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CONVENTION ON THE CONSERVATION OF EUROPEAN WILDLIFE
AND NATURAL HABITATS

Standing Committee
21st meeting

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Document for information

**Tuberculosis in cattle and badgers
(United Kingdom)**

Report by the Government

*Document prepared by
the Secretary of State for Environment, Food and Rural Affairs*

INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

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The Rt Hon Margaret Beckett MP
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18 July 2001

Dear Secretary of State,

I am pleased to send you the third report of the Independent Scientific Group.

In the report we have outlined the progress made since our second report, particularly in consolidating the epidemiology and pathogenesis research programme that underpins the approach that we believe is needed to provide robust scientific results on which future sustainable TB control policies must be based.

Although most media and public interest has focused on the field trial aspect of the epidemiological study, we have again spelled out, consistent with the holistic and objective approach that we have taken, the central importance of gaining a better understanding of the dynamics of the disease in cattle if the objective of controlling TB in cattle while ensuring their co-existence with wildlife is to be achieved.

We were grateful for the immediate response from former MAFF Ministers to our previous proposals that ensured that the cattle pathogenesis programme was speedily put in place. We now advise and seek approval for an extension to this programme; this requires that additional disease containment facilities are built, with some urgency, if essential work is to be done within the timeframe outlined in our second report.

While recognising that the selection of future policy options is a decision solely for Ministers, we see our role as ensuring that all likely future options are adequately underpinned by appropriate science. In pursuit of this we have considered a range of policy options to assist us in our deliberations, and a discussion of these options is included in the report. I would stress that our choice of options should not be interpreted by anyone as indicative of our preference for future policy.

While we would wish to emphasise that there were no delays in the trial implementation timetable during the reporting year, it will be unavoidable that the recent Foot and Mouth disease outbreak, which affects directly some of the trial areas, will have an impact on our work. The inevitable effect will be to extend the time needed to complete the work programme. It will also make some analyses more difficult. However, at this stage we consider the impact to be manageable and also we do have the flexibility to readjust some of the final trial areas. We will, of course, continue to review the situation and provide you with a more detailed assessment of the position when the outbreak has been, or is near to being, concluded, in order that the field work can be completed as quickly as possible. Meanwhile, we are concentrating our efforts on the laboratory work and replanning our work programme and schedules.

As we record in the report, the Group remains grateful to you and your former MAFF colleagues for your continued support and encouragement and for the positive response that we have had from MAFF and its executive agencies.

Yours sincerely

F J BOURNE

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**An Epidemiological
Investigation into
Bovine Tuberculosis**

1. Chairman's Introduction

1.1 It is more than a year since we published our second report [1] in which we outlined in detail the holistic approach adopted with the aim of establishing an information structure to underpin the development of bovine tuberculosis (TB) control strategies. Among other things, we presented our advice to the Ministry of Agriculture, Fisheries and Food (MAFF) on the broad research programme needed to gain a better understanding of the epidemiology of TB in cattle and wildlife - a programme that is now in place. The Independent Scientific Group on Cattle TB (ISG) believes that it is only through this understanding that sustainable control policies can be devised and successfully implemented. This focused epidemiological research programme is complemented by a range of other studies including economic analysis of the impacts of bovine TB both locally and nationally, the ecological impact of reducing badger populations in tracts of the countryside, vaccine development and many other lines of investigation that are listed in Appendix A.

The Field Trial

1.2 The field trial, which forms one part of the epidemiological research programme, was explained in detail in our second report. It was originally conceived on the recommendations of the Krebs report [2] to evaluate the effects of badger culling on the incidence of TB in cattle. However, because our work has the wider objective of better understanding the disease, the trial has been designed by the ISG to provide a baseline of epidemiological and scientific data in addition to addressing the culling issue. Epidemiological data on the incidence and prevalence of TB in badgers, its relationship to population density and social group size and, importantly, the spatial relationship between TB-infected badgers and TB breakdowns in cattle herds will be provided. We also recognise that infectious disease is dynamic, and that disease patterns change over time; the trial allows opportunity to study this, since some of the field trial operations are in areas that were previously subjected to localised badger removal. Data from these particular operations will provide retrospective information on the localised incidence of TB in badgers and its relationship to TB in associated cattle herds and also allow comparison of the contemporary incidence of TB in badgers and cattle and with the incidence in cattle in the intervening years.

1.3 We, therefore, expect a broad range of informative and indeed essential data to result from the trial. The timetable for enrolment of triplets and initial proactive culling was presented in our second report. It was envisaged that all triplets would be identified by the end of 2000, that proactive culling would be completed in seven of the triplets by this time, and that field work would have started on the remaining three triplets in preparation for their initial proactive cull in 2001. This timetable has been met by MAFF's Wildlife Unit (WLU). Statements in the media and elsewhere that the timetable has slipped in the past trapping year are groundless, though we are aware that the outbreak of foot and mouth disease will cause some future delay to the timetable.

TB99 Farm Survey

1.4 Several risk factors, particularly in the area of cattle husbandry, have been proposed as predisposing some farms to TB outbreaks. The TB99 epidemiological investigation questionnaire is designed to address this issue, gathering data in a form amenable to statistical analysis on a range of potential risk factors to cattle TB in an objective, comprehensive and practical manner. Since January 1999 TB99 data have been collected from breakdowns plus 3 control farms in all trial areas. Outside trial areas TB99 data have been collected from every breakdown occurring between January 1999 and June 2000. Data collection was resumed in January 2001, after the interruption caused by the classical swine fever outbreak, but the recent foot and mouth outbreak has had a seriously disruptive effect. An initial analysis is now being conducted of TB99 data, and preliminary results from an initial analysis of data from non-trial farms is included in this report in Chapter 6.

Diagnosis

1.5 The cornerstone of any epidemiological study is the accumulation of accurate data on the prevalence and distribution of infection and appropriate analysis and interpretation of the data. But especially there is a need for accurate (both sensitive and specific) disease diagnosis. The methods

used to diagnose TB in badgers captured in the trial, and also in previous badger removal operations, have been and will continue to be critically assessed and audited. MAFF conduct their own internal quality assurance audit of procedures and we are also arranging an external audit of diagnostic techniques in view of their central importance to the study.

1.6 The accurate diagnosis of disease in cattle is also essential if we are to understand the epidemiology of the disease and put in place effective controls. The cattle pathogenesis research programme has as one of its objectives a study of available diagnostic tests, with a view to improving these and developing alternative tests. The ISG highlighted to MAFF, through the TB Forum, the potential value of the gamma interferon test (IFN) to complement the tuberculin skin test in problem herds and so to increase the sensitivity of the diagnosis. It is encouraging that a small feasibility field trial to study the logistics of using the test is underway, while research work to improve the sensitivity and specificity of this test is receiving high priority.

Pathogenesis

1.7 The ISG recognises that there is a reservoir of TB in wildlife in Great Britain, but its scale, its significance to cattle TB, or whether anything can usefully be done about it is unknown; these are questions that the field trial and related research have been designed to answer. We recognise also that there is an increasing level of infection in cattle in the South West. It is not clear how this is maintained or how this is influenced by any external source of infection or cattle-to-cattle transmission, but previously adopted control policies have neither eliminated nor contained this infection. Because of the rising number of outbreaks we have previously questioned whether cattle TB control in this high disease risk area is actually being constrained by limitations in the tuberculin test itself, since this could be having a major impact on persistence of infection in a reactor herd and its subsequent amplification by cattle-to-cattle transmission. In our second report we emphasised that we do not have sufficient knowledge of the transmission dynamics.

1.8 As a result the ISG has consciously sought to stand back and take an objective view of the TB problem in order to identify, through the best available science, a path for resolving the complex problems posed by bovine TB. We advised that additional work be put in place as a matter of priority to better understand the pathogenesis of TB in cattle. MAFF have responded speedily to this advice and a significant programme of work was initiated in July 2000. The pathogenesis research has been designed to answer a number of key questions. How quickly does the disease develop in cattle? Following infection, at what stage in the disease process is transmission to other animals likely to occur? How early in the disease process can accurate diagnosis be made? This programme ought to shed light on factors influencing the persistence and possible amplification of TB in cattle herds, and thereby contribute to the development and refinement of more effective control procedures. We now further advise that this programme is extended and extra research facilities put in place to facilitate this work.

Policy options

1.9 We have previously emphasised that there is probably no single solution to the problem of TB in cattle and that, in the light of Ministers' stated views that the elimination of badgers from large tracts of the countryside is not acceptable, a strategy based solely on badger culling is not an option for future policy. Consistent with this, therefore, the programme of research now in place has been designed to consider a range of options and to ensure that an appropriate scientific underpinning will be available for each. To construct the research agenda it has been necessary for the ISG to consider what these options might be.

1.10 We have considered a wide range of options from proactive badger culling in certain areas, coupled with improved TB diagnosis and health management in cattle, to a strategy based solely on the cattle element of better diagnosis and health management. Various intermediate hybrids could be adopted, including a situation in which Government accepts responsibility for the protection of public health, and the agricultural industry accepts responsibility for TB control in cattle. We stress that the purpose of this exercise was to aid ISG in its task of advising on an appropriate research programme

that will scientifically support a range of policy options; it does not imply that any particular measure will ultimately be recommended.

1.11 We believe that the breadth of the research programme is appropriate but we will continue to assess research needs, the progress of research and the balance of the programme. We will also continue to review the progression of the disease in the cattle population, both regionally and nationally, and the short-term control options that may be considered, and will provide further advice as appropriate.

Road Traffic Accident (RTA) Survey

1.12 We have previously indicated that future policy options may require information on the prevalence of TB in badgers outside trial areas that may be obtained from a survey of the TB status of badger carcasses collected as victims of road traffic accidents. After considerable delays it was encouraging that the State Veterinary Service had made progress in getting the RTA Survey up and running, although the foot and mouth outbreak has resulted in further delays.

Style of the report

1.13 It is my hope that the report is clear and readable, that it conveys the breadth of the work that is now in place, the holistic approach that we have taken and the value of the information that will be forthcoming from the research programme.

Acknowledgements

1.14 As Chairman of the ISG, I wish to express my gratitude to Ministers and DEFRA senior management for their continued support. The ISG Secretariat team continues to provide excellent service and we are indebted to advisors from the Central Science Laboratory (CSL), the Veterinary Laboratories Agency (VLA) and the Chief Scientist's Group (CSG). We are grateful to the State Veterinary Service for their work with TB99 and to VLA staff for their constructive support, work and advice. My continued appreciation goes to the Secretary of the Group and to the ISG members, who give unstintingly of their time to pursue the many facets of this investigation and who remain committed to the work that we are doing.

John Bourne

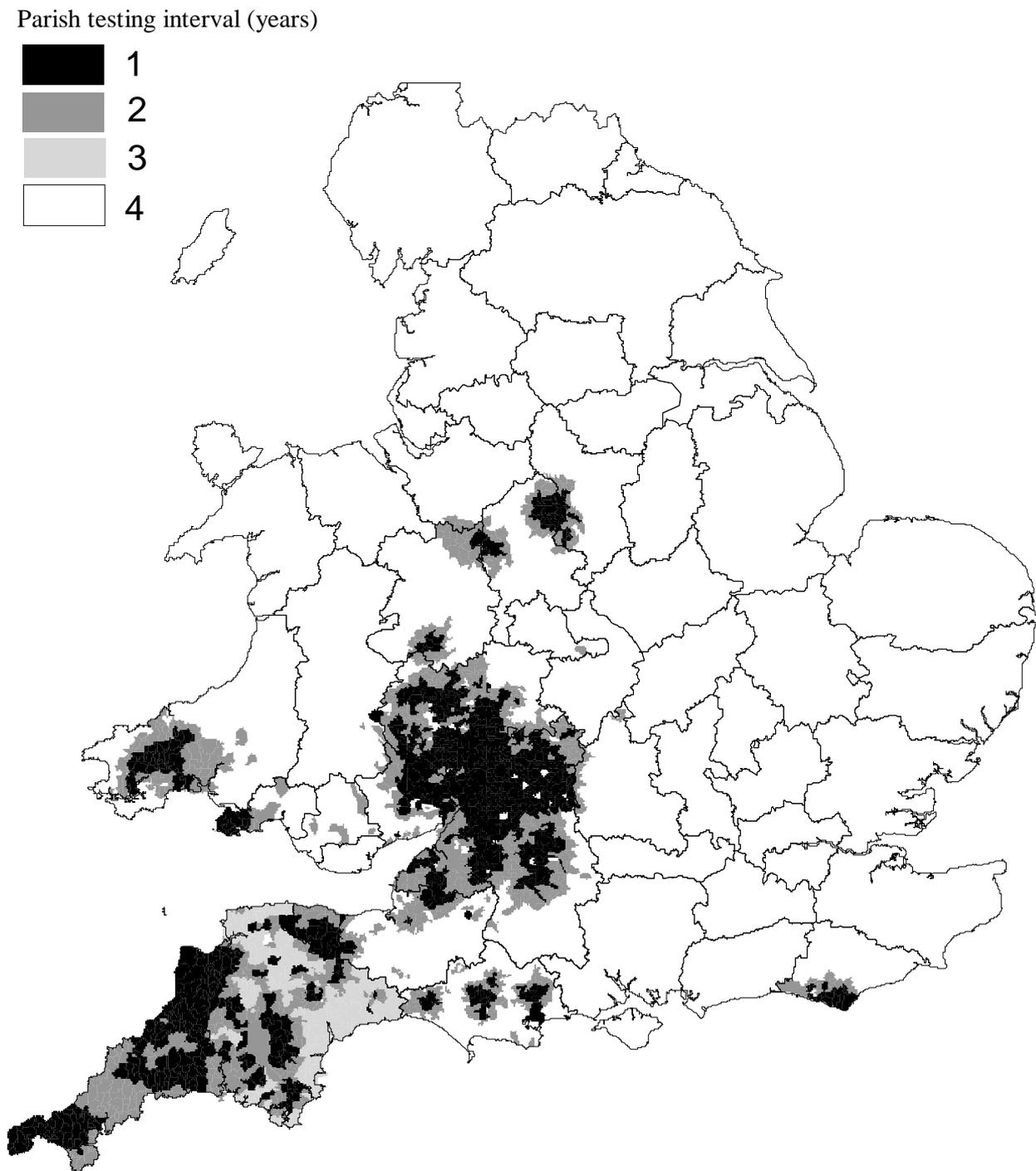
July 2001

2. Towards a sustainable policy to control TB in cattle in Great Britain

2.1 Bovine TB (caused by the organism *Mycobacterium bovis*, abbreviated *M. bovis*) is a serious disease of cattle which resulted in approximately 9000 cattle having to be slaughtered in the year 2000. Its occurrence in a herd leads to major disruption to production and breeding programmes, financial hardship and emotional distress to farmers whose herds are affected, and threats to neighbouring cattle and milk producers. If the national incidence level rises above a critical threshold, this has serious implications in relation to EU regulations and international trade. It is also a potential human health risk.

2.2 Control policies for the past 25 years have relied on the regular testing of cattle and the immediate slaughter of animals found to be infected. This has been successful in lowering the level of and subsequently controlling the disease in most of Great Britain. However, in the South West where foci of infection have persisted, the incidence of the disease remained at higher than average levels and in recent years has increased substantially. The disease has also extended to counties further north. The distribution of the disease is reflected by testing intervals as shown in Fig. 2.1.

Figure 2.1 Parish testing frequencies for England and Wales in 2000.



2.3 The failure to control TB successfully in these areas has been ascribed to the existence of a TB reservoir in wildlife, specifically the badger, whose involvement was first suspected in the early 1970s. Whilst there is some evidence from past investigations that almost complete elimination of badgers reduced the incidence of TB in cattle, these studies lacked controls, making the interpretation insecure. Furthermore, the policy of restricted badger culling, coupled with the removal of tuberculin positive cattle from herds, has not controlled the disease. In an attempt to finally resolve this question, and in order to base future strategy on a sound scientific footing, the Government in 1996 appointed the Krebs committee whose report [2] provided an in-depth review of the situation. It concluded that there was compelling evidence that badgers did contribute to cattle TB, but that with existing knowledge it was neither possible to quantify the contribution they made to the disease nor to assess the value of badger culling to its control. Krebs recommended that a major field trial was put in place to answer these two major questions, and the ISG was established to advise on designing and implementing the field trial.

2.4 From the beginning of its work it was the ISG's view, endorsed and encouraged by Ministers, that to develop a sustainable solution to the problem of TB in cattle it was important to take a holistic approach. The Group concluded that there is probably no simple solution, that cattle TB must be attacked on a number of fronts, and that future control options required a far better understanding of the epidemiology and pathogenesis of the disease in both cattle and wildlife than exists.

2.5 We have previously explained the logic of taking a holistic view in the search for a sustainable scientific base to underpin future control policies. This acknowledges that the elimination of badgers from large tracts of the countryside is not an acceptable option for future policy, and that the overarching objective must be to control cattle TB in such a way as to allow the harmonious co-existence of cattle and wildlife, specifically badgers [1, 3].

2.6 The ISG has consequently developed a wide-ranging epidemiological investigation into TB in both cattle and wildlife. Our working approach is built around identifying the major epidemiological questions that need to be answered and then developing a substantial programme of research to provide answers that can best inform policy development. Major questions relate to factors influencing the prevalence and persistence of the disease in cattle and wildlife, risk factors contributing to the development of the disease in cattle, transmission routes between and within species, the use of effective diagnostic techniques and the effectiveness and relative economic merits of potential control options.

2.7 The multi-faceted investigation includes:

- i) A substantial epidemiological investigation, including a field trial and a questionnaire designed to assess various possible risk factors for disease;
- ii) Studies into cattle pathogenesis, including laboratory based and complementary field studies; and
- iii) Other related research.

2.8 All of these elements are now in place and include in addition programmes to provide information on wildlife ecology, the ecological consequences of badger removal, estimation of badger population density and social group structure, vaccine development and molecular epidemiology. All of these approaches are inter-linked and are being pursued in parallel.

2.9 Major media attention and comment has focused primarily on the field trial. This restricted interest unfortunately fails to recognise that all aspects of our work have relevance to future control policy options. In this respect the studies on cattle pathogenesis of TB which are aimed towards gaining a better understanding of the disease in cattle, its diagnosis and limitation of its spread, are of particular importance.

2.10 The ISG would expect ultimately to present to Ministers, for their consideration, a range of policy options for cattle TB control. The adoption of a control policy for implementation will be a decision solely for Ministers. However, to ensure that whatever options we present are adequately

underpinned scientifically we have considered a range of possible options to guide us in ensuring that research is in place to deliver the scientific and economic base against which such options can be evaluated.

2.11 The options considered range from, a policy incorporating some element of badger removal coupled with improved diagnosis of TB in cattle and more targeted health management of cattle, to a policy of no action against wildlife but a reliance on improved diagnosis and more targeted and improved health management in cattle. Further details of our thinking, can be found in Chapter 7.

3. The Epidemiological Investigation

THE FIELD TRIAL

3.1 The field trial was originally conceived to evaluate the effects of badger culling on the incidence of TB in cattle. However, consistent with the holistic approach taken by the ISG, the trial has been designed to provide additional data on the underlying epidemiology of TB in cattle and badgers.

3.2 The trial design has been detailed in previous reports [1, 3]. It consists of three experimental treatments: “proactive culling” (initial removal of as many badgers as feasible consistent with welfare constraints and thereafter maintaining numbers as low as possible), “reactive culling” (removal of badger social groups with access to a farm in response to an outbreak of cattle TB on that farm) and “survey only” (where no badger removal takes place). All culling operations in the trial are undertaken with full attention paid to badger welfare considerations.

3.3 The trial is being carried out in localities with the highest incidence of TB in cattle. A total of thirty trial areas have been prescribed, each measuring approximately 10,000 hectares (100 sq.km.), assembled into ten sets of broadly matched “triplets”. All trial areas are surveyed at the outset for signs of badger activity to provide indices of badger abundance and distribution, and then each trial area within a triplet is randomly allocated to one of the three treatments. From the badgers that are trapped and culled, epidemiological data will be obtained on the prevalence of TB in badgers and the spatial distribution of infected badgers and social groups, its relationship to population density, social group size and structure, geographical and physical environmental factors and - most importantly - the spatial relationship between TB in cattle and badgers. It is important to recognise that these data cannot currently be obtained in any other way, which demonstrates the crucial importance of the trial to the epidemiological investigation.

3.4 One of the cornerstones of an epidemiological study is accurate and sensitive disease diagnosis. This also can only be achieved in relation to badgers by carrying out the field study, since no reliable TB diagnostic test, or range of tests, can be used in live wildlife to provide the information that is required. Diagnosis can be made only by post mortem examination, and every badger culled is subjected to a rigorous post mortem protocol including bacteriological culture of body tissues.

3.5 The trial will also provide a unique insight into the dynamics of TB in the badger populations. Infectious disease is not static, it continually changes with respect, for instance, to its prevalence and distribution in populations and its virulence and pathology. Being centred in cattle TB hot spots many of the triplets have been subjected to previous badger removal operations (BROs) and thus afford the opportunity to compare past recorded information on disease incidence in badgers and its relationship to cattle TB with that found currently. This could provide additional valuable insights into the epidemiology of the disease, both in badgers and cattle, and their inter-relationship.

Completion of the triplet selection process

3.6 At the time of our last report, the ISG had approved six triplets of trial areas for enrolment into the trial. During the past year, the remaining four triplets in the planned schedule have been enrolled and announced by MAFF. The full list of triplets and their conventional designation by location is therefore:

Triplet A - Gloucestershire/Hereford

Triplet B - Devon/Cornwall

- Triplet C - East Cornwall
- Triplet D - Herefordshire
- Triplet E - North Wiltshire
- Triplet F - West Cornwall
- Triplet G - Staffordshire/Derbyshire
- Triplet H - Somerset/Devon
- Triplet I - Gloucestershire
- Triplet J - Devon

Progress with trial operations

3.7 During the course of the 2000 trapping year, running from May 2000 to January 2001, surveying was completed and initial proactive trapping operations were successfully carried out in Triplets E, F, G and H. This brings to seven the total number of initial proactive operations completed by the end of 2000, achieving the timetable set down by the ISG in our second report [1]. Follow-up proactive culls were completed in Triplets B, C and E, and reactive operations were carried out in Triplets A, B and C. Table 3.1 provides a summary of the number of badgers taken in the trial to date, while further details of trial operations in each of the "live" triplets (those for which an initial proactive cull has been completed) are given at Appendix C together with background data for each trial area within those triplets. In summary, the trial has been conducted to the timetable that the ISG laid down for the MAFF WLU, the group responsible for the culling operations, at the beginning of 2000.

Table 3.1 Summary of number of badgers taken in trial areas.

Triplet	Proactive Area	Reactive Area
Herefordshire/ Gloucestershire	55	34
Devon/Cornwall	397	107
East Cornwall	357	178
North Wiltshire	744	-
West Cornwall	451	-
Devon/Somerset	162	-
Staffordshire/Derbyshire	428	-
Total	2594	319

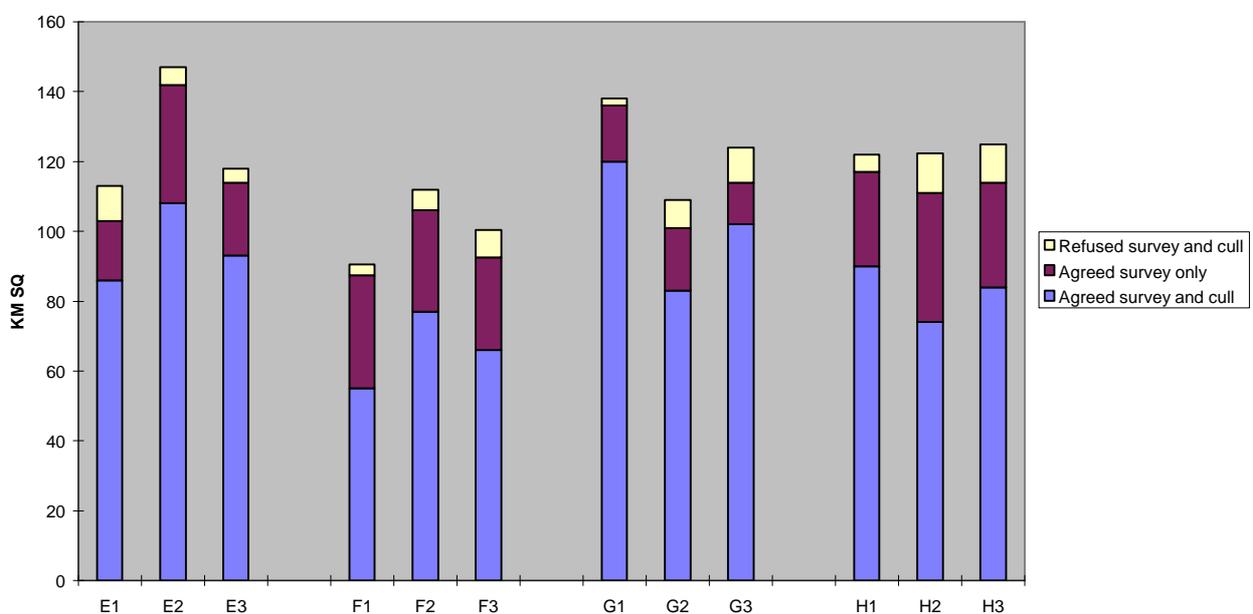
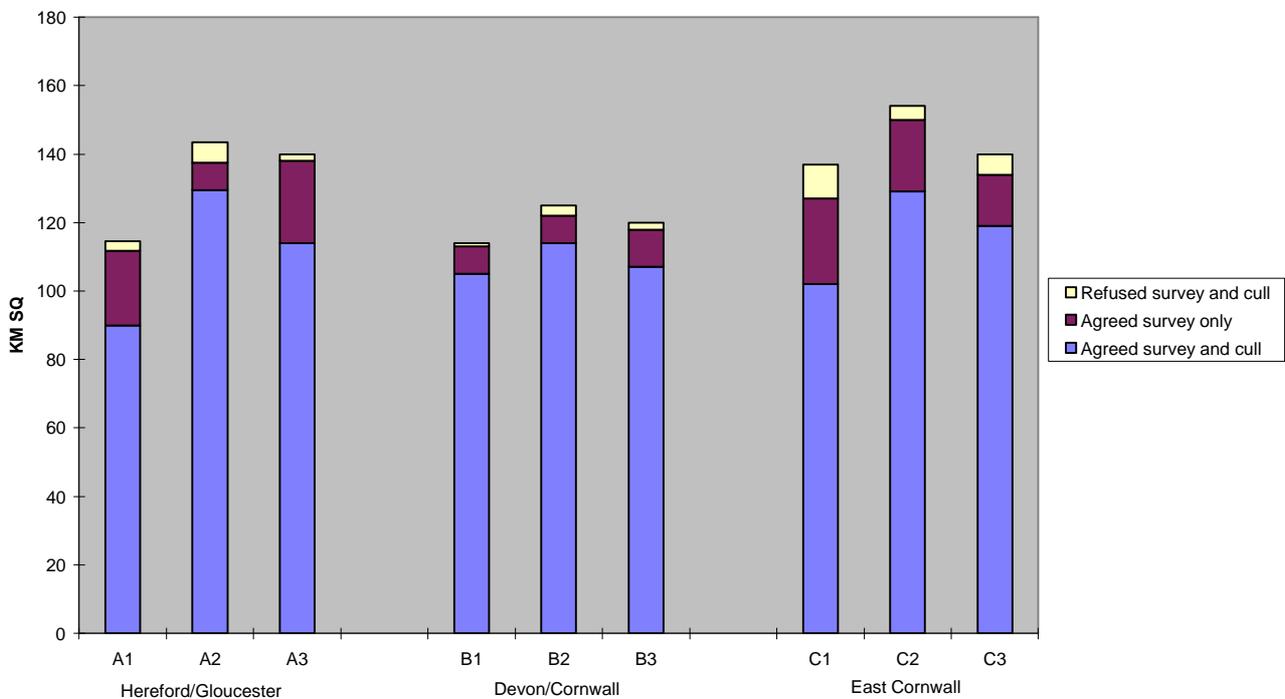
3.8 At the time of the last report, operations in Herefordshire (Triplet D) had been suspended due to significant levels of interference. We advised that a repeat survey would be necessary before trapping operations began in this triplet, due to the length of time that would have elapsed between the initial survey and the likely resumption of trial activity. Surveying had begun and was nearing completion in this triplet and in the most recently announced triplets in Gloucestershire and Devon, prior to the suspension of activities as a result of foot and mouth disease.

Participation in the trial

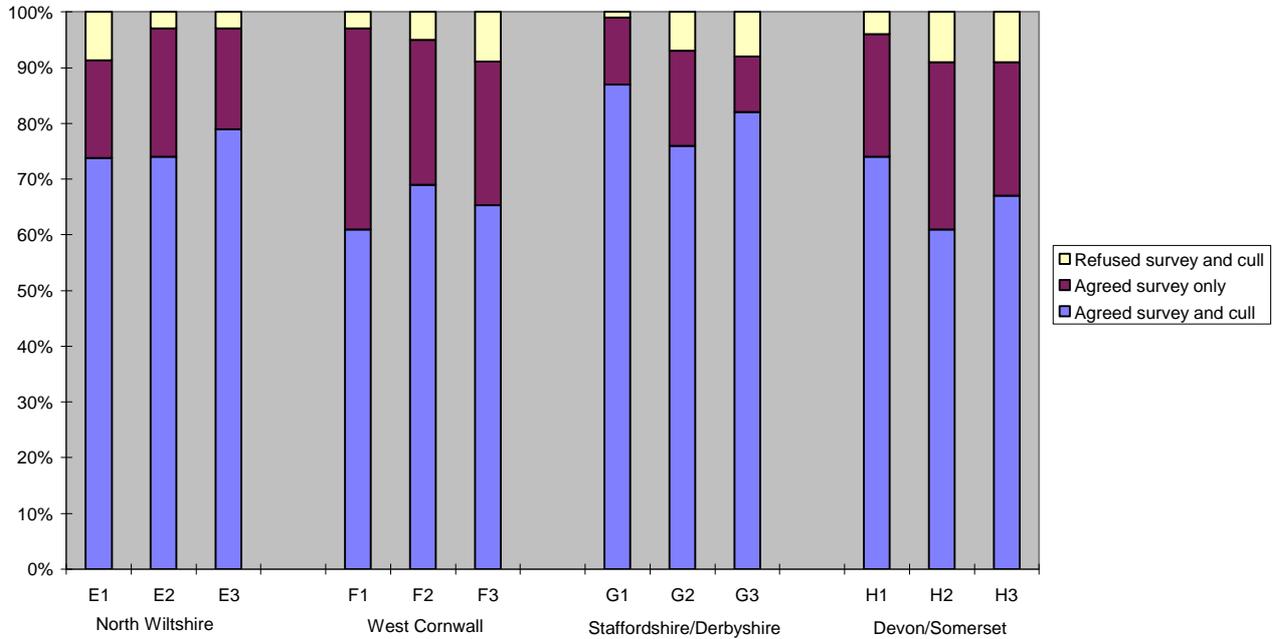
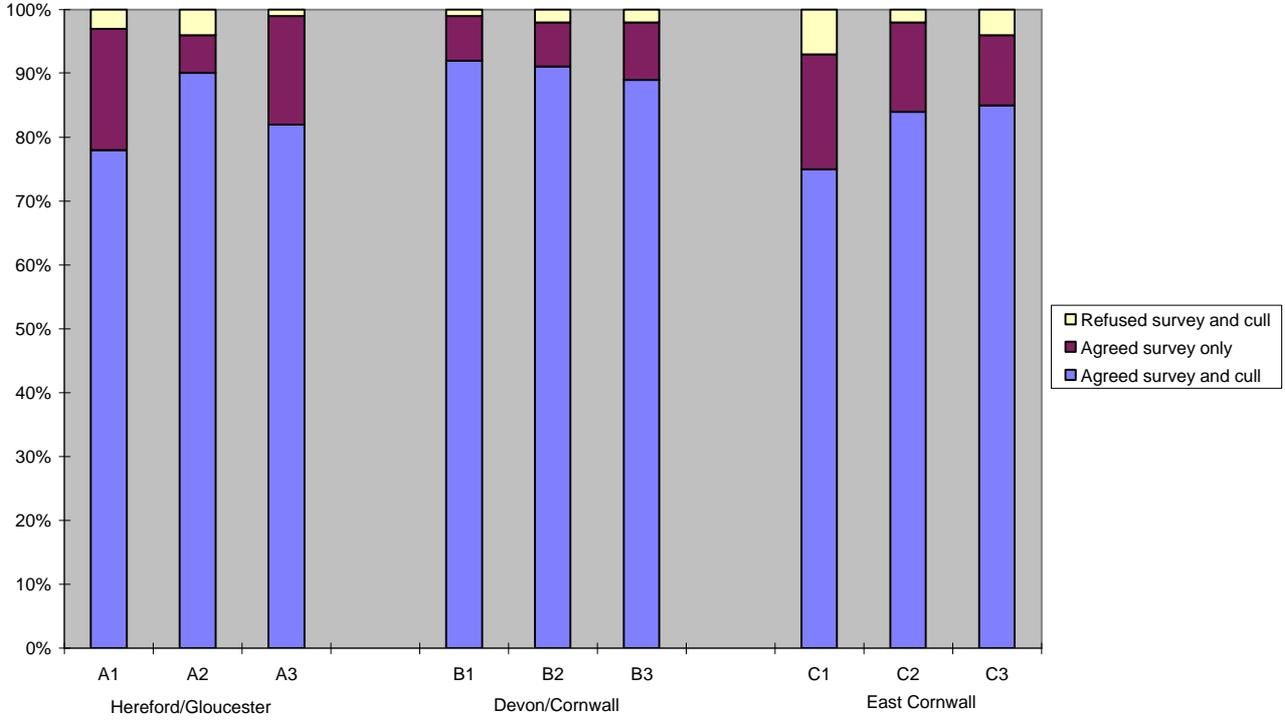
3.9 Once a triplet has been announced, the purpose of the trial is fully explained to farmers and landowners whose land falls within the triplet areas and they are asked to give their consent for two levels of trial activity - surveying and culling or, if they cannot give permission for culling on their lands, they are asked to permit surveying only. The response from land occupiers to MAFF's request to co-operate with the trial continues to be generally positive. Figure 3.1 shows the levels of consent for the seven triplets for which surveying has been completed, indicating that the level of co-operation in the rural community continues to be generally high. The ISG wish to express their gratitude to farmers, landowners and their representatives, including the National Farmers Union, for their support for the trial and other work that is taking place both within and outside trial areas.

Figure 3.1

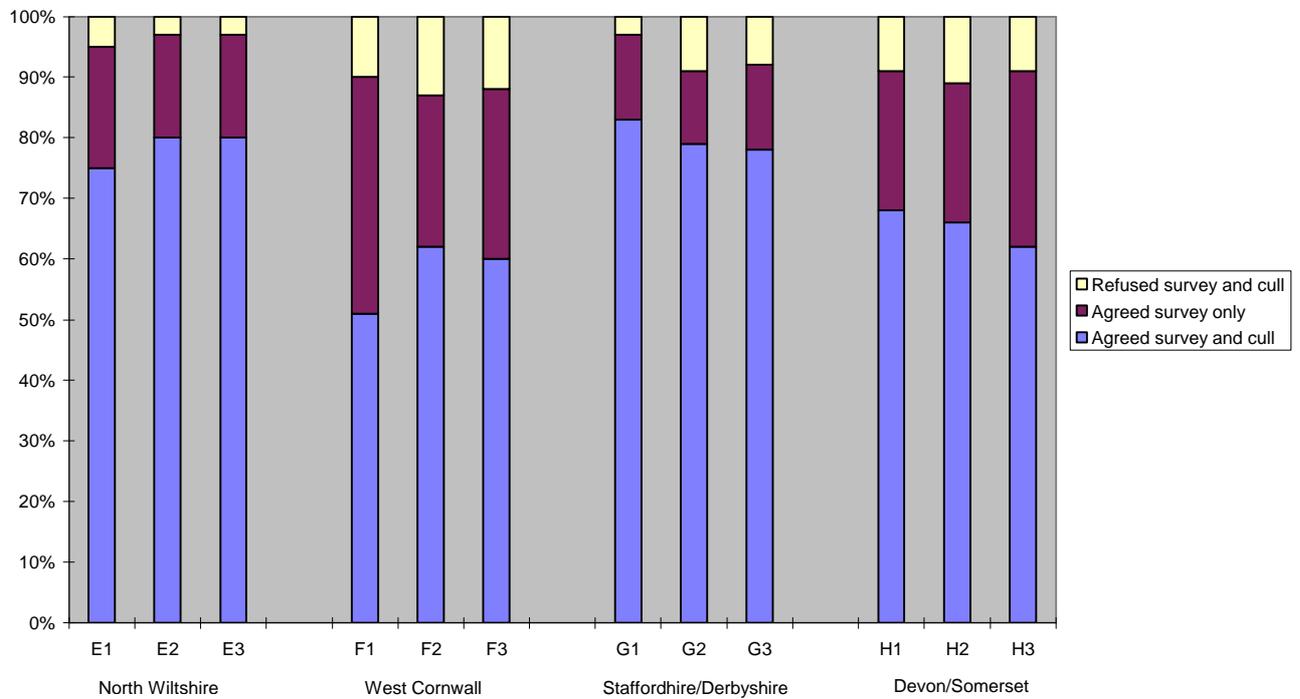
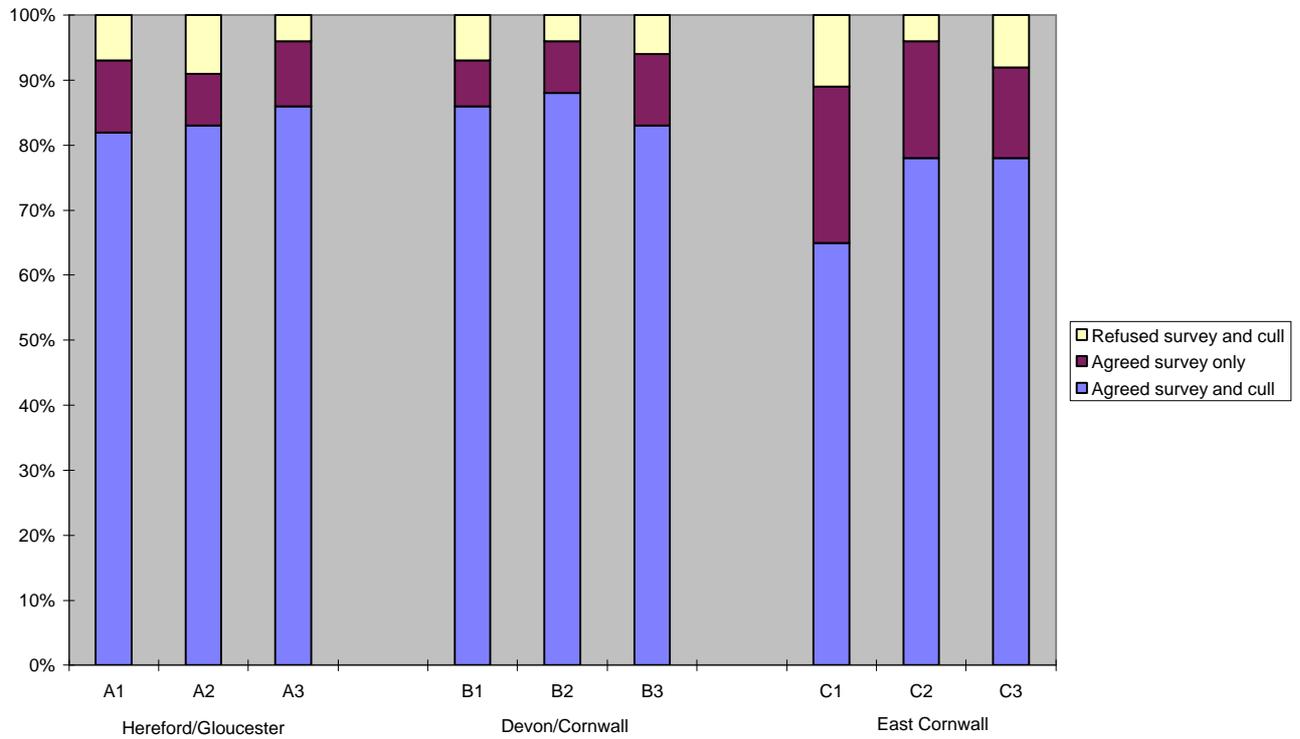
Level of co-operation - results of visits to trial areas and inner buffer zones (total available area for which permission for trial operations was sought).*



Level of co-operation - results of visits to trial areas and inner buffer zones (percentage of available area).*



Level of co-operation - results of visits to trial areas and inner buffer zones (percentage of all occupiers visited).*



* Source: provisional management data

Conduct of the trial

3.10 As we explained in our second report the trial has been designed to maximise the generation of rigorous scientific data for analysis. In so doing we have been careful to take full account of the ethical and environmental implications of our work and of the need to protect animal welfare, since any of the approaches taken may be implemented in future TB control policy.

Trial audit

3.11 The field operations and laboratory procedures conducted by the WLU and VLA are subject to internal audit procedures and scrutiny by members of the ISG. In addition, on our recommendation, field operations have been subject also to independent external audit.

Humane capture and despatch

3.12 In designing and implementing the trial we have given full consideration to animal welfare. Cage traps designed specifically for the capture of badgers are used to allow for easy release of non-target species. We stipulate that traps should be set as late as possible in the day and visited as early as possible the next day to minimise the length of time that captured animals are held in traps. Procedures for the despatch of trapped badgers are kept under continual internal review and in an independent assessment [4], published in October 2000, Dr J Kirkwood of the Universities Federation for Animal Welfare concluded that despatch procedures used in the trial are humane and met high welfare standards.

3.13 Dr Kirkwood made a number of recommendations for training and procedures, all but two of which have been acted upon by MAFF. One related to the use of repeater firearms to reduce the time elapsed between shots on those few occasions when a second shot is required. The Government was unable to accept this recommendation as a result of its acceptance of the Dunblane Report in 1996. Dr Kirkwood also suggested that trapping procedures should be audited at night when trapping occurs. This recommendation could not be implemented because of police advice about the inadvisability of night working against the background of anti-trial activity, but we are keeping this recommendation under review.

Field surveying and social group delineation

3.14 Cresswell Associates Environmental Consultants audited the fieldwork undertaken by WLU staff in the early stages of the trial, November 1998-December 1999, when expertise and survey procedures were evolving. The auditors' report found no fundamental flaws in the carefully specified field operational procedures, and concluded that over 90% of main setts were accurately located (which is the important factor for data gathering and trapping efficiency) and that social group delineation for identified main setts was accurately achieved in every instance. The auditors' report identified some shortcomings in the procedures in place at that time, and made recommendations on the identification and classification of badger setts and the establishment of badger social groups. MAFF has implemented as many of these recommendations as far as is practicable while the auditor's report was in preparation. The ISG is confident that field procedures in the trial have improved and notes that further staff training has been provided since the audit was carried out. We will keep standard procedures under review through the course of the trial.

The closed season

3.15 As described in our previous reports, in designing the trial we adopted a closed season to minimise the risk of capturing female badgers with dependent cubs below ground. This no-cull period covers the months of February, March and April and was defined on the basis of the most compelling scientific evidence available to us on the timing of nidation namely, that the majority of births would occur during the latter part of January to early February.

3.16 As the Group explained to the Agriculture Select Committee an analysis of the capture of lactating females and cubs in the Wiltshire triplet E, which was proactively culled in the last two weeks of May 2000, supported the validity of the definition of the closed season. At the point of trapping WLU staff estimated, based on teat size, that 51 females (out of 602 badgers culled) were

lactating or had recently stopped lactating. On the basis of average litter size of 2 - 3 cubs this number of lactating females would be expected to produce between 120 to 150 cubs. The number of cubs trapped, 162, is consistent with the majority of cubs present having been captured. At subsequent post mortem examination 3 of the 51 post parturient females were found to be actively lactating. At the setts where these lactating females were trapped two cubs were caught at one of the setts and one cub at another. This suggests that the number of cubs dying below ground has been very small. In a culling operation immediately prior to the start of the closed season (in Triplet A in January 2000), pregnancy status was assessed for the 18 females trapped and none of these was found to be lactating although 5 (28%) were found to be pregnant. This is consistent with no cubs being left below ground as a result of MAFF trapping operations. Nonetheless, the ISG continues to re-assess this and all other welfare aspects of the trial.

Interference with the trial

3.17 Trial audits, coupled with our own observations, reassure us that the WLU has translated the design of the trial into field activity very effectively. Unfortunately, the WLU continues to experience obstruction of staff and damage to equipment to varying degrees during the conduct of trial operations. While we recognise that badger culling is an issue which invokes strong emotions, in both those opposed to the trial and in those who advocate action against badgers on a wider scale, we repeat our previous advice that interference to the trial of any kind can only prolong the timeframe over which data would need to be collected before sufficient data were gathered from which dependable conclusions can be drawn. This in turn would delay the development of a broadly acceptable, sustainable TB control policy based on sound science.

3.18 In our last report we recognised and commented upon the careful planning and co-ordination that was necessary in order for the field work to be effectively carried out. We would wish to re-emphasise again our gratitude to WLU staff for their commitment and for the energy, initiative and professionalism they have demonstrated in the field.

Statistical design of the trial

3.19 An analysis of the statistical power of the trial was originally conducted by Krebs to determine the extent of trial activities necessary to generate sufficient data to allow dependable conclusions to be drawn. The Agricultural Select Committee, in its first review of trial operations, could find no flaw in the trial design, but recommended that the original data and accompanying analysis be verified by an independent expert. Professor D Mollison of Heriot-Watt University was appointed by MAFF as the field trial independent statistical auditor and published his first report in November 2000. The Group noted with satisfaction the endorsement of its approach and of the statistical design of the trial and we will continue discussions with Professor Mollison throughout the course of the trial.

TB99 - THE FARM SURVEY

3.20 Several risk factors, particularly in relation to cattle husbandry practices, have been postulated as predisposing some farms to TB outbreaks. Such risk factors are not amenable to experimentation, primarily because of the abundance of variable factors, the impracticability of conducting controlled experiments on commercial livestock farms and the relative paucity (in statistical terms) of TB outbreaks. In an attempt to identify and quantify risk factors we have adopted a "case control" study approach, which is well established in medical and veterinary epidemiology, using the TB99 questionnaire. An initial analysis of TB99 data is provided in Chapter 6.

4. Cattle Pathogenesis

4.1 In our second report we explained that we attached an extremely high priority to assessing the relative importance of cattle-to-cattle transmission of TB, an issue that we considered not to have been adequately addressed in the past and which may be of far greater practical significance than has been appreciated.

4.2 The implicit assumption underlying the long established TB control procedures is that cattle-to-cattle transmission is of critical importance, which is why movement restrictions are imposed immediately reactors to the tuberculin test are found in a herd. This approach, coupled with the removal of reactors, has worked in most parts of Great Britain but the persistence of TB breakdowns in some regions has been interpreted as evidence for a continuing source of infection from wildlife. Because of the higher frequency of tuberculin testing in these high incidence regions, and the prevailing belief that the testing protocols are effective at clearing herds of infection, the possibility of cattle-to-cattle transmission as a dominant cause has been largely discounted. This may or may not be justifiable, however. High risks of infection, irrespective of the source of disease, may place greater demands on the testing programme whose sensitivity, based on the tuberculin test, may not be sufficiently high to deal with a situation where there is repeated introduction of infection.

4.3 The ISG recognises that there is a long-standing disease problem in cattle which the testing and badger culling programmes over many years have failed to eliminate. The fact that cattle TB is increasing in incidence has been interpreted as evidence that TB diseased badgers are continually infecting cattle. However, we believe it necessary to question this view and consider the possibility that, irrespective of its original source, infection persists in herds, giving opportunities for amplification and cattle-to-cattle spread.

4.4 A feature of the disease in cattle (and a possible confusing factor) is its low incidence and generally low but variable rate of transmission, as reflected in some transmission experiments using naturally-infected tuberculin positive cattle [5]. However, other transmission experiments using experimentally infected animals have highlighted the possibility of transmission occurring early in the disease process and this could also have practical relevance. An understanding of these aspects of the disease which directly relate to on-farm disease management are, along with others, being addressed in the cattle pathogenesis programme and we welcome MAFF's prompt support and the immediate provision of funding for research in this area.

4.5 On our advice, following open competition MAFF has commissioned a major collaborative project, involving the Institute for Animal Health (IAH), the VLA and Queens University, Belfast, to investigate the pathogenesis of *M. bovis* in cattle.

Minimal Dose Pathogenesis Study

4.6 This programme, which started in July 2000, uses an intermediate infectious dose sufficient to ensure that all infected animals develop disease and are, therefore, informative. In addition to providing information on disease dynamics, it will explore routes of transmission, the effect of repeated skin testing on the course of the disease, and study other diagnostic tests. It will support the development of mathematical models of transmission and disease development for later use in analysing patterns of infection both within and between herds.

Field-based study

4.7 The laboratory-based pathogenesis study will be complemented by a field study carried out by VLA in collaboration with IAH and the SVS focused on non-reactor cattle removed from TB breakdown herds. The immune status of these animals will be determined and observed for a 60-day period during which any disease development and bacterial excretion will be monitored. It is accepted that not all of the selected in-contact animals will be infected and, therefore, informative. However, essential information on the pattern of disease in a herd, the identification of markers of early disease and pathology in cattle and the diagnosis of disease is likely to be forthcoming.

4.8 A detailed post mortem examination and the further refinement of post mortem techniques on tuberculin positive cattle will form part of this field study in order to provide more information on the pathology of diseased cattle.

4.9 The ISG places great importance on obtaining the fullest understanding of the pathogenesis of TB in cattle and is recommending that this research is extended as a matter of priority in two further areas.

Low dose pathogenesis studies

4.10 We recommended that ongoing studies using intermediate infectious doses of the TB bacterium should be extended to low dose infections, to determine the status (infectivity, immunity) of animals infected with doses that do not result in pathology. The experimental protocols will be similar to those used for the higher dose study, but it will be necessary to maintain these animals under observation for longer periods (at least 12 months, rather than 3 months with the higher dose) to observe intermittent and transient effects and to repeat the infectious challenge. The experimental design recognises that not all animals exposed to low dose infection will become infected, although they may respond immunologically, and consequently experimental groups will of necessity be larger than for the higher dose experiments. All these experimental studies have to be conducted within the protocols of high disease security and this brings particular problems. The need to conduct this extensive research within the timeframe of the field trial, if its findings are to inform our policy advice, highlights the requirement for more disease containment (Category III) facilities in the United Kingdom. We estimate a need for accommodation for up to 80 animals and we would hope that this could become available by the end of 2001 or early 2002.

Tuberculin-positive (reactor) animals

4.11 We also advise that collateral studies on animals from breakdown farms should be extended to holding tuberculin-positive (reactor) animals for long periods (at least 12 months) to gain insight into the changing and intermittent nature of the disease in naturally infected animals.

5. Other Research

5.1 The Ministry supports an extensive programme of research to complement the other measures discussed earlier in this report; ISG keeps this programme under constant review. A full list of currently-funded projects is given at Appendix A.

Vaccine Research

5.2 The use of vaccines in either cattle or badgers remains a potential policy option, although the ISG regard this option as offering prospects only in a long-term context and also caution that success cannot be guaranteed. The demands of an acceptable cattle vaccine are particularly severe since it would need both to prevent the establishment of persistent infection and to eliminate transmission. Additionally it should not give a positive reading in the tuberculin skin test since this would confuse the regular herd testing procedures and create serious regulatory problems. However, an additional concern about the use of cattle vaccination in Great Britain relates to the strong likelihood that a wildlife reservoir of TB infection will persist in the countryside environment and cattle protected by a successful vaccine might then respond immunologically when exposed to natural infection from this wildlife source, thus confusing the skin test.

5.3 Any diagnostic test based upon detecting an immune response would need to distinguish immune responses generated following infection from those elicited following challenge of a protected vaccinated animal. This would be extremely difficult to achieve. In addition to being highly sensitive such a test would have to have a high level of specificity for it to be acceptable, since false positive reactions would trigger a herd breakdown control response.

5.4 Nonetheless, we support continuation of the vaccine research and its co-ordination with human TB research, since new technologies are continually developing which may be applicable to cattle vaccine development. The vaccine research programme should also provide additional information on the immunology and pathogenesis of cattle TB. However, the ISG recognises the need to periodically assess the balance, scope and duration of the vaccine programme to ensure that the limited scientific and physical resource available for laboratory-based cattle TB studies are used effectively to meet both short term and long term objectives.

5.5 By contrast with the cattle situation, vaccination of wildlife would require a less demanding vaccine since, although widespread coverage would be the target, protection of each individual animal would not be essential. The primary role of a wildlife vaccine would be to reduce the severity of

disease in the target species and the consequent rate of transmission to cattle. A wildlife vaccine, however, would only be effective if most cattle TB infections derived from wildlife - a point that, at present, is in doubt.

5.6 Furthermore, even if a wildlife vaccine were available the logistics of vaccinating a badger population in the wild presents enormous challenges. The effectiveness of the strategy is likely to be greatly influenced by the route of vaccination; oral vaccination is likely to be the preferred route for use in the badger but by this route it may be difficult to achieve a protective immune response.

5.7 If the strategy of badger vaccination is to be seriously pursued, experimental facilities to conduct vaccination challenge studies will need to be made available. This will necessitate sourcing TB-free badgers and possibly rearing offspring that can be used for experimental studies in disease secure high containment facilities. A more demanding requirement will be to validate the potential vaccine in the field and to determine how its success would be measured particularly as we currently have no reliable live test for TB infection in badgers. A further consideration is the possibility of transmission of a live wildlife vaccine to other wildlife - and also to cattle - and the impact that might have on tuberculin testing in cattle

5.8 While there is strong pressure from some groups for successful vaccination of badgers to be considered as the preferred strategy there are many difficult issues that must be addressed if this policy is to be pursued. The ISG is now undertaking a detailed study of vaccine development and their potential use, to inform Ministers of the varied and additional research requirements to support this policy.

Molecular Epidemiology

5.9 In our second report we identified the potential value of molecular typing to the epidemiology studies but cautioned that the molecular typing methodologies were not yet sufficiently discriminatory to answer detailed questions. Encouragingly, typing methodologies that are more discriminatory are being developed by MAFF scientists and others, and are being used on *M.bovis* isolated from cattle and wildlife in trial areas. The ISG recognises the importance of this work and is taking steps to involve other research workers including those with expertise in population genetics and molecular and other disciplines in the analysis and interpretation of data.

Research Complementing the Field Trial

5.10 Investigations are being carried out by CSL and the University of Oxford into the risk of cattle contracting TB from wildlife species other than the badger in areas of high herd breakdown risk. There is well-established evidence that certain wildlife species (the possum in New Zealand, the water buffalo in Australia, and the badger in Great Britain and Ireland) can be reservoirs of TB infection. However, it is not clear if other wildlife species in which the organism has also been found are spill-over hosts or whether the disease is self sustaining in the species, or if they are a source of infection for cattle.

5.11 We advised that research is needed on the ecological consequences of badger removal. CSL has started an investigation in field trial areas studying the effect of badger removal on other species, including the effect on populations of foxes, rabbits, hedgehogs and ground nesting birds.

5.12 *If badger population control were to form part of cattle TB control policy in the future, it would be essential to develop accurate methods of assessing badger numbers, which do not involve capture of the animals. Two separate projects conducted by CSL and the University of Bristol are developing these methods. Social perturbation that arises following badger removal might affect the distribution of TB-infected badgers and the incidence of TB in cattle. The trial itself allows us to test theories concerning perturbation and this is complemented by a perturbation study by scientists at the University of Oxford.*

5.13 *CSL, in collaboration with Sheffield University, is undertaking an analysis of badger social structure using molecular genetic techniques by analysing DNA from all individual animals caught in the trial to determine genetic relatedness. All badger samples from reactive and proactive areas will*

be genotyped and fine-scale structure will be examined. Gene flow within the badger population will be followed within culling areas.

Economic evaluation of policy options

5.14 In our second report we recommended support for research into the economic dimensions of cattle TB and its control in order to assist the full evaluation of potential policy options. Research has now been commissioned by MAFF into the farm-level effects of bovine TB and its control and the wider economic impacts of TB in the agricultural sector. In addition, we have advised MAFF to explore the prospects of research in a third area which relates to the valuation of wildlife. Because of the apparent role of wildlife as a disease vector in cattle TB, it is possible that wildlife control could become part of disease control policy. An element of 'cost' associated with such a policy is the value of the wildlife that would be lost as a result. However, it is difficult to place an economic value on particular species of wildlife because they are not bought and sold by groups or individuals. They are genuine economic commodities (because people attach value to them and are prepared to incur financial or other costs to preserve/protect/gain more of them) and so must be included in any comprehensive economic evaluation; but they are not commercial commodities, and so the everyday market system does not produce data that reflects their valuation relative to everything else. It is desirable to have an indication of an economic weighting that can be attached (as a cost) to the badgers that would be removed, or (as a benefit) to those that are not removed, as a consequence of particular disease control options that may be assessed. Without this the economic characterisation of any policy will be incomplete and inconsistent, giving no indication of how "ecological" values and "monetary" values could be considered together.

Road Traffic Accident (RTA) Survey

5.15 Last year we supported the re-introduction of a road traffic accident survey of badger carcasses, as recommended by Krebs, as an important means of collecting data on the prevalence of TB in badgers within and outside of trial areas. We recorded our disappointment that this important element of the programme had not been implemented by MAFF.

5.16 We reported to the Agriculture Select Committee in November our regret that this exercise had been further delayed due to the redirection of State Veterinary Service resources in the autumn to deal with the outbreak of Classical Swine Fever in East Anglia. Since the conclusion of that outbreak, the SVS had made some progress towards re-establishing the RTA Survey on the scale that we had originally envisaged, but was obliged to further postpone the survey due to the operational demands of the foot and mouth outbreak.

Other research

5.17 A number of other research initiatives have been put in place including work on the survival of *M.bovis* in silage, the possibility that the European tick (*Ixodes ricinus*) is capable of transmitting TB and studies on badger visitation to farm buildings. The Group has emphasised the importance of maximising the research opportunities provided by the field trial, subject to constraints on MAFF resources and to data confidentiality considerations. We have in the past recommended for funding a number of research projects which benefit directly from the work on the trial itself. In addition, measures have been put in place to bank serum and genetic material from the badgers culled, to encourage further studies in the future from interested scientists as resources and new technologies become available.

5.18 The ISG has been consulted by MAFF on a number of specific requests to use trial data or biological material from the trial. In most cases, subject to the need to protect the narrow band of trial and other data defined in our second report, we have been pleased to give our support to such requests. Each request for data has been examined by MAFF and the ISG on a case-by-case basis.

6. Preliminary Analysis of Risk Factors Associated with TB in Cattle

6.1 The ISG has overseen the collection of epidemiological data from all farms in Great Britain with a TB breakdown. The data collected will support investigations into the wide range of factors potentially associated with increased risk of TB in cattle, including herd size and composition as well as environmental and husbandry factors. A strength of this approach is the relatively large number of factors that can be investigated, compared to on-farm experiments where only a limited number of comparisons can be made and experimental control would be extremely difficult or impossible to achieve.

6.2 Such data from affected farms (known as cases) are most powerful when compared with data collected from similar farms without TB (known as controls), as these comparisons can provide strong evidence of associations. Control farms are being selected and studied for comparison with case farms within the field trial.

TB99 Questionnaire

6.3 One of the key research undertakings of the ISG has been the extensive revision of the survey form used to collect information on all farms with a TB breakdown. The key principles guiding the ISG were:

- The need for objectivity
- The need to be comprehensive
- The need to provide data amenable to statistical analysis
- The need for practicability.

6.4 Unlike the original form (TB49), the new form has been designed to collect epidemiological data on risk factors as well as to assist the SVS management of the incident. At the end of 1998, the revamped survey form was piloted. MAFF consulted publicly on the piloted questionnaire. The questionnaire, known as TB99, was further refined in light of comments received in the consultation process. To promote the objective collection of data, MAFF implemented a national training programme for staff administering the questionnaire.

6.5 On each farm, TB99 collects data on a wide range of potential risk factors relating to the 12-month period prior to the herd breakdown. The 12-month period was chosen to cover the time period most relevant to disease transmission, to cover a single annual farming cycle and to avoid collecting unnecessary (and possibly incorrectly recalled) data from previous years.

Data collected include:

- Farm location and environment
- Cattle herd composition and health
- Cattle movements
- Herd testing history
- Type of farm enterprise
- Husbandry factors
- Water sources
- Housing/bedding arrangements
- Supplementary feeding practices
- Presence of domestic, farmed and wildlife species
- Steps taken to avoid contact between cattle and wildlife.

In designing the questionnaire, a practicable balance had to be struck between including the widest possible range of potential factors influencing TB incidence in cattle and the need to be concise and easy to use.

6.6 Following a brief second pilot phase, TB99 was launched in April 1999 and data collection backdated to January 1999. The questionnaires are completed by trained SVS staff through personal interviews with the farmers concerned. TB99 data are collected on all farms in Great Britain on

which a confirmed TB breakdown has occurred since the beginning of 1999. In areas enrolled in the field trial, every breakdown incident, regardless of confirmation, is the subject of a TB99 questionnaire. Since its launch, more than 1500 TB99 questionnaires have been completed and the ISG wishes to express its appreciation to those farmers who co-operated in carrying out this important part of the epidemiological study.

6.7 Amongst farms in the badger culling field trial, the main epidemiological analysis of the TB99 data will be the comparison of TB99 data from farms with TB breakdowns (cases), with similarly collected data from three comparable herds (including, if possible, one contiguous herd) without TB breakdowns (controls). Systematic differences between the cases and controls may indicate factors that enhance the risks of TB breakdowns, suggesting possible strategies for intervention in future.

6.8 At present, insufficient data are available on control farms from trial areas to support such an analysis. However, a large body of data on the farms outside of the trial areas which have experienced recent TB breakdowns throughout Great Britain are available, and this forms the basis for a range of descriptive analyses. More importantly, some preliminary comparative analyses can also be conducted which are illustrative of the value of the TB99 risk analysis indicating the types of question that will be addressed.

6.9 From this non-trial data, farms with multiple reactors can be compared with farms with single reactors to investigate predictive factors. These analyses are, in a sense, using the multiple reactor herds as cases and the single reactor herds as unmatched controls. This chapter describes preliminary analysis of the TB99 data. When data are analysed for individual counties, only the six counties in which more than 100 TB99 questionnaires (outside of trial areas) were available for analysis (Cornwall, Devon, Dyfed, Gloucestershire, Herefordshire and Worcestershire, and Wiltshire) are analysed.

Herd size, cattle ages and location

6.10 *Demographic aspects of farms, such as the size of the cattle herd, the ages of the cattle, or simply the location of the farm, may be associated with greater or lesser risks of TB infection. In this section, preliminary analyses of these factors are presented. An examination of the distribution of herd sizes, compared to holdings in Great Britain as a whole, illustrates the epidemiological principle that larger populations (herds) are more likely to have at least one individual (cow) with disease. Table 6.1 presents the comparison for herds on annual testing intervals, but similar results were seen for herds on 2-, 3- and 4-year testing intervals.*

Table 6.1 Distribution of herd size by total number of cattle for annually tested herds affected by TB, annual tested herds in Great Britain and the expected distribution if each animal poses an identical risk.

	1 to 9	10 to 29	30 to 39	40 to 49	50 to 69	70 to 99	100 to 199	200 and over
Herds affected by TB	2%	8%	3%	4%	8%	10%	32%	33%
Herds in Great Britain	27%	16%	5%	5%	7%	9%	18%	13%
Expected if each animal poses an identical risk	2%	4%	2%	2%	5%	9%	30%	45%

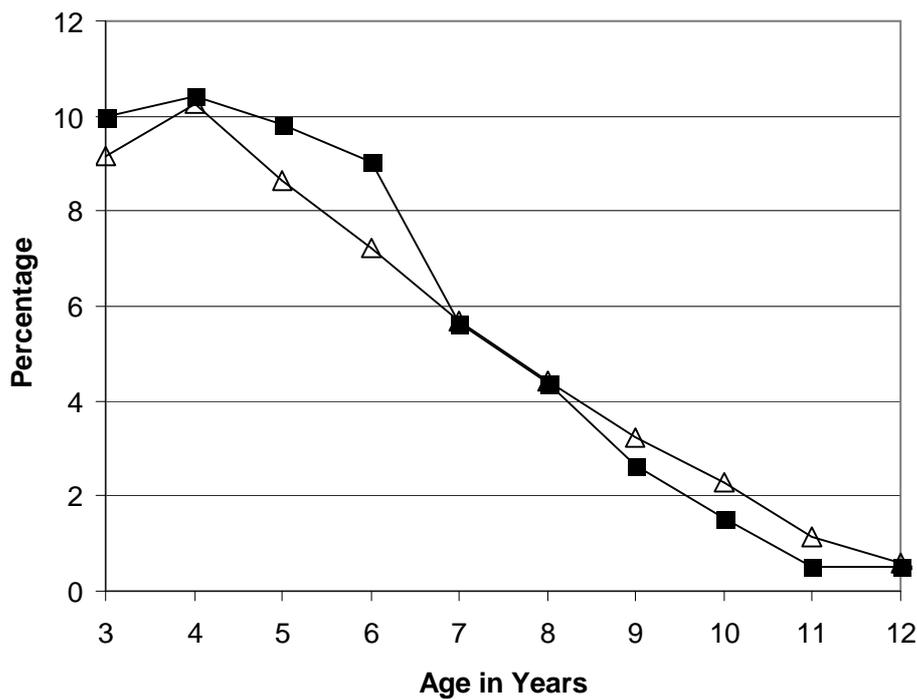
6.11 Ignoring the possibility of within-herd cattle-to-cattle transmission, if each cow had a P% chance of having a disease the probability that a herd of size n were to have no cases of disease would be: $(1-P/100)^n$.

Thus, as n increases, the probability of at least one case of disease increases, and herds of different sizes are at different risks of disease. To determine the distribution of herd sizes that would be expected were each animal at risk, P is estimated such that the sum of expected breakdown herds approximately equals the number of breakdowns for which we have herd size data. Table 6.1 presents the expected distribution of herd sizes obtained using this model that assumes each animal has an identical risk of infection (regardless of herd size). The observed distribution of herd sizes in the herds affected by TB is considerably closer to that expected assuming animals pose identical risks than to the distribution in all tested herds in GB, results are presented in Table 6.1 for annually tested herds but similar results were obtained for herds on longer testing intervals.

6.12 To examine whether age might affect the probability that an animal would test positive for *M. bovis* infection, we examined the age distribution of reactors (Figure 6.1). Since some categories of young cattle are not TB skin tested (for example, in beef fattening herds), the age distribution cannot be directly compared with that of the national herd. Although it can be seen from Figure 6.1 that there are more 5- and 6-year-old reactors and fewer 9- to 11-year-old reactors than expected, the age distribution of older reactors, those three years of age and older, is quite similar to the age distribution predicted for British cattle [6].

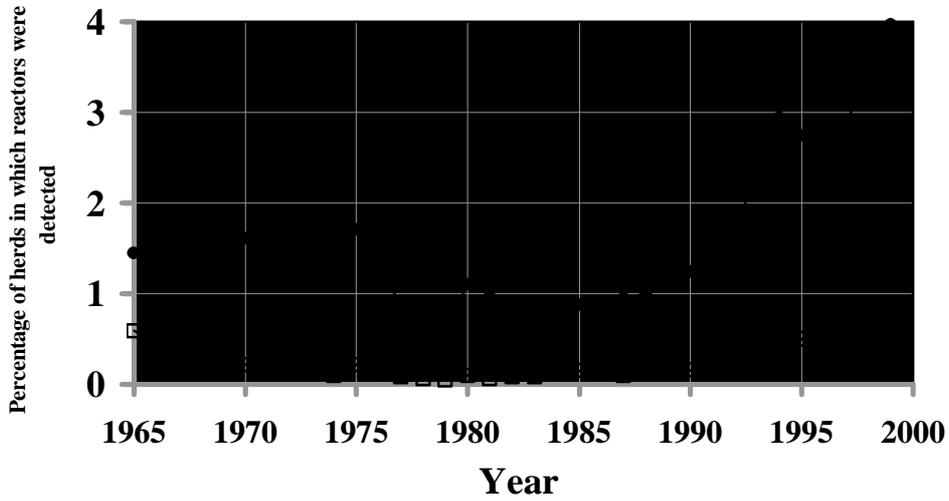
6.13 Taken together these two results indicate that individual cattle appear to be at equal risk of being a reactor regardless of herd size or age.

Figure 6.1 Age distribution of TB reactors as recorded on TB99 questionnaires (square) compared to that predicted by a survival model for British cattle (triangle).



6.14 One of the sources of variation that simple herd- or animal-based models fail to incorporate is regional variation in TB incidence. That is, cattle living in different regions of Great Britain experience very different risks of TB infection. Since 1980, the annual incidence of TB breakdowns has been steadily increasing throughout England and Wales, with a sharper rise in South West England where incidence has historically been greatest (Figure 6.2). Two additional areas showing greater than average incidence, in the past decade, are West Staffordshire and a large area in Gloucestershire [2]. Figure 6.3 shows the spatial distribution of TB breakdowns in 1999.

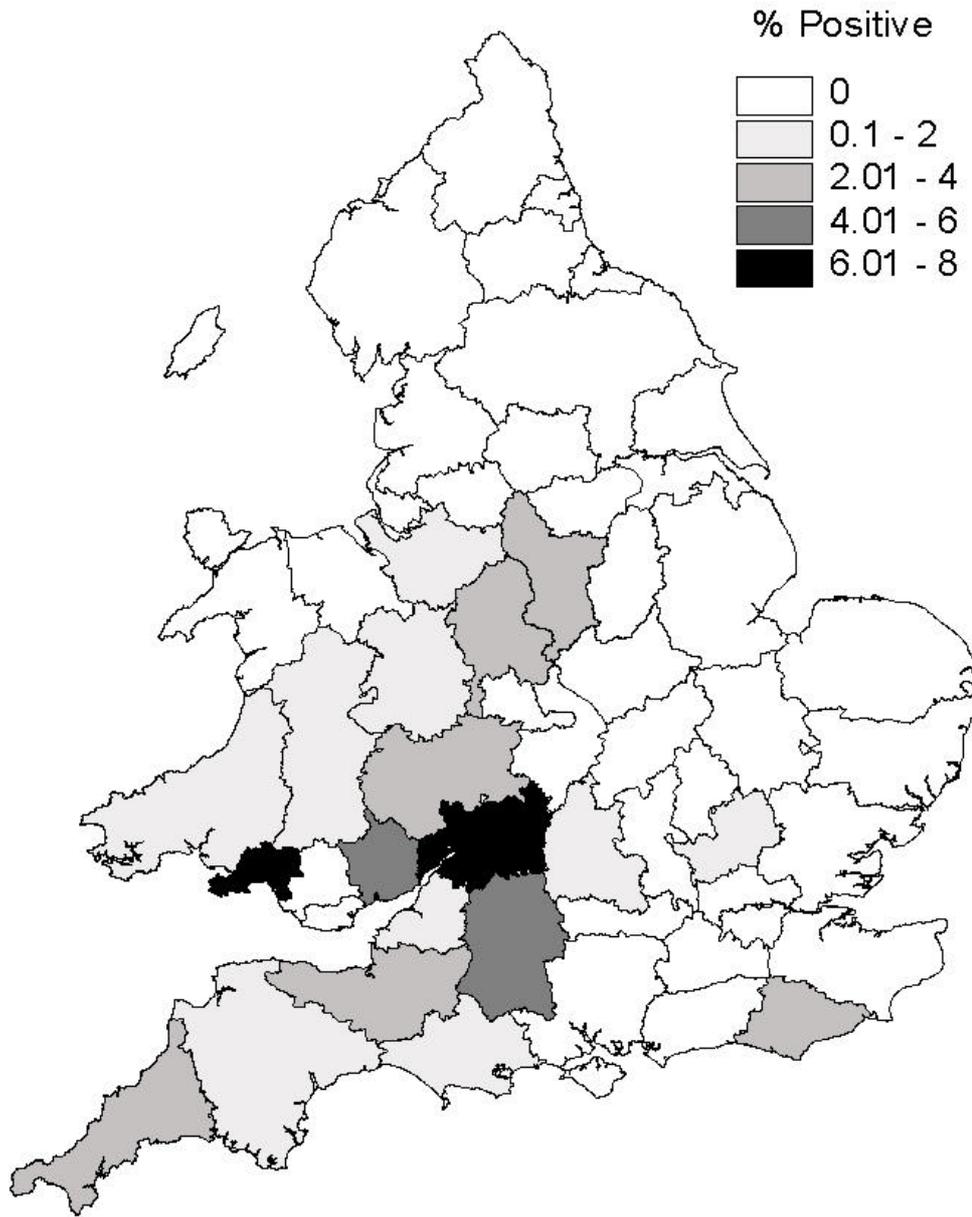
Figure 6.2 Annual Occurrence of Reactor Herds in England and Wales, 1965 – 2000.



—●— 1) In the South western Region

—□— 2) Elsewhere in England and Wales

Figure 6.3 County-specific occurrence of confirmed TB incidents in 1999.



Environment

6.15 In addition to herd and animal characteristics, data were collected on the farm environment. The specific questions ranged from soil type and land cover to whether or not the farm was run organically. In this preliminary analysis of potential risk factors multiple reactor farms are compared with single reactor farms.

6.16 For each farm, the type of soil on the cattle premises (loam, clay, sand, Cotswold Brash, peat, chalk, and other) was recorded with approximate percentages. The soil on cattle premises on the average farm was:

- I. 45% loam,
- II. 29% clay,
- III. 6% sand,
- IV. 4% Cotswold Brash,
- V. 3% peat,
- VI. 1% chalk and
- VII. 12% other.

The current data give no indication that type of soil affects the probability that a breakdown farm will have multiple reactors.

6.17 For the average farm, the land cover on the cattle premises summarised from a 17-class system is:

- 83% pasture / meadow / amenity grass,
- 6% rough pasture / dune grass / grass moor,
- 6% tilled (arable crops),
- 1% marsh/rough grass,
- 1% deciduous/mixed wood and
- 3% other.

The current data give no indication that land cover affects the probability that a breakdown farm will have multiple reactors.

6.18 A number of questions can be addressed from the data, for example, it can be seen that the proportion of farms with cattle grazing areas subject to flooding was very similar in multiple reactor farms (25%) to that in single reactor farms (23%). The proportion of farms run organically was also similar in multiple reactor farms (5%) to that in single reactor farms (7%). However, with currently only 76 of the farms with TB breakdowns reported to be run organically, there was very little power with which to detect such an association.

Other Animals on the Farm: Domestic, Farmed and Wildlife

6.19 Data were collected on other animals on the farm, both domestic, farmed and wildlife species on the holding. In the case of wildlife, farmers were asked about both sightings and signs of wildlife on the premises. In this preliminary analysis multiple reactor farms are compared with single reactor farms to determine whether farms with multiple reactors were more or less likely to have specific species on the farm. Table 6.2 presents the proportion of farms reporting the presence of domestic and farmed animals. Each of the species in Table 6.2 was listed individually on the questionnaire.

Table 6.2 The percentage of farms with TB breakdowns reporting the presence of domestic and farmed animal species.

Domestic and farmed species	Percentage of TB breakdown farms reporting presence of domestic and farmed species
Buffalo	<1%
Cat	60%
Chicken	24%
Deer	
Red	<1%
Roe	1%
Other	<1%
Dog	73%
Ducks	7%
Game	1%
Geese	6%
Goat	3%
Horse	28%
Llamas	<1%
Pigs	7%
Poultry (other)	3%
Sheep	53%
Turkeys	2%
Any domestic and farmed animals	80%

6.20 The presence of each domestic and farmed animal species was analyzed for its association with multiple reactor breakdowns for each herd size category (<50, 50-99, 100-199, 200 and above). This revealed no consistent indication that the presence of any domestic or farmed animal was associated with the risk of multiple reactor breakdowns.

6.21 Table 6.3 presents the proportion of farms reporting the presence of wildlife species. Each of the species in Table 6.3 was listed individually on the questionnaire. Although there was also a question regarding 'other' wildlife species in which farmers were asked to specify the species, these species are not reported here, as the data may not be comprehensive enough to be of use. For example, although only 1% of farms reported the presence of mice, it seems likely that mice are more widespread but not seen as important enough to report.

Table 6.3 The percentage of farms with TB breakdowns reporting sightings and signs of wildlife species on the premises used by the reactor cattle over the 12 months prior to the TB incident, as well as the *M. bovis* infection prevalence of each species based on animals sampled by MAFF [2]. The tested badgers are those submitted by the public to MAFF between 1972 and 1994. The sample size, n, is given for each prevalence estimate.

Wildlife species	Percentage of TB breakdown farms reporting presence of wildlife	<i>M. bovis</i> infection prevalence (n)
Badgers	80%	4% (n=21,731)
Birds	67%	-
Deer		1% (n=1817)
Fallow	12%	
Muntjac	9%	
Red	1%	
Roe	2%	
Sika	1%	
Feral cats	20%	0% (n=25)
Ferrets/Polecats	6%	4% (n=26)
Foxes	83%	1% (n=954)
Geese	7%	-
Hares	42%	0% (n=14)
Hedgehogs	41%	0% (n=23)
Mink	14%	1% (n=172)
Moles	72%	1% (n=166)
Rabbits	80%	0% (n=144)
Rats	76%	1% (n=412)
Stoats / Weasels	35%	0% (n=66)
Wild boar	<1%	-
Any	88%	

6.22 The presence of specific wildlife species was analysed for its association with multiple reactor breakdowns by county. This revealed no consistent indication that the presence of any wildlife species was associated with the risk of multiple reactor breakdowns.

Human TB Infection

6.23 Data were collected on possible risk factors for a human source of TB infection on the farm. 63% of the farms had footpaths and/or bridleways on the farm, 14% had adjacent road lay-bys, 13% had sewage outfalls, 5% had human sewage sludge, 3% had campsites and 3% had a medical history of TB infection in the farmer, farm employees and/or their families. Overall, 70% of farms had risk factors for a human source of TB infection, but we cannot make any statement at this stage on whether they are significant in terms of a causal association.

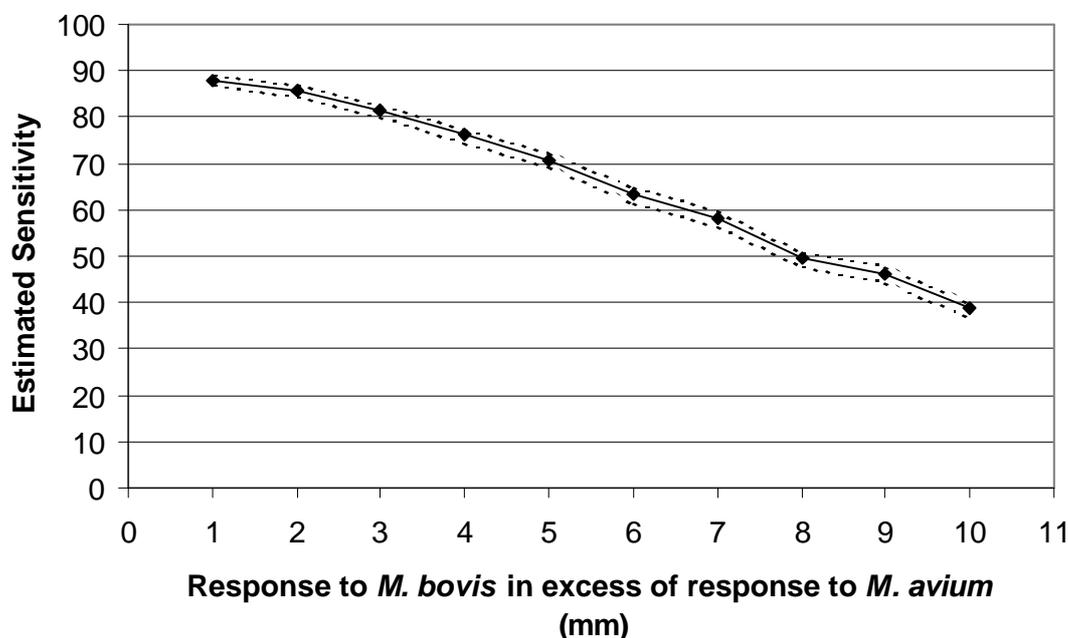
Tuberculin skin test

6.24 In addition to information on potential risk factors, the TB99 dataset also provides valuable information on the performance of the tuberculin skin test. Diagnosis of TB is based on the detection of a specific immune response to *M. bovis*. Due to cross-reaction, the cattle are skin tested using purified protein derivative (PPD) from both *M. bovis* and *M. avium*. The standard level of interpretation is to classify reactors as those with a greater reaction to *M. bovis* PPD than to *M. avium* PPD of 5mm or more. The severe level of interpretation classifies cattle as reactors if they have a greater reaction to *M. bovis* PPD of 3mm or more. The TB99 dataset includes data on both tests for

reactors as well as slaughtered direct contact animals. Thus, it is possible to investigate the ability of the skin test to predict the presence of visible lesions and a positive *M. bovis* culture result.

6.25 The culture and post-mortem lesion results were recorded for each animal. Data on the 3555 animals with either fully negative or *M. bovis* positive culture results and complete data on the presence of visible lesions were analysed to estimate the sensitivity of the skin test as a function of the excess in the response to *M. bovis* PPD compared with the response to *M. avium* PPD. As expected, with an increased skin test threshold for the excess *M. bovis* response, sensitivity decreases (Figure 6.4). The estimates were virtually identical when the skin test is used to predict the presence of visible lesions and to predict either indication of infection (*M. bovis* culture or visible lesions). Due to the high likelihood of exposure of the negative animals in these data to positive animals within the same herd, the data were not used to estimate specificity.

Figure 6.4 The sensitivity (with 95% confidence interval) of the *M. bovis* skin test to predict a positive result (*M. bovis* culture and/or visible lesions), as a function of the excess in the response to *M. bovis* PPD compared with the response to *M. avium* PPD.



6.26 For the 5mm standard interpretation of the skin test, the estimated sensitivity (71%; 95% confidence interval: 69-72%) is somewhat lower than those reported previously [5]. Sensitivity estimates depend on the value of the ‘gold standard’ (here culture or identification of visible lesions) to identify all infections correctly. Also the use of different or complimentary tests, the IFN test for example, might identify additional, or perhaps just different, infected animals causing the resulting estimates of sensitivity to differ. Clearly, the methods used to evaluate skin test performance should be made known to facilitate comparisons between studies.

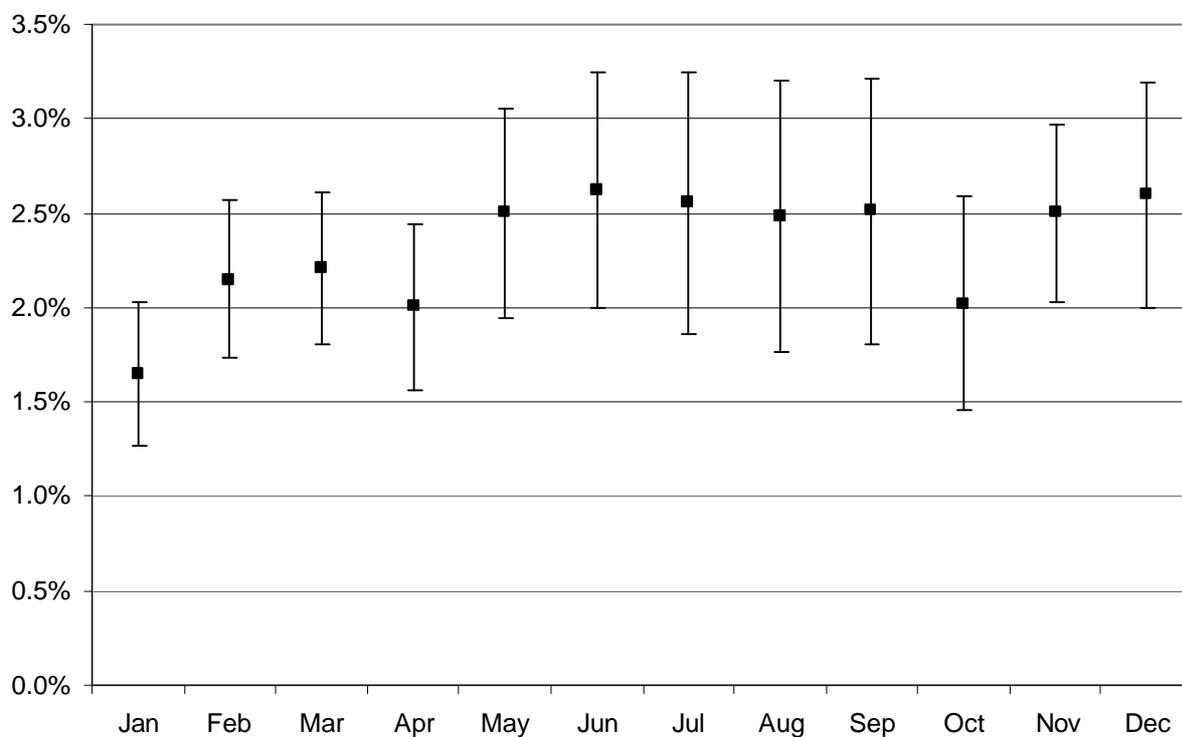
6.27 The frequency with which herds are routinely tested depends on past TB incidence in the surrounding region. Herds in the majority of the country are tested every four years, but in parts of South West England, South Wales and the Midlands it will be more frequently (every 3 years, 2 years or annually), (Figure 2.1) though cattle herds experiencing a TB breakdown will typically be tested every 60 days. Since routine testing frequency is determined by past TB incidence and areas often experience similar levels of TB incidence over several years, shorter testing intervals will be

associated with increased TB incidence even though the testing interval was not causally related to the incidence of TB breakdowns. The key point is that annual testing of all herds will give a true measure of annual incidence whereas testing at 2, 3 or 4 year intervals will not, because some of the infections detected could have been initiated in previous years.

6.28 It is possible that once one cow has been infected with TB, a longer testing interval would allow more time for cattle-to-cattle transmission within the herd. However, there was no association between a herd having multiple reactors and the testing interval.

6.29 Finally, although the raw data for 1999 indicate that more TB breakdowns are confirmed in November, February and March, adjustment for monthly variation in the number of routine tests performed reveals that tests performed between January and April are less likely to be confirmed positive (Figure 6.5). Unfortunately, since tests are performed every 1, 2, 3 or 4 years, seasonal variation in TB infection incidence cannot be estimated.

Figure 6.5 Percentage of routine TB herd tests resulting in confirmed TB incidents as a function of the month of the test in 1999.



Potential Value of the TB99 Data and Future Research

6.30 These initial investigations, on the data provided by the TB-affected farms outside the field trial, revealed that animals of different ages and in different sized herds experience similar levels of TB infection risk, but that the risks do vary regionally. The risk factors considered here, preliminarily provided no consistent evidence of the presence of particular species (whether domestic or wildlife) being associated with an increased risk of multiple reactors.

6.31 Once data are available on a sufficient number of the matched control farms, further more powerful analyses of the wide range of risk factors (including environmental and wildlife factors, as well as husbandry and biosecurity factors) will investigate whether particular factors are associated with increased risks of TB generally, as well as increased risks of the breakdown involving multiple reactors.

6.32 In addition to these risk factor studies, analyses of the sensitivity of the tuberculin skin test will be broadened to examine whether the age or other characteristics of the infected cattle affect test sensitivity. Furthermore, alternative interpretation strategies (including consideration of the absolute level of response, as well as the relative *bovis/avium* responses) will be investigated.

7. Future Policy Options for TB control

Introduction

7.1 In our view, future policy options available to the Government for the control of cattle TB are likely to be multi-factorial and be dependent upon answers to major scientific questions highlighted in the Group's second report. These relate to the need for a better understanding of the epidemiology and pathogenesis of TB in cattle and wildlife, particularly badgers. In addition to these central questions relating to the disease itself, and to the technical effectiveness of control measures, we anticipate that Ministers will need to take into account issues such as the economic importance of the disease, the cost-effectiveness of potential control strategies, and the ecological and environmental impact of individual options.

7.2 It is important that future potential policy options for TB control are appropriately underpinned by the research programme; the research being carried out must be sufficiently informative to support rigorous predictions and comparative assessments. We need to consider whether additional work needs to be done, and whether the balance of the programme, with respect to need and available resource, is appropriate. In what follows, we identify a number of potential elements of a future TB control policy. Others may emerge as a result of discussions in the TB Forum or as data become available from the research programme. We will keep these options under review, and refine them where appropriate, as an integral part of our future work programme.

7.3 In identifying potential future control options the ISG recognises that a reservoir of TB infection exists in badgers. However, we are not aware of its scale or significance to cattle, nor whether and to what extent selective control of the badger population has a role to play in the control of cattle TB. The field trial is designed to answer these and other related questions.

7.4 Given the increased incidence of cattle herds affected with TB, and the incomplete sensitivity of the tuberculin test, it is likely that increasing numbers of infected cattle are remaining undetected. Whether these particular animals contribute to transmission of infection we do not know. However, current and past control policies, which have included a substantial component of badger culling in many locations, have failed to control the cattle disease. This is the dilemma that has led to the current programme of epidemiological research including the field trial. It is crucial to understand how infection in cattle and badgers are linked, and the extent to which the culling of infected cattle, with or without the culling of badgers, can progressively lower the level of infection in cattle.

7.5 Bovine TB is a low incidence infectious disease with, based on the evidence, a low transmission rate. Nonetheless, the implicit assumption underlying the long established controls is that cattle-to-cattle transmission is of critical importance, which is why movement restrictions are imposed immediately when reactors are found in a herd. This approach, coupled with the removal of reactors, has been successful in reducing the incidence of TB in most parts of Great Britain over past decades and keeping incidence at a low level. However, the persistence of TB in cattle in some regions has been interpreted as evidence that there must be a continuing source of infection from wildlife, rather than due to inadequacies of the cattle testing system and movement control, or both. We have questioned this view as part of our overall consideration of the persistent TB problem. This has led us to consider the possibility that irrespective of its original source, infection persists in cattle herds despite regular tuberculin testing, thereby providing opportunities for amplification within herds and for cattle-to-cattle spread.

7.6 The policy options that we have considered in our overall review range from, at one extreme, proactive culling of badgers in defined areas coupled with improved diagnosis and cattle health management, to, at the other extreme, a policy based only on the element of better diagnosis and health management in cattle.

CATTLE OPTIONS FOR CONTROLLING TB

i. Elimination of TB-infected or exposed cattle

TB testing- Diagnosis

7.7 We have identified as a priority for any improved control policy the development of better tools for the diagnosis of the disease in cattle to improve on or supplement the tuberculin skin test that is laid down as the statutory test in EU legislation. MAFF are committed to an evaluation of the gamma IFN test as an adjunct to the statutory test. The Group continue to review the potential merit for wider use of this supplementary test in the light of emerging research findings from work commissioned in the MAFF-funded programme and elsewhere.

Herd slaughter

7.8 At present, animals testing positive for TB according to the tuberculin skin test are removed from the herd as reactors as a first step in the disease control programme. Additional culling, amounting to partial or complete herd removal, is carried out at the discretion of the MAFF Divisional Veterinary Manager. The Ministry is in the process of developing central guidance for the use of the SVS, to identify on a consistent basis the circumstances where whole or partial herd removal is justified. The Group will examine data on the effects of this approach where it has been applied and will keep this option, and its practical effects, under review.

Removal of TB excretor animals

7.9 The present TB control strategy is based upon the identification and elimination from the herd of animals that are immune responsive to *M.bovis*. A complete change of strategy could be based on the detection and elimination of animals shedding the TB bacillus. Cattle herd health and human health would be protected by the elimination of these bacterial excretors. However, while this approach may present itself as a considered option in the future, current techniques for the detection of tubercle bacilli in the live, non clinically affected animal are too insensitive to be of value. The question of frequency of testing would also need to be resolved.

ii. Herd health management

7.10 MAFF offers advice to farmers on animal husbandry, disease management and biosecurity measures which could be employed in order to reduce the risk of transmission of the disease. The independent Husbandry Panel recommended a number of potential improvements in husbandry practice.

7.11 Data from the TB99 epidemiological study should provide useful insights into the risk factors associated with husbandry practice and biosecurity. In addition, the programme of research into cattle pathogenesis should yield data that will advance our appreciation of the role that cattle-to-cattle transmission plays in the spread of TB and inform future strategies for disease control and herd health management.

7.12 Within the context of the TB Forum, the British Cattle Veterinary Association has produced proposals for the assessment of risk of exposure to TB and the development of strategies for reduction of that risk through improvements in animal husbandry practice. The Group is assessing these proposals with a view to identifying those elements that could be tested alongside the field trial and the current research programme.

iii. New cattle movement controls

Movement restrictions and pre-movement testing

7.13 MAFF is proposing to introduce movement restrictions on herds where an official tuberculin test has not been carried out by the due date. It is also proposed that the movement of an animal in the period between the first and second stages of an official tuberculin test will be prohibited. There is currently no statutory requirement for cattle to be tested for TB prior to sale and transport in addition to the normal scheduled official test. It is currently possible for purchasers to insist on a pre-sale or

pre-movement TB test, but in practice this is not done to any significant extent. It would be possible to strengthen current TB controls to require any cattle sold to have evidence of a sufficiently recent TB test and possibly to complement the tuberculin skin test.

7.14 A possible mechanism for the transmission of the disease from cattle to cattle would be eliminated if the licence system was changed to require animals destined for slaughter to be routed directly to abattoirs, rather than through markets where if infected they could infect cattle destined for transport to farms.

7.15 A further option would be to limit or prohibit the movement of cattle from areas with a relatively high TB incidence in cattle to other parts of the country. This would have the intention of limiting the potential for inter-regional cattle-to-cattle transmission of the disease.

7.16 The validity of these options will be assessed against the results from the laboratory- and field-based research on cattle pathogenesis and diagnosis.

iv. Cattle vaccination

7.17 The ISG has supported the Ministry's vaccine development programme but cautions that the successful development of a TB vaccine for cattle is a speculative policy option which may not provide the total solution to the problem posed by TB. If a successful wildlife vaccine was developed (and/or the wildlife source of the disease was eliminated) and if wildlife made a significant contribution to cattle TB, a cattle vaccine would be unnecessary.

7.18 The ISG advises that the use of cattle or wildlife vaccines should be kept under active consideration as a long term future policy option, but its judgement is that such a strategy is unlikely to offer a viable vaccine within the timescale for reassessment of policy in the light of the field trial and the TB research programme.

v. Breeding; disease resistance

7.19 It has been suggested [7] that selective breeding for resistance to TB infection could be an option that could provide a means of achieving a reduction in the general level of the disease. This approach would be extremely long-term, expensive and of uncertain outcome. Given that current TB control policy is based on detection and removal of all infected animals irrespective of the severity of disease, genetic resistance would only be exploitable if it prevented the establishment of persistent infection. While there is anecdotal evidence that some family lines of cattle are more likely to succumb to the disease, this, even if substantiated, might be due to factors other than genetic susceptibility. There are to our knowledge no identifiable populations of TB-resistant cattle which would allow experimental studies of the scientific basis of resistance to *M. bovis* infection. Initial studies would, therefore, be needed to determine if there is evidence of resistance in the field. This could possibly be done by analysis of pedigree information on affected dairy herds but because of the low prevalence of infection in the cattle population the sensitivity of this approach will be low. We understand that scientists in the Republic of Ireland are carrying out such a desk study and we await the outcome of this with interest (for further details, see Appendix B).

WILDLIFE OPTIONS FOR CONTROLLING CATTLE TB

i. Badgers

Removal/population control

7.20 In principle, if a persistent source of infection were in wildlife, then one option for control would be to remove that source. Ministers have made clear that they would not consider the widespread elimination of badgers but a complete analytical appraisal of options needs to consider the potential role of at least partial and strongly focused culling. The field trial is designed to evaluate the effects of badger culling on the incidence of TB in cattle. The policy options of either proactive or reactive culling are being evaluated. With the epidemiological data on the spatial prevalence of TB in badgers, its relationship to population density and badger social group structures, and the spatial

relationship of TB in badgers to TB in cattle that will be gained from the trial it may be possible to identify other wildlife control options.

Elimination of TB-infected badgers

7.21 A refinement of this option would be to target only TB-infected badgers for removal. This would require the development of a rapid sensitive live test for TB status in badgers, something which was proposed in 1986 in the Dunnet review [8] on badgers and TB, but is still not available. Work is in hand to attempt to develop a sufficiently sensitive and specific test but this must realistically be viewed as a long-term research target.

ii. Removal/population control of other wildlife

7.22 Studies are in place to assess the prevalence of *M.bovis* infection in wildlife species other than the badger. These studies have been designed to determine their potential significance as reservoirs of infection and hence allow appraisal of population control of such species, or possibly the use of vaccines, as a further means of control of the disease in the cattle population.

iii. Vaccination

7.23 If it is the case that most cattle infection derives from badgers, then vaccination of badgers, in theory, presents a more realistic and possibly less long-term option than cattle vaccination for TB control. The badger vaccine option is included in the current research programme but if it is to be seriously pursued experimental facilities to conduct vaccination challenge studies will need to be made available and methods devised for field validation.

OPTIONS FOR DECENTRALISING TB CONTROL

7.24 Government responsibility is to protect human health and the security of the food supply system. The risks to human health posed by exposure to *M. bovis* are relatively small and largely controlled by pasteurisation of milk and carcass inspection at slaughter. There is no reported transmission of *M. bovis* to humans from meat or meat products but it would be possible to strengthen further the food standards legislation already in place by banning the sale of unpasteurised milk and excluding TB reactors from the food chain. Placing greater responsibility for TB control directly onto farmers could be supported by the measures set out below.

i. Commercial insurance/statutory levy to cover consequential losses

7.25 Rather than compensating farmers for the slaughter of infected animals the Government could require them to carry compulsory commercial insurance cover for the losses they incur associated with a TB breakdown. Alternatively, such cover could be provided through a compulsory levy on the livestock industry, generating a fund to compensate affected farmers rather than placing the burden on the public purse. A Government-industry working party is looking at the principle of such insurance, albeit in the context of exotic diseases such as classical swine fever and foot and mouth disease, rather than TB, but there may be some read across.

ii. Redirected Government funding

7.26 The Government could make any form of compensation to farmers conditional upon the attainment of minimum standards of husbandry and biosecurity. Government grants for specific improvements in animal husbandry practice or biosecurity measures could also provide incentives for better TB control action by farmers.

7.27 The costs and benefits of various options will be assessed within the research on economic impact of cattle TB.

8. Looking Ahead

8.1 We continue to advise on the implementation of the field trial and the wider research programme, and remain alert for new research and new technologies which could facilitate investigation of these issues.

8.2 We have now enrolled all ten triplets in the field trial and would have expected proactive culling to have been completed in all triplets during 2001, consistent with the timetable prescribed in our second report to Ministers, had not trial operations been disrupted by the foot and mouth outbreak. We shall continue to work closely with DEFRA and the WLU on the implementation of the trial and continue to review operating procedures.

8.3 As the trial progresses an increasing amount of data will become available from the TB99 risk analysis epidemiological questionnaire, from other analyses being carried out as part of the current DEFRA programme based on pre-trial data, and from the field trial. Analysis of some of these data has already started and will continue.

8.4 We have in this and earlier reports highlighted the critical importance of accurate disease diagnosis and for this reason have encouraged MAFF to consider the complementary use of the gamma IFN test alongside the tuberculin skin test in certain problem herds which show a history of repeated breakdowns. The logistics of this approach are currently being evaluated in a small field trial by DEFRA. Additionally, the ISG is collating data, from work being done in the current research programme and elsewhere, to advise on improving the sensitivity and specificity of the test and its potential for wider use in TB-infected herds.

8.5 We are also extending the epidemiological investigations outside trial areas to a consideration of TB breakdown clusters in Shropshire, West Sussex, South West Wales and Staffordshire/Derbyshire.

8.6 In this report we have commented on the potential of vaccination of cattle and wildlife, recognised the significant challenges that have to be met and cautioned against over optimism. In order to better inform Ministers on the research, statutory and other requirements for development and use of either a cattle or wildlife vaccine, the ISG has embarked on a vaccine scoping study to consider this issue in greater depth.

8.7 A number of research workshops have been held, including one on mathematical modelling, and a further workshop on molecular epidemiology has been arranged for the current year.

8.8 Our overwhelming concern is to ensure that a scientifically rigorous understanding of the disease is established as quickly as possible, and we will advise Ministers immediately when we have sound scientific evidence that could assist the development of TB control policy.

9. References

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APPENDIX A

Summary of Current MAFF-funded TB Research Work

	PROJECT TITLE AND CONTRACTOR	START DATE	TOTAL COSTS (£)
A	Generation of vaccine candidates against <i>Mycobacterium bovis</i> VLA	01/04/99	1,566,005
B	Testing of vaccine candidates for bovine tuberculosis using a low dose aerosol challenge guinea pig model VLA	01/07/99	1,068,045
C	Testing TB vaccines in cattle VLA	01/04/99	1,316,635
D	Development of badger vaccines VLA	01/04/99	304,250
E	Antigen presenting cells and T cell responses to <i>Mycobacterium bovis</i> IAH	01/04/99	1,200,000
F	Development of badger immunological reagents VLA	01/04/99	419,560
G	Development of a turf model to assess the biological control of <i>Mycobacterium bovis</i> using myco-bacteriophage CAMR	01/07/99	80,000
H	The effect on viability of <i>Mycobacterium bovis</i> of freezing samples prior to cultural testing VLA	01/09/98	30,872
I	Improved diagnostics for cattle VLA	01/04/99	511,347
	PROJECT TITLE AND CONTRACTOR	START DATE	TOTAL COSTS (£)
J	Cost-effectiveness of using the gamma interferon test in herds with multiple tuberculin reactors VLA	01/04/00	124,682
K	<i>Assessment of the economic impacts of TB and alternative control policies</i> Reading University	01/05/01	156,959
L	Development and evaluation of strain typing methods for <i>Mycobacterium bovis</i> VLA	01/09/99	1,124,682
M	<i>An integrated approach to the application of Mycobacterium bovis genotyping for the control of bovine tuberculosis in GB</i> VLA	01/04/01	917,801
N	Detection and enumeration of <i>Mycobacterium bovis</i> from clinical and environmental samples VLA	01/04/99	297,046
O	<i>Survival of Mycobacterium bovis in laboratory made silage</i> VLA	01/04/01	4,408

P	<i>Mycobacterium bovis</i> pathogenesis <i>IAH, Queen's University Belfast, VLA</i>	01/07/00	2,440,159
Q	Pathogenesis and diagnosis of tuberculosis in cattle - complementary field studies <i>VLA</i>	01/10/00	2,591,017
R	A spatial analysis using GIS of risk factors associated with TB incidents in cattle herds in England and Wales <i>VLA</i>	01/01/99	188,373
S	Ecological correlates of tuberculosis incidence in cattle <i>Warwick University</i>	16/08/99	374,181
	PROJECT TITLE AND CONTRACTOR	START DATE	TOTAL COSTS (£)
T	Multivariate analysis of risk factors affecting incidence of TB infection in cattle <i>Royal Veterinary College</i>	10/05/99	37,563
U	Multivariate analysis of risk factors affecting tuberculosis incidence in cattle herds - phase 1 <i>VLA</i>	01/04/99	137,479
V	Quantification of the risk of transmission of bovine TB from badgers to cattle within localised areas <i>VLA</i>	01/04/99	167,504
W	Integrated modelling of <i>M. bovis</i> transmission in badgers and cattle <i>CSL</i>	01/04/99	890,769
X	The risk to cattle from <i>Mycobacterium bovis</i> infection in wildlife species other than badgers <i>Oxford University</i>	01/05/99	998,803
Y	The risk to cattle from wildlife species other than badgers in areas of high herd breakdown risk <i>CSL</i>	01/01/00	608,095
Z	Understanding the route of TB transmission from badgers to cattle <i>Bristol University</i>	01/10/99	266,942
AA	The potential of ticks as vectors of <i>Mycobacterium bovis</i> <i>Oxford University</i>	01/01/00	49,942
BB	Develop innovative methods to estimate badger population density <i>CSL</i>	01/04/99	882,089
CC	Novel methods of estimating badger numbers in the wider countryside <i>Bristol University</i>	01/10/99	230,426
DD	An integrated study of perturbation, population estimation, modelling and risk <i>Oxford University</i>	01/04/99	1,252,592

	PROJECT TITLE AND CONTRACTOR	START DATE	TOTAL COSTS (£)
EE	A molecular genetic analysis of badger social structure and bovine tuberculosis <i>CSL</i>	01/01/00	766,069
FF	Ecological consequences of removing badgers from an eco-system <i>CSL</i>	01/02/99	1,000,810
GG	Using herd depopulation for effectively controlling TB <i>VLA</i>	01/04/01	26,758
HH	Exploratory study to model the distribution and spread of bovine TB using multi-temporal satellite imagery <i>Oxford University</i>	01/06/01	42,450
	TOTAL RESEARCH COST		22,074,313

Contractor Key:

- CAMR** - Centre for Applied Microbiology and Research
- CSL** - Central Science Laboratory
- IAH** - Institute of Animal Health
- VLA** - Veterinary Laboratories Agency

APPENDIX B

*The ISG's response to the Husbandry Panel Report***INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB****Chairman: Professor John Bourne MRCVS****Secretary: Dr David Lees**

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Mr Roy Hathaway

TBZ Division

Ministry of Agriculture, Fisheries and Food

1A Page Street

London SW1P 4PQ

3 August 2000

Dear Roy,

TB AND CATTLE HUSBANDRY: REPORT OF THE INDEPENDENT HUSBANDRY PANEL MAY 2000

The Independent Scientific Group on cattle TB (ISG) has carefully considered the report of the Husbandry Panel and this letter sets out our conclusions

As we recorded in our second annual report, the Group supported the Agricultural Select Committee's recommendation for an independent assessment of the measures which might contribute to a TB control strategy, although we had some doubts that new solutions for TB control would emerge from such an assessment.

The Panel's report provides a comprehensive catalogue of the available literature on cattle TB, animal husbandry and other factors. It comprises a useful reference document. The Panel is to be congratulated for covering so much ground in so short a time and time constraints probably explain why, in most cases, the literature has not been critically assessed in the report.

The report states that, in the absence of definitive knowledge of the transmission routes of the disease, the Panel assessed a wide range of potential routes and associated husbandry practices. The report concludes that badgers are likely to be the main wildlife reservoir of bovine TB in the UK. This is, of course, an open question and precisely what the badger culling trial is intended to investigate.

The Group was somewhat surprised that the Panel has not devoted more attention to issues such as the importance of the maintenance of herd biosecurity. However, we were reassured to note that the Panel has in effect endorsed the advisory literature on good animal husbandry practices provided by MAFF, which in part covers this area.

It was also reassuring that the report did not identify any significant scientific initiatives that had not been considered previously by the ISG and MAFF. The current MAFF research programme on cattle TB is specifically designed to improve our knowledge of the epidemiology, routes of transmission, pathogenesis and risk factors associated with the disease all of which are identified by the Panel. In our view, many of the issues identified by the Panel for further research are being actively researched or are secondary to those being covered by current projects. We do, however, believe that research work to improve diagnosis of cattle TB is a high priority.

The ISG also wishes to comment on the proposal that research work, albeit a desk exercise initially should focus on genetic resistance to TB in cattle.

The recommendation of the Husbandry Panel appears to be based on the premise (hat some animals when exposed to *M. bovis* are able to resist infection. However, there is no evidence for the existence of cattle that are completely resistant to infection, since experimental studies with high doses of *M. bovis* invariably have resulted in persistent infection and pathology in 100% of animals.

The greater variability in disease outcome in animals receiving lower doses of organisms suggests that there are genetic differences in susceptibility to disease although this may be due to differences in infective dose. Whether or not some cattle are able to clear infections with *M. bovis* and resist the establishment of permanent infection is not known. It has been assumed that in experimental animals that do not develop pathology or skin test reactivity following low dose infection ($10^2 - 10^3$ organisms) that infection has merely failed to establish. However a recent unpublished observation from a study at CVL that such animals mount a cellular immune response to *M. bovis* (measured using in vitro assays) suggests that transient infection might occur. This aspect of the pathogenesis of the disease in cattle requires further investigation, and such a study is currently being planned.

Since the practical aim in cattle TB control programmes is to identify and remove all infected animals irrespective of the severity of the disease and that these are identified by a cellular immune response there may be limited scope to exploit genetic resistance that affects disease severity. Such resistance could reduce the extent of cattle-to-cattle transmission of disease, although this cannot be predicted without having more information on what parameters affect transmission. Genetic resistance that afforded complete resistance or that enabled animals to clear infection without a permanent identifiable cellular immune response would potentially be exploitable although it is unclear that such resistance occurs.

There are also difficulties in studying genetic resistance using current technologies. While there is anecdotal field evidence that certain family lines of cattle are more likely to succumb to the disease this, even if substantiated, might be due to factors other than genetic susceptibility. There are however no identifiable populations of TB-resistant cattle which would allow experimental studies of the genetic basis of resistance to TB. Initial studies would therefore be needed to determine whether or not there is evidence of resistance in the field.

While this could theoretically be done by analysis of pedigree information on affected dairy herds there are a number of difficulties in undertaking such studies. First, only those animals that have been exposed to *M. bovis* will be informative. The incidence of detectable infection in most herds is very low and there is no way of identifying animals that have undergone transient infection with recovery, if indeed it does occur. The sensitivity of analysis of pedigree will be very low. Ultimately such studies would need to identify specific lineages of animals that could be subjected to further genetic studies to identify the genes involved.

Because of the low and unpredictable exposure to infection in the field, these genetic studies would need to be carried out experimentally. While it is by no means certain that studies of pedigrees would identify lineages of cattle with sufficiently divergent disease susceptibility to allow further experimental investigation, the resource requirements for generating experimental animals and holding these under category III containment over prolonged periods of time in order to obtain meaningful results would be massive.

The Group welcomed the opportunity to comment on the report before MAFF publishes its response and I hope that the above comments are useful. If I can help further, please let me know.

F J BOURNE

APPENDIX C

Background Data from Trial Areas Subjected to Initial Proactive Culling Operations

TRIPLET A

	Herefordshire/Gloucestershire		
	Blaisdon A1	Dymock A2	Broadway A3
1. Triplet name			
2. Trial area			
3. Number of cattle herds in trial area	135	91	74
4. Historical incidence of TB in cattle in herds in trial area			
confirmed breakdowns: 3 year (1995-97)	54	37	39
12 month (1997)	17	14	12
annual incidence: 3 year (1995-97)*	0.1333	0.1355	0.1757
12 month (1997)*	0.1259	0.1538	0.1622
5. Total surface area (trial area and inner buffer zone) (km ²)†	163	165	155
6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km ²)‡	115	144	140
7. Number of land occupiers visited in trial area and inner buffer zone	250	299	179
8. Treatment	Reactive	Survey only	Proactive
9. Number of Traps (to date)	48	Not applicable	310
10. Number of Badgers Caught	34	Not applicable	55
11. Non-target species caught	0	Not applicable	102
12. Non -target species found dead in traps or dispatched	0	Not applicable	12
13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.			
- Total number of badgers caught	300	165	86
- Percentage of badgers caught found to be infected with TB	36%	49%	76%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

‡ - Source: provisional management data

TRIPLET B

Devon/Cornwall			
	Hartland B1	Putford B2	Bude B3
1. Triplet name			
2. Trial area			
3. Number of cattle herds in trial area	90	153	129
4. Historical incidence of TB in cattle in herds in trial area			
confirmed breakdowns: 3 year (1995-97)	37	48	35
12 month (1997)	16	26	11
annual incidence: 3 year (1995-97)*	0.1370	0.1046	0.0904
12 month (1997)*	0.1778	0.1699	0.0853
5. Total surface area (trial area and inner buffer zone) (km ²)†	119	143	130
6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km ²)‡	114	125	120
7. Number of land occupiers visited in trial area and inner buffer zone	164	270	232
8. Treatment	Reactive	Proactive	Survey Only
9. Number of Traps (to date)	352	1663	Not applicable
10. Number of Badgers Caught	107	397	Not applicable
11. Non-target species caught	107	135	Not applicable
12. Non -target species found dead in traps or dispatched	5	24	Not applicable
13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.			
- Total number of badgers caught	306	377	331
- Percentage of badgers caught found to be infected with TB	32%	20%	37%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

‡ - Source: provisional management data

Data in 3 and 4 are for trial areas after surveying. The figures in the Second Report [2] were for the proposed trial areas before surveying.

TRIPLET C

East Cornwall			
	Otterham C1	Launceston C2	Lanreath C3
1. Triplet name			
2. Trial area			
3. Number of cattle herds in trial area	151	180	107
4. Historical incidence of TB in cattle in herds in trial area			
confirmed breakdowns: 3 year (1996-98)	21	16	14
12 month (1998)	7	9	5
annual incidence: 3 year (1996-98)*	0.0464	0.0296	0.0436
12 month (1998)*	0.0464	0.0500	0.0467
5. Total surface area (trial area and inner buffer zone) (km ²)†	145	157	151
6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km ²)‡	137	154	140
7. Number of land occupiers visited in trial area and inner buffer zone	259	315	237
8. Treatment	Reactive	Survey only	Proactive
9. Number of Traps (to date)	306	Not applicable	1300
10. Number of Badgers Caught	178	Not applicable	357
11. Non-target species caught	5	Not applicable	59
12. Non -target species found dead in traps or dispatched	0	Not applicable	1
13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.			
- Total number of badgers caught	162	360	257
- Percentage of badgers caught found to be infected with TB	19%	24%	22%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

‡ - Source: provisional management data.

Data in 3 and 4 are for trial areas after surveying. The figures in the Second Report [2] were for the proposed trial areas before surveying.

TRIPLET E

North Wiltshire			
	Cold Ashton E1	Charlcott E2	Poulshott E3
1. Triplet name			
2. Trial area			
3. Number of cattle herds in trial area	96	104	123
4. Historical incidence of TB in cattle in herds in trial area			
confirmed breakdowns: 3 year (1996-98)	18	14	24
12 month (1998)	7	5	10
annual incidence: 3 year (1996-98)*	0.0625	0.0449	0.0650
12 month (1998)*	0.0729	0.0481	0.0813
5. Total surface area (trial area and inner buffer zone) (km ²)†	149	156	152
6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km ²)⌘	113	147	118
7. Number of land occupiers visited in trial area and inner buffer zone	205	211	207
8. Treatment	Reactive	Survey only	Proactive
9. Number of Traps (to date)	0	Not applicable	1235
10. Number of Badgers Caught	0	Not applicable	744
11. Non-target species caught	0	Not applicable	69
12. Non -target species found dead in traps or dispatched	0	Not applicable	13
13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.			
- Total number of badgers caught	479	240	140
- Percentage of badgers caught found to be infected with TB	24%	30%	40%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

⌘- Source: provisional management data

TRIPLET F

West Cornwall			
	Madron F1	GodolphinF2	Stithians F3
1. Triplet name			
2. Trial area			
3. Number of cattle herds in trial area	137	206	253
4. Historical incidence of TB in cattle in herds in trial area			
confirmed breakdowns: 3 year (1997-99)	20	25	17
12 month (1999)	6	19	8
annual incidence: 3 year (1997-99)*	0.0487	0.0405	0.0224
12 month (1999)*	0.0438	0.0922	0.0316
5. Total surface area (trial area and inner buffer zone) (km ²)†	145	149	164
6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km ²)‡	90	112	100
7. Number of land occupiers visited in trial area and inner buffer zone	252	527	658
8. Treatment	Proactive	Survey only	Reactive
9. Number of Traps (to date)	513	Not applicable	0
10. Number of Badgers Caught	451	Not applicable	0
11. Non-target species caught	31	Not applicable	0
12. Non -target species found dead in traps or dispatched	2	Not applicable	0
13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.			
- Total number of badgers caught	447	246	441
- Percentage of badgers caught found to be infected with TB	13%	13%	21%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

‡ - Source: provisional management data

TRIPLET G

1. Triplet name

2. Trial area

3. Number of cattle herds in trial area

4. Historical incidence of TB in cattle in herds in trial area

confirmed breakdowns: 3 year (1998-2000)

12 month (2000)

annual incidence: 3 year (1998-2000)*

12 month (2000)*

5. Total surface area (trial area and inner buffer zone) (km²)†

6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km²)‡

7. Number of land occupiers visited in trial area and inner buffer zone

8. Treatment

9. Number of Traps (to date)

10. Number of Badgers Caught

11. Non-target species caught

12. Non -target species found dead in traps or dispatched

13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.

- Total number of badgers caught

- Percentage of badgers caught found to be infected with TB

Staffordshire/Derbyshire		
Nettly Knowe G1	Lady Edge G2	Cubley Brook G3
114	241	132
20	25	27
8	10	13
0.0585	0.0346	0.0682
0.0702	0.0415	0.0985
156	151	154
138	109	124
263	299	247
Reactive	Proactive	Survey only
0	631	Not applicable
0	428	Not applicable
0	1	Not applicable
0	0	Not applicable
0	0	0
0%	0%	0%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

‡ - Source: provisional management data

TRIPLET H

1. Triplet name

2. Trial area

3. Number of cattle herds in trial area

4. Historical incidence of TB in cattle in herds in trial area

confirmed breakdowns: 3 year (1998-2000)

12 month (2000)

annual incidence: 3 year (1998-2000)*

12 month (2000)*

5. Total surface area (trial area and inner buffer zone) (km²)†6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) (km²)‡

7. Number of land occupiers visited in trial area and inner buffer zone

8. Treatment

9. Number of Traps (to date)

10. Number of Badgers Caught

11. Non-target species caught

12. Non -target species found dead in traps or dispatched

13. Aggregated data on badger removal operations in trial areas under the 'interim strategy' 1986-1997.

- Total number of badgers caught

- Percentage of badgers caught found to be infected with TB

Devon/Somerset		
Brendon Hills H1	Tarr Steps H2	Huntsam H3
80	68	136
13	17	18
7	9	4
0.0542	0.0833	0.0441
0.0875	0.1324	0.0294
145	146	149
122	122	125
176	224	317
Reactive	Proactive	Survey only
0	568	Not applicable
0	162	Not applicable
0	332	Not applicable
0	5	Not applicable
61	49	31
23%	37%	23%

* - Number of breakdowns divided by total number of herds (per annum), expressed as a decimal figure.

† - Some of this surface area will automatically be unsuitable for trial operations (including, for example, settlements, airfields, roads, rivers, lakes, quarries etc.)

‡ Source: provisional management data

APPENDIX D

Discussions with Interested Parties and Participation in Meetings and Conferences

1. Agriculture Select Committee oral evidence session - 15 November 2000

2. Organisations met:

Farmers Union of Wales
Forestry Commission
Lakeland Veterinary Association
National Farmer's Union, South West Region
National Farmer's Union, Newton Abbot, Moretonhampstead and Chagford Branch
The National Trust
Northern Ireland Assembly – Department of Agricultural and Rural Development
The Parliamentary and Scientific Committee
Royal Association of British Dairy Farmers
Scientific Committee for *M. Bovis*
Welsh Institute of Rural Studies
National Federation of Badger Groups South West Region (Gloucester)
University of Cambridge Veterinary School
National Beef Association
NFU (Pembrokeshire Branch)

3. Public Meetings and Conferences Attended

Triplet F - Open Meeting - Penzance - *February 2000*
Triplet G - Open Meeting - Ashbourne - *May 2000*
Triplet H - Open Meeting - Wheddon Cross - *May 2000*
Third International Conference on *Mycobacterium bovis* - St John's College, Cambridge - *August 2000*
National Federation of Badger Groups – Annual Conference, Durham - *September 2000*
Triplet J - Open Meeting - Exeter - *December 2000*
Triplet I - Open Meeting - Cheltenham - *Jan 2001*
Royal Show (Demonstration and lecture)

4. Members of the ISG met a number of individuals during the report period.

APPENDIX E
Glossary of key terms

BADGER POPULATION DENSITY

The number of badgers per unit area, normally per square kilometre.

BADGER REMOVAL

The culling (killing) of badgers in a specific countryside area.

BOVINE TB

A disease caused by the mycobacterium *M.bovis*.

BREAKDOWN

MAFF define a breakdown (or a TB incident) as occurring when one or more reactors are revealed by the tuberculin skin test or when disease is suspected in either live cattle showing clinical disease or in carcasses with lesions at post-mortem examination.

CONFIRMED BREAKDOWN

A herd breakdown where the disease has been confirmed in one or more animals, usually reactors, by detection of lesions at post-mortem and/or through culture of *M.bovis*.

DIAGNOSIS

The identification of an illness or disease by clinical signs or response to laboratory tests.

DNA

Deoxyribonucleic acid.

EPIDEMIOLOGY

The study of the distribution and dynamics of disease in a population. Its purpose is to identify factors which determine the occurrence of disease, and to provide a basis for intervention programmes. Epidemiological methods are also used to assess the variance, severity and magnitude of disease and related risks.

GAMMA INTERFERON

A product of white blood cells generated during an immune response.

GENOTYPE

The distinctive DNA fingerprint distinguishing one individual from another.

INCIDENCE

The rate at which new cases of infection arise in a population.

INCIDENT

(see breakdown)

MYCOBACTERIUM

A family of related bacteria characterised by a lipid-rich waxy coat that results in acid fast staining, which include species that cause TB.

NIDATION

Attachment of the fertilised ovum within the uterus at the start of pregnancy.

PATHOGENESIS

The processes within an individual involved in the development of disease.

PERTURBATION

The disruption of the social organisation or spatial structure of badger populations, such as that caused by culling.

POWER (STATISTICAL)

The probability that a difference between treatments will be detected given a particular magnitude of underlying difference between these.

PREVALENCE

The proportion of a population infected at a particular time.

REACTOR

An animal which gives a positive result to the tuberculin skin test.

SENSITIVITY

The proportion of true positives detected by a diagnostic method.

SETT

A burrow system which badgers use for shelter and breeding.

SOCIAL GROUP

A group of badgers (averaging six to eight in a group, although a maximum of 25 has been recorded) occupying one or more setts within a well-defined territory from which badgers of other social groups would be excluded.

SPECIFICITY

The proportion of true negatives detected by a diagnostic method.

TREATMENT

A term used to refer to the relevant action, i.e. proactive culling, reactive culling or survey only, which will be applied in the trial areas. Each triplet has three trial areas and each trial area will be subject to one of the three different treatments

TRIPLET

A group of three trial areas, each subject to a different treatment. Within each triplet, one area will be allocated to proactive culling, one to reactive culling and one to survey only.

TUBERCULIN

A sterile protein extract derived from the tubercle bacterium and used to diagnose TB in cattle by skin testing (also known as Purified Protein Derivative or PPD).

VACCINE

That used to prevent disease by stimulation of an immune response to the causative agent.

APPENDIX F

Membership of the Independent Scientific Group on Cattle TB**Professor John Bourne MRCVS CBE (Chairman)**

Former Professor of Veterinary Medicine at the University of Bristol (1980 – 1988), former Director of the Institute for Animal Health and Professor of Animal Health at the University of Reading (1988 – 1997), and Professor of Animal Health at Bristol since 1988.

Dr Christl Donnelly (Deputy Chairman)

Reader in Epidemiological Statistics in the Department of Infectious Epidemiology at Imperial College School of Medicine

Sir David Cox FBA, FRS

Honorary Fellow Nuffield College, University of Oxford since 1994.

Professor George Gettinby FRSE

Professor in the Department of Statistics and Modelling Science at the University of Strathclyde.

Professor John McInerney OBE, FRSA, FRASE

Glenn Professor of Agricultural Policy and Director of the Agricultural Economics Unit at the University of Exeter.

Professor Ivan Morrison FRSE

Head of the Division of Immunology and Pathology at the Compton Laboratory of the Institute for Animal Health.

Dr Rosie Woodroffe

Assistant Professor and Conservation Biologist, Department of Wildlife, Fish and Conservation Biology, University of California, Davis.