition may be enhanced by comprehensive analysis of case studies where this approach has been successful.

101. There is a need for countries to further analyse disease problems to establish opportunities where genetic elements may effectively contribute to sustainable management and define the process by which these options can be integrated into management programmes. ***This requires investment in collaborative development activity amongst technicians of different backgrounds and different***

skills. The skills that need to be brought together include animal production, animal health, genetics, livestock systems and community development. Individual contributions will come from local, national and international agencies. Investment could be in a pilot demonstration project on an identified problem of global importance with a high probability of success. Combined with other ongoing research and development activity in this field, a focussed example could provide a framework for wider application. Current examples may revolve around tick infestations in cattle or nematode infections in sheep. Looking forward, diseases affecting smallholder poultry production systems may provide excellent case studies for situations where both the development and implementation of technology are required.

102. There is a need to develop specific genetic options for disease management and integrate these into whole-system solutions. Stakeholder and community participation is an essential part of this process. ***This requires investment in implementation of genetic elements into integrated disease management strategies in communities which depend on livestock***. The whole-system solutions developed for specific diseases and livestock production systems need to be implemented in a wider range of livestock production systems. Essential to this process is a feedback and communication between people involved in the pilot project and those involved in implementing genetic elements into disease management strategies in other situations. Activities that contribute to success will include training programmes, workshops and exchange of trained personnel.

6. FOR CONSIDERATION

103. Diseases and their management form major recurring and complex contributors to the cost and security of food and agriculture production from livestock. Disease management requires the development of integrated management programmes. Genetic approaches will offer an additional tool to currently used strategies for many diseases and are likely to be an important element of sustainable integrated disease management programmes. To achieve this desired situation the following should be considered:

(1) To efficiently realise the sustainable management of those animal diseases that are important to food security and poverty alleviation, and in view of the rapid development in genetic technologies, it is timely that countries and other stakeholders evaluate opportunities for increasing the cost-effectiveness and sustainability of disease management programmes.

(2) To evaluate opportunities for increasing the cost-effectiveness and sustainability of disease management programmes it is necessary to provide for the further development and use of multidisciplinary approaches in evaluating, planning and implementing cost-effective and sustainable disease management strategies.

(3) When evaluating the efficacy of existing approaches to management of those animal diseases of importance in the livestock sector, recognition should be made that genetic options may contribute to disease management and provision should be made for the evaluation of these genetic options.

(4) When developing sustainable approaches to management of those animal diseases of importance in the livestock sector, provision should be made to develop specific genetic options and evaluate their incorporation into integrated management strategies.

(5) To reduce costs and add value to disease and performance management strategies, the potential for integrating the recording and information systems for animal health and production performance should be considered.

(6) Carrying out the activities required to undertake evaluation of disease management strategies, evaluate genetic options, incorporate genetic elements into the disease management strategies and integrate recording and information systems requires capacity building. In particular, consideration should be given to investing in the development of:
    a. Multidisciplinary teams of specialists to evaluate opportunities for enhancing disease management strategies
    b. Teams of technicians of different skills to design integrated disease management strategies
    c. Teams of technicians, including information scientists, to design integrated recording and information systems
    d. Teams of operational technicians and social scientists to effectively and efficiently implement integrated disease management strategies

7. BIBLIOGRAPHY

Bacon, L.D. (1987). Influence of the major histocompatability complex on disease resistance and productivity. Poultry Science, 66: 802-811.

Baker, R.L., Mwamachi, D.M., Audho, J.O., Aduda, E.O. and Thorpe, W. (1999). Genetic resistance to gastro-intestinal nematode parasites in Red Maasai, Dorper and Red Maasai X Dorper ewes in the sub-humid tropics. Animal Science, 69: 335-345.

Baker, R.L., Mwamachi, D.M., Audho, J.O., Carles, A.B. and Thorpe, W. (2002). Comparison of Red Maasai and Dorper sheep for resistance to gastro-intestinal nematode parasites, productivity and efficiency in a humid and a semi-arid environment in Kenya. Proc. 7th World Congress on Genetics Applied to Livestock Production.

Bennett, R.M., Christiansen, K. and Clifton-Hadley, R.S. (1999). Modelling the impact of livestock diseases on production: case studies of non-notifiable diseases of farm animals in Great Britain. Animal Science, 68: 681-689.

Falconi, C.A., Omamo, S.W., d'Ieteren, G. and Iraqi, F. (2001). An *ex ante* economic and policy analysis of research on genetic resistance to livestock disease: trypanosomosis in Africa. Agricultural Economics, 25: 153-163.

Friars, G.W., Chambers, J.R., Kennedy, A. and Smith, A.D. (1972). Selection for resistance to Marek's Disease in conjunction with other economic traits in chickens. Avian Diseases, 16: 2-10.

Frisch, J.E. (1999). Towards a permanent solution for controlling cattle ticks. International Journal for Parasitology, 29: 57-71.

Frisch, J.E., O'Neill, C.J. and Kelly, M.J. (2000). Using genetics to control cattle parasites – the Rockhampton experience. International Journal for Parasitology, 30: 253-264.

Gasbarre, L.C and Miller, J.E. (2000). Genetics of helminth resistance. In Breeding for Disease Resistance in Farm Animals, 2nd Edition. Axford, R.F.E., Bishop, S.C., Nicholas, F.W. and Owen, J.B. CAB International, Wallingford, UK.

Gordon, C.D., Beard, C.W., Hopkins, S.R., and Siegel, H.S. (1971). Chick mortality as a criterion of selection towards resistance or susceptibility to Newcastle disease. Poultry Science, 50: 783-789.

Jeggo, M.H., Gorman, B., Corteyn, A.H. and Davidson, I. (1985). The virulence of bluetongue virus for British breeds of sheep. Research in Veterinary Science, 42: 24-28.

Kristjanson, P. (1997). Returns to disease-resistance helminthiasis research. In: Measuring Returns to ILRI's Research. Systems Analysis and Impact Assessment Working Paper No. 97-1. ILRI, Nairobi, Kenya. pp. 35-41.

Kistjanson, P., Swallow, B.M., Rowlands, G.J., Kruska, R.L. and de Leeuw, P.N. (1999). Measuring the cost of African animal trypanosomosis, the potential benefits of control and returns to research. Agricultural Systems, 59: 79-98.

Lillehoj, H.S., Ruff, M.D., Bacon, L.D., Lamont, S.J. and Jeffers, T.K. (1989). Genetic control of immunity to *Eimeria tenella*: interaction of MHC genes and non-MHC linked genes influences levels of disease susceptibility in chickens. Veterinary Immunology and Immunopathology, 20: 135-148.

Maurer, F.D. & McCully, R.M. (1963). African Horse-Sickness - with emphasis on pathology. American Journal of Veterinary Research, 24: 235-266.

McLeod, R. and Kristjanson, P. (1999). Economic impact of ticks and tick-borne diseases to livestock in Africa, Asia and Australia. Report to the International Livestock Research Institute, Nairobi, Kenya.

McLeod, R. (2000). Economic impact analysis: Internal parasites of small ruminants in Asia and Australia – Preliminary analysis. eSYS Development Report to the International Livestock Research Institute, Nairobi, Kenya.

Perry, B.D., McDermott, J.J., Randolph, T.F., Sones, K.R. and Thornton, P.K. (2002). Investing in animal health research to alleviate poverty. International Livestock Research Institute (ILRI), Nairobi, Kenya.

Rosenberg, M.M. (1941). A study of the inheritance of resistance to *E. tenella* in the domestic fowl. Poultry Science, 20: 472.

Simm, G. (1998). Genetic Improvement of Cattle and Sheep. Farming Press, Ipswich, U.K.

Veerkamp, R.F., Stott, A.W., Hill, W.G. and Brotherstone, S. (1998). The economic value of somatic cell count payment schemes for UK dairy cattle breeding programmes. Animal Science, 66: 293-298.

Witter, R.L. (1998). The changing landscape of Marek's disease. Avian Pathology, 27: S46-S53.

Table 1. *Examples[1] of diseases for which there is documentation or strong anecdotal evidence of genetic variation in host resistance or tolerance, in major domestic livestock species. The nature of the genetic variation varies between diseases and pertinent details are commented upon.*

Species	**Infectious agent**	**Disease**	**Comment**
Chicken	virus	Marek's disease	MHC resistance gene used in breeding programmes
	virus	Infectious laryngitracheitis	Inbred lines differ in resistance. MHC genes involved
	virus	Avian leukosis	Single dominant gene affects resistance
	virus	Infectious bursal disease	Breed differences in resistance
	virus	Avian infectious bronchitis	Inbred lines differ in resistance
	virus	Rous sarcoma	Selection for resistance successful. MHC genes involved
	virus	Newcastle disease	Heritable differences in resistance long established
	bacteria	Pullorum	Inbred lines differ in resistance
	bacteria	Fowl typhoid	Inbred lines differ in resistance
	bacteria	Salmonellosis	Well established resistance effects
	protozoa	Coccidiosis	Inbred lines differ in resistance. MHC genes involved
	nematode	Ascaridia galli	Differences between commercial lines in resistance
Pigs	virus	African swine fever	Individual animals survive epidemics
	virus	Foot-and-mouth disease	Anecdotal breed effects. Possibly tolerance
	virus	Atrophic rhinitis	Within and between breed variation in resistance
	bacteria	Neonatal diarrhoea	Major gene conveys complete resistance
	bacteria	Postweaning diarrhoea	Major gene conveys complete resistance
Cattle	virus	Foot-and-mouth disease	Anecdotal breed effects. Possibly tolerance
	Virus	Rinderpest	Documented breed resistance
	virus	Bovine leukaemia	Strong evidence for MHC effects
	bacteria	Paratuberculosis (Johnes)	Within-breed resistance variation. Nramp is candidate
	bacteria	Mastitis	Genetic effects subtle but well established
	bacteria	Tuberculosis	Within & between-breed variation in resistance. Nramp?
	bacteria	Brucellosis	Within & between-breed variation in resistance.
	bacteria	Salmonellosis	In vitro evidence from Brucellosis resistant cattle
	bacteria	Dermatophilosis	Verified breed differences
	bacteria	Cowdriosis (heartwater)	Historical field observations only
	protozoa	Trypanosomosis	Tolerant breeds exist
	protozoa	Theileria (*Theileria annulata*)	Breed differences, possibly tolerance
	protozoa	Theileria (*T. sergenti*)	Combination of resistance and tolerance
	protozoa	East Coast Fever (*T. parva*)	Breed differences, possibly tolerance
	protozoa	Babesia	Breed differences, tolerance
	nematodes	Helminthosis[2]	Combination of resistance and tolerance
	ticks	Ticks	Combination of resistance and tolerance

Sheep & Goats	prion	Scrapie	Variation in resistance dominated by a known gene
	bacteria	Footrot	Variation in resistance & vaccine response
	bacteria	Mastitis	Genetic effects subtle but well established
	bacteria	Paratuberculosis (Johnes)	Anecdotal evidence of within breed variation
	bacteria	Dermatophilosis	Selection for resistance successful in Merinos
	bacteria	Salmonellosis	Heritable within-breed resistance. Nramp implicated.
	bacteria	Cowdriosis (heartwater)	Breed tolerance
	protozoa	Trypanosomosis	Tolerant breeds exist
	nematodes	Helminthosis[2]	Combination of resistance and tolerance
	plathyhelminths	Liver fluke (*Fasciola hepatica*)	Combination of resistance and tolerance
	flies	Cutaneous myiasis (flystroke)	Selection for resistance successful in Merinos

---

[1] For almost every disease that has been intensively and carefully investigated, evidence for host genetic variation has been found. Almost certainly, there will be genetic variation in resistance or tolerance for a wide variety of additional diseases.

[2] For brevity, genetic variation in resistance to several different genera of nematode parasites (independently verified examples) is counted as one example of host genetic variation in resistance.

Appendix 1: Factors influencing the possible rate of parasite evolution, in response to genetic changes in the host.

All control measures that aim to reduce numbers of parasites can lead to genetic change in the parasite population to evade the control strategy. This is best documented in the case of control by chemicals and antibiotics. This could also happen as the result of using genetics to manage or control parasite populations. Although this has been documented in plants, there are currently no recorded examples of this occurring in domestic animal populations.

Risk of genetic change in the parasite is minimal when it is tolerance of infection that is being managed. In this case the parasite can complete its lifecycle unimpeded. Thus, there is no selection pressure placed upon the parasite to change its transmission characteristics. Many apparent differences seen between populations in disease occurrence are due to tolerance of infection, and these differences have often been stable for very long time periods, e.g. thousands of years.

Management of infection may, in some circumstances, place selection pressure upon the parasite to change. The greater the selection pressure placed on the pathogen the more likely the parasite population is to respond. With sufficient resistance in animal populations to ensure quick disease eradication, the risks of parasite evolution are effectively zero. Slower disease eradication may allow the parasite to gain a niche in the population and hence a fleeting opportunity to evolve resistance. However, weak selection pressure, as would be seen with quantitative selection of individual animals for resistance places only slight selection pressure on parasites. In this case, the majority of parasites are shed by the least resistant animals. This places very little selection pressure upon parasites.

Genetic heterogeneity in the host, i.e. the number of genes and hence mechanisms used by the host to control infection, is critical to the rate of effective parasite evolution. The greater the number of resistance mechanisms, the less the risk of the parasite evolving resistance. Thus, strategies that rely upon a single gene that does not confer complete resistance have the greatest risk of parasite evolution.

Evolution rates also depend upon the type of parasite, especially their rate of generation turnover. For this reason, parasite evolution is more likely to be problematic for viruses or bacteria. As a broad summary, host genetic resistance to organisms such as nematodes that uses several mechanisms is likely to be robust to parasite evolution, whereas strategies that use a single gene to control viral or bacterial diseases are most at risk.

Rates of parasite evolution are not known, nor are the time periods over which genetic strategies for managing infection will be sustainable. However, ongoing genetic management strategies that use the response of the host to the parasite, e.g. selection of hosts with a greater degree of resistance to infection, will always be against the current strain of parasite. Hence they will always be appropriate.

Appendix 2. The persistence of genetic variation in host resistance to disease.

Complex host-parasite interactions guide the evolution of both hosts and parasites, and are one of the major reasons for the maintenance of genetic variation in natural populations. Combining genetic theory and epidemiology can give insight into why genetic variation in host resistance to infection persists. Firstly, selection pressures, especially those for disease resistance, will act in different ways across time and environments. This maintains genetic variation for all traits, in both wild and domestic populations. Secondly, natural selection will not make populations of animals completely resistant to infection. This is because as natural selection moves a host population towards resistance, the selection pressure for resistance decreases. There exists, for each disease, a certain proportion of susceptible animals that can be carried in the population without exposing the population as a whole to risks of disease. Once the number of genetically susceptible animals falls below this level, selection pressure for resistance ceases. Hence, genetic variation for resistance to infection remains in the population. Thirdly, modern domestic livestock populations have been selected for other characteristics. Together, these factors explain why genetic variation in resistance has been observed for diseases that have been comprehensively studied.

Appendix 3. Genetic factors underlying resistance and tolerance.

Much is already known about mechanisms of tolerance and resistance to infection. Several processes may control tolerance or resistance. For example:

- The animal may have an appropriately targeted immune response against the pathogen. This may enable the animal to successfully combat the infection or avoid pathogenic effects of disease
- The animal may have non-immune response genes that preclude infection, or limit infection in target organs. Examples include the binding protein genes that allow specific strains of *E. coli* , e.g. those with K88 or F18 fimbriae, to attach to the gut of the pig resulting in pre-weaning or post-weaning diarrhoea. Absence of appropriate binding proteins results in resistance to infection.
- The animal may have physical attributes which make infection by the pathogen difficult. An example is the role of skin thickness in conferring resistance to ticks.
- The animal may have behavioural attributes which enables it to avoid infection. An example is the hygienic behaviour of honeybees. This is their dominant natural defence against brood diseases such as American Foulbrood, Chalkbrood and, possibly, the Varroa mite.

Genetic resistance to infection or tolerance of infection may, in some cases, be due predominantly to a single gene. Examples include resistance to *E. coli* diarrhoea in pigs (described above) and the PrP gene which is associated with resistance to scrapie in sheep. In other cases, resistance or tolerance is due to the combined effects of several or many genes. Examples of this include nematode resistance in ruminants, mastitis resistance in dairy cattle and sheep, and trypanotolerance in locally adapted breeds of cattle.

Although resistance and tolerance are sometimes qualitative phenomena, as in the case of *E. coli* diarrhoea in pigs, more often they are quantitative phenomena. That is, they show continuous variation from one extreme to the other. Continuous variation is seen when resistance or tolerance is due to the combined effects of several genes.

Disease resistance tends to be specific to particular diseases rather than general to all diseases. This is because genetic resistance to different diseases is controlled at least to a major degree by different mechanisms. Thus, different genes will generally influence resistance to unrelated diseases. However, similar genes may influence resistance to closely related infections. An example is the often-observed strong genetic correlation between resistance to different species of gastrointestinal nematode parasites.

Appendix 4. Principles of genetic markers

Molecular genetic markers allow the identification of individual animals that are (partially) genetically resistant to infection or (partially) genetically tolerant of infection. They can be used to identify such animals in the absence of a disease challenge. They require the application of molecular technology. The aim is identify alleles (variants) at specific genes that confer partial or complete resistance to infection or tolerance of infection. Sometimes, the causative allele can be identified and utilized. More often, it will be a genetic marker that is "linked" to the causative allele that will be identified. "Linked" means the marker and the allele occur close together on the same chromosome, and hence are inherited together. With linked genetic markers it is not always necessary to know the causative gene because an inferred linkage, derived from data, will often suffice. However, the marker must be closely linked to the causative gene and identified in the target population, as the degree and nature of linkage between marker and causative allele may differ between populations.

Appendix 5. Cost benefit analyses of incorporating genetic elements in disease management strategies for four diseases

Ticks and Tick-Borne Diseases

Tick worry and tick-borne diseases cause considerable production losses throughout tropical and subtropical cattle production systems, although they are generally ranked below helminth and several other infections in terms of economic impact. Tick-borne diseases include anaplasmosis, babesiosis, cowdriosis, theileria and East Coast fever. McLeod and Kristjanson (1999) provide estimates of the economic costs due to production losses and mortality. For example, in Australia the total annual costs have been estimated at $US20.8m, $4.0m in Indonesia, $24m in Zimbabwe, $57.6m in South Africa, $132.6m in Kenya and $355.4m in India.

Selection of individual animals with enhanced tick resistance for breeding, based simply on tick counts, can quickly lead to reduced tick infestation. Frisch *et al.* (2000) demonstrated that with as little as 6 years of continuous selection, a nucleus herd could be created that has tick burdens sufficiently low to be of little consequence. Frisch *et al.* (2000) costed the within-herd benefits of selection *vs*. the benefits of using acaricides for controlling ticks. Offsetting acaricide costs against production benefits, there was a net annual benefit of AUD$4.5/animal. Offsetting data collection and processing costs against the production benefits from genetic selection, costs were higher than benefits for the first 10 years, subsequently returns were greater than costs and cumulated annually thereafter. In addition to these calculations, no acaricide treatment is required after 10 years of continuous selection, increasing the financial benefits and reducing future problems of acaricide resistance. In these calculations, the nucleus breeding herd bears the full cost of data recording. When the nucleus is used to breed sires for widespread use, the value of resistant sires would far exceed the relatively small cost incurred over the 10 years required to produce them. Moreover, acaricides costs are incurred throughout the industry, whereas genetic selection costs are incurred predominantly in the nucleus herds.

The benefits of enhanced tick resistance may be scaled up to the national level, in the situation where selection takes place on nucleus farms. It is assumed from Frisch *et al.* (2000) that after 10 years the costs of selection are balanced by the benefits on the nucleus farm. The nation-wide benefits are then a function of the extent to which production losses are offset by using the genetically more resistant animals and the penetration (uptake) of these genotypes into the national herd. Assuming that populations containing animals with genetically enhanced resistance have half the production losses and costs due to tick infestations, and that a national penetration of 20% is achieved, then the benefits from the genetic elements of tick management equate to 10% of the total losses. This is annually $US2.1m in Australia, $2.4m in Zimbabwe, $5.8m in South Africa and $13.3m in Kenya.

These calculations do not assume high-level technological input. A gene conferring essentially 100% resistance in some genetic backgrounds is known to exist (Frisch, 1999), although genetic markers still need to be identified for this gene. Once identified, this gene could be used to considerable effect in various situations through crossbreeding programmes that use genetic markers to ensure retention of the gene. The benefits, but also the costs, of this approach are potentially considerably greater than those described above.

Finally, the use of genetic elements in the overall disease management strategies will reduce long-term selection pressure for acaricide resistance in the tick population and hence reduce future production losses once available acaricides become less effective.

Helminth Infections

Helminth infections in ruminants constitute the single greatest disease problem to domestic livestock, worldwide. Comprehensive costings of production losses and treatment costs in Asia and Australia are presented by McLeod (2000). For example, total annual production losses and costs to the Australian sheep industry are estimated at $US123m, $13m in Indonesia, $3.6m in the Philippines, $81m in India and $4m in Nepal.

Breed substitution can produce immediate and substantial benefits. For example, in Kenya there is the issue of whether livestock keepers should use the native Red Maasai breed or the apparently more productive Dorper breed. In semi-arid conditions there is little difference between the breeds in overall output or efficiency, however under humid conditions where parasite challenge is high, the Red Maasai has an output three times greater than the Dorper and is 5 times more efficient (Baker *et al*., 2002). When scaled up to the regional or national level, this represents a very large benefit achievable at little cost.

In terms of within-breed selection for enhanced resistance, inputs and outputs are most easily costed in western-style market-oriented production systems. Research in the UK to demonstrate the benefits of selecting sheep for enhanced resistance to nematode infections, and to convince the industry that such selection should be implemented, cost £270 000. A direct consequence of this research has been the implementation of self-funding breeding programmes in which measurements of nematode resistance are expected to increase the total benefits of selection for increased productivity by 25%. Using current levels of uptake, selection for increased productivity is expected to return £16.6m annually to the industry, discounted over a 20-year time horizon (Simm, 1998). Therefore, the benefits of selecting for nematode resistance potentially contribute an additional £4.1m annually to the UK sheep industry, once selection for nematode resistance is as widespread as selection for performance.

Returns to livestock industries in economies where cost structures and returns are lower will be somewhat less in absolute terms than in high-cost western production systems, however they are still substantial. Proportionately these returns may well be higher and more important given the importance of livestock to family livelihoods in many developing countries. As described in section 2, the proportionate impact of disease in developing countries is greater than in developed countries. Selection of animals for resistance to the major tropical nematode helminth, *Haemonchus contortus*, can be performed cheaply using faecal egg counts and observed eye-lid colour, an indicator of anaemia. As a conservative example of annual benefits, assume that animals selected for enhanced resistance have production losses and costs that are reduced by 10%, and that the national penetration of resistant stock is 15%. Then a 1.5% annual compounding of saving in costs and losses can be achieved by using genetic elements in the disease management strategy. This equates to annual savings of $1.8m in Australia, $0.2m in Indonesia, $1.2m in India and $0.06m in Nepal. These estimated benefits are similar to those presented by McLeod (2000) for sustainable (non-genetic) endoparasite control (SPC) strategies in the same Asian countries. However, the logistics and level of technology required for the genetic elements are less than that required for SPC, thus the level of uptake and benefits may well be higher. Additionally, continued selection will lead to ever-greater reductions in production losses. If resistant breeds are identified and utilised, benefits will be considerably greater and will be realised at little cost.

A formal closed-economy model of the benefits of genetic management of helminth infections was presented by Kristjanson (1997), for genetic management using phenotypic measurement and for management using genetic markers. The model assumed a population of 312 million sheep and goats in developing countries at risk due to anthelmintic resistance. Net benefits to both consumers and producers (discounted at 5%) were calculated over a 30-year time horizon, subtracting research costs, assuming a probability of success of 0.5, elasticity of demand of 0.58 and elasticity of supply of 0.8. For management using phenotypic measurement, the assumed increases in productivity and adoption levels were 10% and 15%, respectively (the same as above). The net present value of the total benefits, after subtracting research costs of $2.5m, was $387m corresponding to an IRR of 78.9% and a benefit:cost ratio of 180:1. For the genetic marker model, adoption remained at 15% but the productivity benefits were increased to 15%. However, assumed research costs were higher ($3m) and time to implementation was longer. Thus, the net present value was lower at $160m with an IRR of 40.7% and a benefit:cost ratio of 70:1.

Trypanosomosis

Trypanosomosis is an important constraint to livestock production in tropical Africa. Trypanosomes are borne by tsetse flies and Kristjanson *et al.* (1999) estimated that at least 46 million cattle are kept in tsetse infested environments, of which 17 million are treated with medication at an annual cost of $35million. Total annual costs, including production losses, mortality and reduced fertility, are estimated to exceed $1billion (Falconi *et al.*, 2001). Conventional control options are unavailable (vaccines), expensive (chemotherapy) or difficult to implement effectively (vector suppression).

Trypanotolerance can be genetically improved by a combination of breed substitution, within-breed selection of tolerant animals and, in the near future, molecular genetic markers. In particular, the N'Dama and West African Shorthorn breeds appear able to tolerate moderate infection pressure and remain productive.

A formal economic analysis of the outcome of research into genetic tolerance of trypanosomosis (Falconi *et al.*, 2001) has considered both field observation-based research, i.e. that which leads to either breed substitution or within-breed selection of superior animals using phenotypic measurements alone, and breeding schemes that use genetic markers associated with enhanced resistance to identify superior animals for breeding. Assuming adoption rates of 10% and 50% for the field observation and genetic marker approaches, the Falconi *et al.* (2001) model predicts substantially larger benefits from utilising genetic markers, although the return upon research investment for the two scenarios is similar. Assuming a 5% discount rate and summing across 50 years, the field observation approach yielded benefits of $32million, a benefit:cost ratio of 5.1:1 and an IRR of 32%. In contrast, the genetic-marker approach yielded benefits of $281million, a benefit:cost ratio of 5.2:1 and an IRR of 12%.

Mastitis

Mastitis is the single most important disease in dairy cattle in developed counties and is also of major importance in developing countries. Economic impacts include milk loss, premature culling, occasional mortality (more common in sheep mastitis), and high treatment costs. In particular, treatment by antibiotics is problematic in light of the need to decrease antibiotic usage in livestock production systems. Furthermore, in livestock production systems where farmers are paid according to milk quality, enhanced somatic cell counts (SCC) due to subclinical mastitis incur financial penalties. Selection against subclinical mastitis using SCC is now widespread in developed countries. Selection for resistance to clinical mastitis is a component of dairy cattle breeding programmes in Scandinavia.

A full economic appraisal of the costs of clinical mastitis in the UK is given by Bennett *et al.* (1999). The UK dairy herd suffers approximately 40 cases of clinical mastitis per 100 cows per year, and total annual costs of clinical mastitis to the UK dairy industry, not including penalties on subclinical mastitis were £187m. Selection to decrease mastitis or limit the rate of increase of mastitis, with a cumulative impact of 1% per year and a national penetration of 50% would result in a national benefit of £0.9m/year. Additional benefits from improved milk quality through decreased SCC depend critically upon the current mean SCC. At national average SCC, the benefit of reducing SCC by 1% is £0.50/cow (Veerkamp *et al.*, 1998). At a national penetration of 50% this translates to a cumulative annual benefit of £0.6m. Thus, total benefits from using genetics to help manage clinical and subclinical mastitis cumulate at £1.5m/year to the UK dairy industry.

Appendix 6. The terms of reference

To prepare documentation on opportunities for the use of genetically-based technologies in the management of the range of animal diseases that impact the development of the important farm livestock species and the spectrum of important farming systems of the developing and developed world. The documentation should be comprehensive technically and also cover important policy issues to be addressed. The documentation should cover the following areas:

1. Background
2. Current technologies and their applications
3. Future opportunities
4. Cost-effectiveness of development and use of these applications
4. Risks and threats both in the development of these technologies and in their application
5. Priority areas both in terms of the technologies and the diseases to be addressed.
6. Policy issues for consideration

The final document is expected to be around 12,000 – 15,000 words.

This report will form part of a larger paper that will provide comprehensive state-of-the-art documentation on the topic: “Opportunities for the use of genetic elements in the management of farm animal diseases, including those that relate to policy”.

It is envisaged that this documentation may be utilised in three ways:

1. As a technical description of the state-of-the-art, to also go on the FAO Web-page.
2. For use in crafting intergovernmental documentation to be considered by both FAO's Committee on Agriculture and the Commission on Genetic Resources for Food and Agriculture to assist countries to develop policy for incorporating genetic elements in management of diseases. It is particularly necessary given the rapid advances underway in the development of a range of powerful molecular genetic tools with a broad range of potential applications in understanding, monitoring and controlling diseases and their agents. This will include economic dimensions particularly as these relate to developing country benefits and costs.
3. To be crafted into documentation being developed by FAO as the core of a decision support system for country capacity development in the genetic improvement of livestock.

Appendix 7. The Authors

- *Stephen Bishop*

Advisor to the Government of UK on their disease research programme and the National Scrapie Plan. Principal Investigator, Roslin Institute, specialising in disease genetics, epidemiology and animal breeding; Visiting Professor, Glasgow Veterinary School (1998-2001); Special Professor, School of Biosciences, Nottingham University (2001-). Council member, President's Committee member and Chairman of Programme Committee for British Society of Animal Science. More than 190 Scientific Publications including: Axford, RFE, Bishop, SC, Nicholas, FW and Owen, JB. (2000). "Breeding for Disease Resistance in Farm Animals", 2nd Edition. CAB International. Editor for journals: Animal Genetics and Journal of Agricultural Science.

- *Mart de Jong*

Advisor to the Government of The Netherlands and other national governments on FMD control, and BSE and Scrapie eradication. Advisor to the Government of The Netherlands on control of Classical Swine Fever and eradication of Aujesky's disease in pigs and IBR in cattle. Leads the research group Quantitative Veterinary Epidemiology across Universities and the Ministry in the Netherlands, involving some 20 Epidemiologists. Professor of Quantitative Veterinary Epidemiology at the Universities of Wageningen and Utrecht.

- *Douglas Gray*

Regional Coordinator for the International Livestock Research Institute in South East Asia; 20 years experience and 70 publications on parasite control, especially genetic approaches to helminth control on sheep and goats, including "Breeding for Disease Resistance in Small Ruminants (eds Gray, GD, Woolaston RR and Eaton, BT), Australian Centre for International Agricultural Research" Technical Monograph no 34, 1995; co-founder of the 'Nemesis' program for breeding Merino sheep in Australia for resistance to nematodes; leader of ACIAR project "Breeding prolific, worm-resistant sheep for Maharashtra, India (1994-1998) and Sustainable Endoparasite Control for Small Ruminants in South East Asia (1998-2002).

Box 1: Eradication of Transmissible Spongiform Encephalopathies in Sheep using Genetics

Breeding programmes to eradicate scrapie are in place. Monitoring is long term.

Background: Transmissible spongiform encephalopathies (TSE) are diseases supposedly caused by prions. A prion is a wrongly folded specimen of a protein called PrP that is normally produced in the correct folding in cells of animals. This wrongly folded PrP results in newly produced PrP in the cells of animals also being wrongly folded. This is a problem as the wrong folding makes the PrP resistant to enzymes that normally breakdown proteins. Hence the prion protein accumulates as clots in the brain. These clots damage and kill cells. These damages lead to serious clinical symptoms and eventually the death of the affected individual. Known TSE's included scrapie in sheep and Creuzfeld Jacob's Disease (CJD) in humans. Some 20 years ago a new TSE arose in cattle which was called BSE. BSE entered the human food chain and has caused cases of CJD that were distinct from previously reported cases. This was remarkable as scrapie (the TSE from sheep) is assumed after epidemiological research to be not transmissible to humans. Because of its human health implications, BSE in cattle is rigorously eradicated to prevent further human cases of the new variant CJD.

Problem: BSE might have entered the sheep population and cannot currently be distinguished from scrapie. Therefore all TSEs need to be eradicated from the sheep population.

Genetic solution: The gene having the genetic code for the protein PrP is known. Certain variants of this gene lead to scrapie susceptibility whereas other variants of the gene result in sheep being resistant to scrapie. Therefore, the genetic composition of sheep populations, with respect to the PrP gene, should be changed so that eventually all sheep will be resistant. Current programmes in different European countries seek to achieve this by selection such that rams used for breeding are all homozygous for resistant PrP variants. Scrapie is transmitted from sheep to sheep. Scrapie will be eradicated once sufficient sheep are resistant to block transmission of infection. Genetic change in the sheep populations will take many years, especially once the frequency of the susceptible variants is low. The main reason for this is that selection is currently only on the males. However, disease eradication should occur before all sheep become genetically resistant.

Box 2. Breeding for Resistance to Nematode Parasites in Small Ruminants

Important breeding decisions can now be made for integrated worm control. Additional techniques that will make breeding even more effective are becoming available.

Background: Nematode parasite infections are overwhelmingly the livestock disease condition with the greatest impact upon animal health, productivity and world poverty (Perry *et al.*, 2002). This is an obvious problem in developing countries, however sheep and goat production in western countries is equally threatened. Integrated management strategies are becoming urgent for nematode infections. In all production systems nematodes are evolving to make chemical dewormers ineffective, and in most smallholder systems chemicals are both expensive and difficult to obtain. Additionally, long-promised vaccines against nematode parasites are still not commercially available. Therefore, breeding approaches to decrease the impact of nematode worms on the goats and sheep are becoming increasingly important.

The greatest genetic change in modern times in developing countries has been to decrease **the resistance of indigenous breeds by the introduction of exotic breeds with greater dependence on chemicals for worm control. This has hastened the need for using genetics optimally to improve resistance. Paradoxically, it has demonstrated that genetically changing the resistance genotype of host populations can be simple and rapid.**

Selection of breeding stock with enhanced resistance is straightforward. Measurement of resistance is by collection of faeces from young sheep under challenge and counting the nematode eggs in a laboratory. This number, combined with production measurements, is used to select the next ram, buck or breeding female. Eyelid colour may also be used to assess infection-induced anaemia.

Implementation: Convincing research has shown that many breeds of goats and sheep have better performance in the presence of worm challenge than other breeds available to the farmer (Gasbarre and Miller, 2000). These include the Red Maasai, Barbados Blackbelly and Garole sheep and East African goats. One simple breeding approach is to replace the currently used breed, which may have been introduced quite recently, with an adapted breed of proven productivity and reduced need for other inputs for worm treatment. An example of the superiority of locally adapted breeds is the Red Maasai, which produces three times more meat per year than the apparently more productive Dorper, when raised under environmental conditions in which there are substantial parasitic challenges (Baker *et al.*, 1999).

There is also sufficient genetic variation in resistance to nematodes within breeds of sheep to allow selection for increased resistance. This has happened in the field in Merino, Romney, Suffolk and Texel sheep, and Cashmere and Guadeloupe goats. In Australia, New Zealand and the UK there are commercial breeding schemes that include resistance to nematodes in the breeding objectives. Additionally, genetic markers are being sought to make selection of goats and sheep possible without necessarily exposing them to infection.

Benefits:	The immediate benefits of using worm measurements to select breeding stock come from the monitoring of disease levels and improved worm control. This usually results in decreased use of expensive and increasingly unreliable chemicals. Additionally, improved productivity will be a consequence. Genetic resistance can be used as part of an integrated health programme, along with adoption of rotational grazing systems, improved nutrition and management, confinement during risk periods and better use of chemicals.

Box 3. Genetic Strategies for Managing Poultry Diseases in Smallholder Production Systems

Research is promising but new knowledge is needed to take genetic approaches to Newcastle disease, coccidiosis and nematodes to smallholder systems

Background: Diseases have a major impact upon poultry production systems in both intensive and smallholder production systems. In intensive systems, Marek's disease is a viral tumour-causing disease associated with intensive production. Intensive poultry production is often not possible without efficient control of Marek's disease. In terms of effects on world poverty, in developing countries, two of the most important diseases are Newcastle disease and coccidiosis (Perry *et al*., 2002).

Poultry livestock production systems require the smallest investment of the major livestock species. Hence they are characteristic of subsistence smallholder production systems. The low unit value in poultry production systems also dictates genetic improvement strategies – these tend to be facilitated by the transfer or sale of animal genetic resources rather than the selection of outstanding animals within the production system.

Blueprint: Genetic management of Mareks's disease is well established in intensive poultry production systems. Selection for resistance based on both response to infection (Friars *et al*., 1972) and genetic markers (Bacon, 1987) has been used for many years to assist in disease management. Concurrent vaccination strategies have apparently had deleterious consequences as evolution of ever more pathogenic strains of virus has followed each new vaccine (Witter, 1998). Arguably, intensive poultry production would no longer have been possible in many circumstances without genetic selection. Therefore, genetic management strategies have been central to the sustainability of intensive poultry production. This provides a blueprint for the utilisation of genetics to manage diseases in other production systems.

Opportunities: Genetic management strategies have an equal role to play in smallholder poultry production systems. Both Newcastle disease and coccidiosis are diseases for which genetic variation in resistance is well established (e.g. Gordon *et al*., 1971; Rosenberg, 1941; Lillehoj *et al*., 1989). This includes between-breed variation. Hence genetic management strategies are potentially feasible. These would contribute to the alleviation of poverty amongst smallholders and increased security of food supply.

Way forward: Although there appear to be opportunities to use genetic approaches to help to manage Newcastle disease and coccidiosis, effort is required to realise these potential benefits. Firstly, research is required to identify genetically resistant animals or breeds from amongst the currently used animal genetic resources. Once identified, stakeholder involvement is required to ensure fair and equitable dissemination of these genetic resources amongst smallholders, with due regard to current ownership rights of these resources. However, if this can be achieved, gains in terms of poverty alleviation are potentially enormous, with very little cost incurred once genotypes with enhanced resistance have been identified.