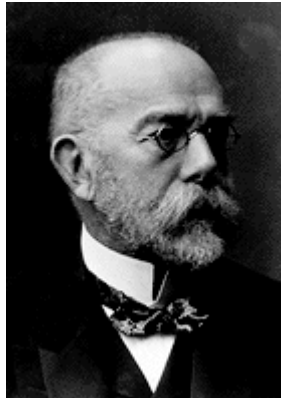# AN EPIDEMIOLOGICAL INVESTIGATION INTO BOVINE TUBERCULOSIS

TOWARDS A SCIENCE-BASED CONTROL STRATEGY

Fourth Report of the
Independent Scientific Group on Cattle TB

Presented to the Secretary of State for Environment, Food and Rural Affairs
The Rt Hon Margaret Beckett MP
December 2004

Robert Koch
(1843-1910)
Proved that human TB was caused by
a mycobacterium
- *Mycobacterium tuberculosis*

Koch expressed doubt that bovine TB (*Mycobacterium bovis*) could infect man, but acknowledged that he had little evidence upon which to base his opinion.

"A Royal Commission was quickly set up to explore the situation. In an unprecedented move, it was charged with conducting its own research, rather than simply collecting evidence from supposedly independent, but usually biased, witnesses.

The Commission, which published an interim report in 1904, demonstrated transmission of the organism from cow to man, and called for urgent legislation to combat the menace." *

*Taken from *The White Death - a History of Tuberculosis*
Thomas Dormandy, Hambledon Press 1999

INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

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The Rt Hon Margaret Beckett MP
Secretary of State
Defra
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<div align="right">23 December 2004</div>

Dear Secretary of State,

I am pleased to send you the Fourth Report of the Independent Scientific Group on Cattle TB.

Since our Third Report genuine progress has been made in developing a clearer understanding of the bovine TB complex. The research programme that we had recommended is now providing a flow of valuable data on a range of topics, including not only those that are directly trial-related but also on other important areas including pathogenesis, epidemiology, diagnosis, risk factors and economic aspects.

As scientists we would always prefer to collect as much data, and over as long a time frame as possible, before making recommendations. However, given the seriousness of the escalating problem of TB in cattle, we recognise our responsibility as your advisers to interpret emerging data which, although incomplete, we believe will allow reasonably secure scientific conclusions to be drawn. We consider this necessary in order to assist wider understanding, inform and guide thinking, contribute to scientific debate, help identify further lines of enquiry and, above all, assist in the formulation of effective evidence-based disease control options.

Two significant events have occurred since our last report, both of them unforeseen. The loss of a complete year of fieldwork due to the FMD epidemic was regrettable, and has extended the timetable of the trial to a projected end date of early to mid-2006. However, our assessment is that the overall impact of FMD on the trial was not large. Furthermore, on the positive side it has

provided a unique opportunity to collect epidemiological data from farms that were restocked as a result of FMD, both within and outside trial areas. These data are already proving to be extremely promising.

The second major development was the finding from our analysis of trial data that led you to terminate reactive culling in November 2003. Although we had recommended continuing culling and data collection a little longer, the ISG nonetheless felt able to support your decision, since we recognised that reactive culling as carried out in the trial could not contribute to the control of the disease in cattle.

The flow of new scientific data will increase over the next two years as the trial nears its projected end. By that time, which coincides with the end point of a number of trial-related and other research investigations, a substantial database will be in place. This, we expect, will underpin a range of robust and focussed analyses on the basis of which Defra should be able to make policy decisions far better informed than has been the case in the past. The ISG will continue to commit itself to supporting this objective.

As we acknowledge in the Report, the Group remains grateful to you and your Ministerial colleagues for your continued support and encouragement.

Yours sincerely

F J BOURNE

Contents

Appendices

List of Tables and Illustrations

1. CHAIRMAN'S SUMMARY AND OVERVIEW

1.1   The ISG has been working for some years now and over that period has developed a substantial base of understanding and new insights into the problem of controlling TB in cattle. It seemed appropriate now, therefore, to present not just an account of events since our Third Report[1] was published in 2001, but to discuss a wider range of issues that our work has covered. It is hoped this will help create a more coherent appreciation of the overall problem than emerges from the sometimes simplistic and narrow focus on specific aspects offered in much of the commentary and writings on the subject.

Background

1.2   From the very beginnings of its work, the ISG recognised that outbreaks of TB in cattle were the consequence of a complex and poorly understood system of determinants. Control policies at the time were based largely on questionable dogma and on limited or non-existent scientific evidence; to make a substantial impact on what was becoming a major problem for the UK cattle farming industry, new approaches needed to be developed on a wider horizon than heretofore. Although our origins were in a recommendation for a badger culling trial contained in the Krebs report[2] we quickly recognised that the development of TB control policy required far more than simply an enhanced empirical focus on badger culling, especially since Ministers declared that the widespread elimination of badgers from large tracts of the countryside was not an option. An overriding consideration was that any policy or policies had to be 'sustainable', meaning that as well as being technically effective in controlling the disease, any interventions had to be both feasible in the context of commercial cattle farming and consistent with public sensitivities and concerns over wildlife and the environment.

1.3   The ISG identified the lack of a coherent and dependable science basis for TB control policy as a severe constraint on progress. Aside from the establishment and monitoring of the Randomised Badger Culling Trial (RBCT) therefore, a great deal of our work has been directed towards developing a better understanding of the disease in cattle and in wildlife, fostering a wide range of scientific studies, questioning established but scientifically unfounded presumptions and considering the information needed from which future policy might reasonably develop. The necessarily holistic approach to our remit that we adopted, extending far beyond the RBCT, has been consistently pursued with the support of Ministers, and is now providing important scientific results to inform future policy.

Randomised Badger Culling Trial (RBCT)

1.4 The RBCT was designed to test the effect on the incidence of bovine TB of two different approaches to badger culling, each of which represented a potential practical policy option. The ISG recognised from the outset that it was conducting a scientific enquiry, not of the impact of complete badger removal, but rather of the effects of two culling strategies implemented under field conditions and in a way that could be extended into a viable policy. The Krebs Committee[2] originally envisaged an experiment involving "the complete or near complete removal of badgers from experimental areas", but it was evident to the ISG from the outset that implementation in the field could not, for valid reasons of both badger welfare and practicality, meet this objective. However, we concluded that this would not detract from the validity of the RBCT, which, by careful design and analysis, would be able to evaluate for the first time the effects of badger culling on the incidence of TB in cattle. It is unrealistic to believe that, for a disease involving a complex of inter- and intra-species transmission, any other quantitative measure could be made irrespective of culling methodology or efficiency, including the total elimination of badgers. For these reasons, which are considered in more detail in this report, the ISG has repeatedly referred to the RBCT as a "trial of two policy options".

1.5 As detailed in the report, field trial work was interrupted by the Foot and Mouth disease (FMD) epidemic, which commenced in February 2001, but picked up again with a resumption of trapping at the start of the culling season in May 2002. The enforced delay did unfortunately result in the loss of one whole year's fieldwork, with the consequence of extending the timetable for the proactive component of the trial from the originally projected end date of 2005 to early to mid-2006. The reactive strategy was also interrupted due to no herd testing being done for some ten months, and also because breakdown farms that had been identified but not culled prior to the imposition of FMD restrictions were either never subjected to the reactive culling treatment or had an extended delay before the culling was eventually done. However, we believe the impact of FMD overall was not large - and certainly does not justify the alarmist claim of having had a huge impact on the integrity of the trial and its outcome. A positive outcome of the FMD epidemic, and one that may subsequently be seen to be very significant in terms of scientific understanding, was the opportunity to carry out a detailed epidemiological study - particularly in parts of the country that had previously been relatively free of the disease - in herds that were depopulated as a result of the FMD slaughter policy and subsequently restocked. As highlighted in this report a number of these restocked herds have subsequently suffered TB breakdowns and are providing a valuable insight into the dynamics of the disease in cattle.

Control options

1.6   We fully sympathise with and share the frustration felt by farmers who observe an ongoing unchecked progression of TB both within and outside hotspot areas. However, strident calls for action to be taken against badgers in the face of rising herd incidence levels, while understandable, have little merit when there is no clear science base on which to develop that action and therefore no means of predicting its effects. Furthermore, the claim by some commentators that little has been achieved or done to better understand and control this disease is to ignore the genuine progress that has been made in developing a clearer understanding of the TB complex and the research findings that can now influence policy action. The research programme put in place by Defra, on which the ISG has advised, has, in the last few years, been providing a stream of data, albeit incomplete, on a range of topics, including epidemiology, pathogenesis, diagnosis and risk factors, but which we believe is substantive enough to allow interpretation in a way that can now guide the formulation of control options. Reliable scientific interpretation of data is always dependent on the quality and extent of the data. While the ISG would have preferred to have more data, collected over a much longer time frame, we do not have the comfort of this. Given the seriousness of the escalating cattle disease problem, we have a responsibility to interpret emerging data which we believe is such as to allow reasonably secure conclusions to be drawn. This is necessary to inform thinking and the formulation of effective evidence-based control options. As will be seen in the report, we have attempted to do this, with the expectation that these new insights will help Defra design and, in cooperation with the farming industry, implement an improved TB control policy.

1.7   In Chapter 9 we discuss options for controlling this complex disease, explaining why we believe these need to embrace consideration of a wildlife control element, a cattle control element and a general farm management plan to improve local on-farm biosecurity.

Badger culling

1.8   Having been a central feature of government control policy for the past 30 years, some form of reactive culling strategy was seen by many as the most feasible potential future control policy option - despite the fact that the benefits of such badger culling have not been particularly evident. It was for this reason that the reactive treatment was included in the RBCT. However, a recent and important finding from the trial has been that reactive localised culling does not offer a beneficial effect large enough to make it useful as a practical policy option, and that there is substantial but not overwhelming evidence of an adverse effect of the reactive strategy. On the basis of these findings the Ministers suspended the reactive component of the RBCT in November 2003, and localised culling as conducted in the trial cannot therefore be considered as

a future control option. By contrast, the contribution that proactive badger culling can make to the control of cattle TB has yet to be determined and the implementation of this treatment in the trial is continuing. On the basis of the analysis of available data so far, we assess that an answer will become available by early to mid-2006, and this view is shared by the independent statistical auditor to the trial[3]. The findings from the RBCT, along with those from the field trial in the Republic of Ireland (RoI), when they are ultimately published and evaluated, can provide a strong empirical base to inform policy decisions - although consideration of the RoI data must take into account the different environmental and ecological features and public attitudes in the RoI compared to those prevailing in Great Britain.

Better diagnosis

1.9 Information to guide the design of a control element focussed specifically on cattle is also being provided by on-going research, which highlights the strong possibility that there are currently many infected animals remaining in herds, either because they have not been recently tested or because the tuberculin skin test fails to detect them. Future control actions *must* therefore include more effective diagnosis of the disease in individual cattle to allow the identification and removal from the herd of as many animals as is technically feasible which have been exposed to TB and are potential disease transmitters. A critical requirement in this respect is an accurate and sensitive diagnostic test for TB, since any attempt at eliminating a disease by removal of individual infected animals is totally dependent on the accurate identification of those animals. We have consistently questioned the effectiveness of the conventional tuberculin test in situations of high disease incidence. Its value as a herd test is fully accepted, but as a test to identify individually infected animals it is far less dependable. The opportunities for disease transmission from infected animals at all stages of the disease process, and the difficulties of diagnosing some of these animals using the established skin test, have been demonstrated in laboratory and field studies on the pathogenesis of TB in cattle. We believe, therefore, that the case for developing improved techniques of diagnosis is overwhelming, and have repeatedly advised that far more emphasis be placed on this particular objective. It is for this reason that we have given continuing support to the development and field evaluation of the gamma interferon (IFN) test (although as yet not perfect) as offering the best prospects for more effective identification of TB-infected cattle. We have advised that complementary use of this test with the tuberculin test is the only realistic way of tackling the substantial reservoir of disease in cattle that appears to be present in some areas, and also to reduce radically the risk of transmission of disease to new areas of the country. Defra's unwillingness to accept our advice on the design of a field trial of the IFN test which would be rigorous enough to yield the kind of data on its performance that are essential to provide an informed basis for its

use in a range of control options, has been disappointing and extremely worrying.

Cattle movement

1.10 The research also highlights the need for much more rigorous restrictions on the movement of cattle from herds which have had a confirmed TB breakdown, as this appears to be an important means by which the disease is spread to other herds and to new areas of the country. In addition, an important contribution must be clear advice on restocking and replacement policies for previously infected herds to ensure that disease is not reintroduced by replacement animals. We emphasise the need for the acceptance of shared responsibility between Defra and the farming industry if bovine TB is to be brought under control. This will involve farmers putting in place well understood measures for infectious disease control that are in practice no more than sensible, implementable disease security measures. The necessity for a more dependable TB test is self-evident, too, if the spread of disease is to be effectively controlled by pre- or post-movement testing as a requirement of any cattle movements between farms.

TB99 Epidemiological study

1.11 The implementation of appropriate on-farm husbandry and wildlife management practices based on a common-sense approach has often been advocated to aid control of the disease, but the scientific basis for specific recommendations is not yet clear. Some information is being gained from the TB99 epidemiological risk analysis survey, but we have been continually concerned at Defra's inability to pursue this project in the way we have advised. Very poor progress has been made in achieving the target of completing a detailed questionnaire for each 'case' (TB breakdown) in trial areas along with three comparable 'control' farms - the core of the methodology on which the study is based. The completion of case forms has often fallen well below target, while the collection of control farm data has not been given sufficient priority. As a result, we have been unable to undertake the extensive analysis of risk factors planned, and which perhaps would have provided substantive guidance on sensible on-farm practices that might be implemented now. Sadly, therefore, only findings based on an initial analysis are available for us to present in this report. However, as a result of ISG initiatives and enhancements to Defra's national livestock database, the TB99 questionnaire has been redesigned and simplified to take on board the views of the auditor[4] and other TB stakeholders. A renewed effort is being made to deliver the data that the survey can offer using a new form, in a study to be launched in 2005.

Vaccines

1.12   Vaccination, whether of cattle or wildlife, may or may not offer an effective means for TB control, but it can only be considered as a possible control option in the long term. Its prospects have been explored in depth by the ISG and one of its subgroups, the Vaccine Scoping Study Sub-committee (VSSSC)[5].   The idea of a vaccine strategy is often spoken about quite simplistically, reflecting a presumption that a vaccine for either cattle or badgers is scientifically, technically and operationally relatively easy to put in place. This is a naïve view which ignores the formidable scientific difficulties that have to be overcome in developing and implementing a successful vaccine, as well as the high financial and time requirements to validate the vaccine in the field before any widespread action could be taken. We have advised that there is currently no promising suitable vaccine available that could be considered for use in cattle, and no potential candidates seem to be on the horizon. Although the vaccine currently used for humans, Bacillus Calmette Guerin (BCG), might be considered for use in badgers, the reality is that the field trials to determine its value would necessarily have to be very extensive in scope, would be logistically difficult to put in place, and need to be guided by the outcome of the RBCT and its associated research. The ISG recommends that both cattle and badger vaccine options continue to be pursued, recognising that the generic enabling research would be applicable for both species and would greatly benefit from the ongoing international collaboration with researchers trying to develop an improved human vaccine against *M. tuberculosis*. It is thus imperative that the international position gained by the Veterinary Laboratories Agency (VLA) vaccine research team be sustained. It is also necessary that appropriate diagnostics are developed to support a vaccine control strategy.

House of Commons Environment, Food and Rural Affairs Committee

1.13   A matter worthy of comment is the challenge to Defra by the Parliamentary Select Committee[6] and others to develop a so-called 'Plan B' for controlling the growing problem of TB in cattle. This was apparently based on the assumption that 'Plan A' (badger culling) might have no future because of the possibility that the RBCT might yield an ambiguous outcome, or even clear evidence that badger culling as carried out in the trial was ineffectual.

1.14   In practice, any policy may well include a combination of actions - a prospect which the ISG had already embraced, recognising from the outset that future TB control policies would inevitably have to be multidimensional because of the complexity of the disease system. Furthermore, while they may or may not include a badger culling component, they would undoubtedly require a strengthened cattle control element, and this could be developed only following further research. The RBCT was deliberately designed by the ISG to

be robust in implementation so as to ensure that the effects of the two culling options being trialled could (unless there was massive interference, and this has not materialised) be unambiguously evaluated. The outcome of proactive badger culling is not yet known but we do not discount the possibility that long-term sustainable TB control in cattle will not include badger culling.

1.15   Consequently the wide-ranging and integrated Defra funded research programme on which the ISG advised, embracing not only the RBCT but also, in particular, work on the epidemiology and pathogenesis of the disease in cattle, was designed to provide the underpinnings of any cattle control element. The ISG therefore considers that both 'Plan A' and 'Plan B' (a focus on cattle control), neither of which are mutually exclusive, are adequately catered for by the intellectual and scientific research approach we have adopted.

1.16   The ISG considers vaccination of either cattle or wildlife (which might constitute 'Plan C' as an additional component) to be a much longer term option. But given the urgency to respond to the rising incidence of herd breakdowns and the spread of the disease into new areas of the country, there is a critical need for immediate, well-directed short term policy responses. Actions based on improved measures for cattle control are now being informed by research findings, and the ISG has given Defra its advice on how such approaches should be pursued.

The Independent Review of the RBCT

1.17   A feature of our work has been the large number of audits[3,4,7-13], many ongoing, covering all aspects of the work programme and instituted at the insistence of the ISG. When it was announced, therefore, we accepted the independent review of the progress of the RBCT. It is reassuring that in its report[14], Professor Godfray's Review Group supported the scientific approach adopted by the ISG and did not identify the need for any further research that was not already in place or advocated, or which had not been carefully considered and discussed. There were a number of other observations that were supportive of the ISG, for which we are grateful. Some other observations of the Review Group related to internal structures and working practices in Defra that do not directly relate to the ISG but could bear on the work of similar advisory groups in the future.

1.18   However some major recommendations were made that we believe add confusion rather than clarification, and contribute nothing to understanding the aims and outcome of the RBCT and future policy development. In particular, the Review Group's failure to appreciate that the RBCT could only measure the 'contribution' of badger culling to the overall TB problem, represents a basic misunderstanding. So, too, does its presumption that there were (unspecified) better ways of undertaking badger culling, implying the Review Group did not appreciate that animal welfare considerations and the realities of field

operations had to be taken into account. More worrying was an eschewing of scientific practice by their recommendation for the premature release of trial data, an action that would violate the generally accepted principles of conducting trials of this sort while offering no clear guidance as to how policy might be improved. In addition, the advice that Defra should plan future TB control policy - irrespective of the outcome of the RBCT - on the basis that badgers are implicated in the cattle TB complex seems far from constructive. It is obvious that badgers are 'implicated', simply because we know they are susceptible to bovine TB infection and therefore inevitably a part of the overall disease complex; but that does not suggest what, if anything, should be done about it. The RBCT was established to address exactly this question, and for the Review Group to advise taking (again unspecified) action without the benefit of the trial's findings runs directly counter to Defra's own avowed advocacy of basing policy decisions on good science, an aim which the ISG has striven to support. We strongly advise Ministers that the Review Group's recommendations on these matters cannot form any reliable basis for policy decisions on achieving a better control of cattle TB.

Collaboration, participation and extension

1.19   Finally, I should report that we have at all times continued to work closely with Defra in their efforts to tackle this worrying cattle disease, meeting with them regularly and including officials in our discussions of the work that we oversee. We participate fully in the meetings of the TB Forum, while I personally have attended and spoken at numerous meetings of interested groups around the country to explain our work, widen understanding of the nature of the issues faced in TB control, and foster discussion on the way ahead. Other members of the ISG do the same, though to a lesser extent. We continually explore new avenues that might offer productive insights or prospects for greater understanding of the *M. bovis* complex, analyse data as these emerge, develop concept notes, examine the feasibility of new studies, comment on research proposals and outcomes, and generally embrace the whole range of issues that underlie the objective of gaining the rigorous information needed for better TB control. We also make our findings available through conferences and scientific publications, subject to peer review, in accordance with open government practices. It is a hard and concentrated task, but the same members of the Group have been involved from the outset and our enthusiasm and commitment remain undiminished.

Acknowledgements

1.20   As Chairman of the ISG, I wish to express my gratitude to Ministers for their support, and also to Defra senior management. The ISG Secretariat team provides excellent service and advice and I am indebted to advisors and other staff members from the Central Science Laboratory (CSL), the Veterinary Laboratories Agency (VLA) and Defra's Veterinary Research Division. The

Defra Wildlife Unit (WLU) do an excellent job. I am continually grateful for their skill and professionalism, and also for the contribution of field staff from the VLA. I wish also to record the scientific contribution made by university-based researchers in the United Kingdom who contribute to the research programme and enlighten scientific discussions, and particularly to acknowledge the large contribution of scientists at the VLA Weybridge Laboratory, the Veterinary Research Laboratory, Stormont, Northern Ireland, the Institute for Animal Health (IAH), Compton and CSL (Woodchester Park).

1.21   My continued appreciation and gratitude goes to my colleagues in the ISG, and our two research assistants, Dr Andrea Le Fevre and Dr Tom Johnston. They all give unstintingly of their time, respond to ever greater demands to pursue the many facets of this investigation and create the dynamic environment in which we work and interact.

PROFESSOR JOHN BOURNE

2. INTRODUCTION

2.1   From the beginning of its work in 1998, the ISG's view was that, because of the evident complexity of the disease system associated with *M. bovis*, future policies for the control of TB in cattle would need to be based on the application of a range of control measures. In order to be devised and implemented in practice, these measures would require the information that would come from the RBCT with respect to the impact of these forms of badger removal, but importantly, it would also require a far clearer scientific understanding of the epidemiology and pathogenesis of the disease in both cattle and badgers than has been available until now.

2.2   Consequently, as described in earlier ISG reports[1,15-16] to Ministers, our approach to our remit has been to develop a wide ranging epidemiological investigation into TB in cattle and badgers which extends well beyond the trial on badger culling that was originally proposed in the Krebs report[2].

2.3   The RBCT was developed primarily to test the impact of two different badger culling strategies on the incidence of TB in cattle herds. But the trial has been purposefully designed and implemented to ensure that it will provide an additional wealth of epidemiological data in both cattle and badgers - data that cannot be gained in any other way[1]. When it is all finally available, this will include information on the prevalence of *M.bovis* infection in badgers, the relationship of infection prevalence to population density and badger social group structures, the spatial relationship of infected badgers to infected cattle, and the pathology of TB in badgers. In addition, linked to the RBCT are studies designed to identify risk factors associated with development of the disease in cattle, the prevalence of TB in the wider badger population outside trial areas, and a number of ecological projects relating to the badger, other wildlife and cattle.

2.4   Of central importance is a comprehensive programme of work on the epidemiology and pathogenesis of the disease in cattle which complements the above epidemiological studies in the badger, involving both laboratory and field studies.   These have been designed to provide information on the pathology and dynamics of the disease in cattle, the development of new diagnostic tests, the development of effective vaccines and in particular to understand factors influencing prevalence and persistence of TB in cattle and wildlife and transmission routes between and within species. Work is also being developed to enable the relative economic merits of potential control options to be evaluated. The elements of this comprehensive programme are each discussed in various chapters of this report, which together amount to a detailed review of the issues that must be confronted in the development of a coherent and effective policy to control the continuing problem of TB in British cattle herds.

2.5   The extent of the research programme that Defra has put in place based on the advice of the ISG is outlined in Appendix M. The broader programme of research has run in parallel with the RBCT, and although some of the research work will inevitably continue to deliver information beyond the predicted end point of the RBCT (mid 2006) we would expect a range of data to be available to inform control options at this time. Indeed as discussed in Chapter 9, some of the research findings are, we believe, already substantive enough to direct policy.

2.6   The major issue of interest to many people is, of course, the progress of and findings from the badger culling trial, and we report extensively on this in the following chapter. However, the reader is urged to study the report in its entirety in order to appreciate fully how the breadth and detail of the ISG's activities extends beyond the RBCT, and to recognise how the work in these other areas represents an integral component of the holistic approach necessary to better understand the complex problem of TB in cattle.

3.   THE RANDOMISED BADGER CULLING TRIAL (RBCT)

3.1   The principal question addressed by the randomised badger culling trial (RBCT) is "what contribution can proactive and reactive badger culling make to controlling cattle TB?" It is a trial of two different approaches to the culling of badgers, either of which might represent an option for future control policy. The culling methods and procedures employed therefore take account of the practical difficulties of field work, landowner permission, and the public sensitivities concerning badger welfare; in this respect the methods closely approximate how culling as a policy could be implemented in practice. The design of the RBCT has been presented in previous reports[1, 15,16].

3.2   There have been two main developments with the RBCT since the ISG's Third Report[1]. First, restrictions on field activities as a result of the Foot and Mouth disease (FMD) epidemic suspended all trial operations over the 2001 culling year, from May 2001 to January 2002. Second, the reactive component of the RBCT was suspended by Ministers on 4 November 2003, as is described in detail later in this chapter.

Design of the Trial

3.3   The trial has involved three experimental regimes: (i) proactive culling, (ii) localised reactive culling, and (iii) no badger culling, referred to as 'survey-only'. The objectives of proactive culling are to reduce badger densities to low levels across entire trial areas and to maintain low density by further culling on a regular basis within constraints imposed by issues of animal welfare (see 3.46-3.63). In contrast, reactive culling was initiated in response to confirmed TB cattle herd breakdowns and subject to similar welfare concerns. Culling was undertaken across badger social groups occupying home ranges that overlapped the area used by reactor cattle. Survey-only areas receive no badger culling but are subject to regular field surveys to record signs of badger activity and interference with setts.

3.4   Thirty trial areas, each of approximately 100 square kilometres, were selected as ten matched groups and labelled for identification purposes as triplets A,B,C,…..J. The three treatments were then allocated to areas within each triplet, each triplet being regarded as becoming active after the completion of its initial proactive cull. Since the last report[1], the final three triplets, D, I and J have received their initial proactive culls. Summary data on the ten triplets is at Appendix D. A security constraint prevented the random allocation of treatments in triplet I, but treatments were randomly allocated in all other triplets. Many aspects of the trial have been subjected to independent audit[3, 7-13].

Relevance of the culling strategies

3.5   The trial measures the impact of culling badgers on the level of TB in cattle herds, by comparing the incidence rates of herd breakdowns in the trial areas subject to culling with those in the survey-only areas. Assessment can also be made of the consistency of treatment effects in the 10 triplets and of the precision of the estimates.

3.6   In addition to addressing the effect of culling, the RBCT has been designed to provide baseline epidemiological and other scientific data. Epidemiological data on the 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 gained from both proactive and reactive culling areas. We also recognise that infectious disease is dynamic, and that disease patterns change over time, and the RBCT allows the opportunity to study this. Because some of the field trial operations are in areas that were previously subjected to localised badger removal (so-called 'badger removal operations', BROs), data collected when those particular operations were undertaken will provide retrospective information on the localised prevalence of TB in badgers and its relationship to TB in associated cattle herds.

Participation in the trial

3.7   As commented on in earlier reports, the levels of consent for the trial from land occupiers has been, and continues to be, generally high (Figs 3.1-3.3).

3.8   The ISG wishes to express its gratitude to farmers, landowners and their representatives for their support for the RBCT and other work that is taking place both within and outside trial areas. We are especially grateful, too, for the professionalism and commitment of the staff in Defra's WLU who have undertaken the field work in the trial, and to the police forces in the trial areas for their close collaboration and support in the face of the often persistent interference by those members of the public opposed to the trial.

Figure 3.1 Level of co-operation - in treatment areas and inner buffer zones (total available area for which permission for trial operations was sought)
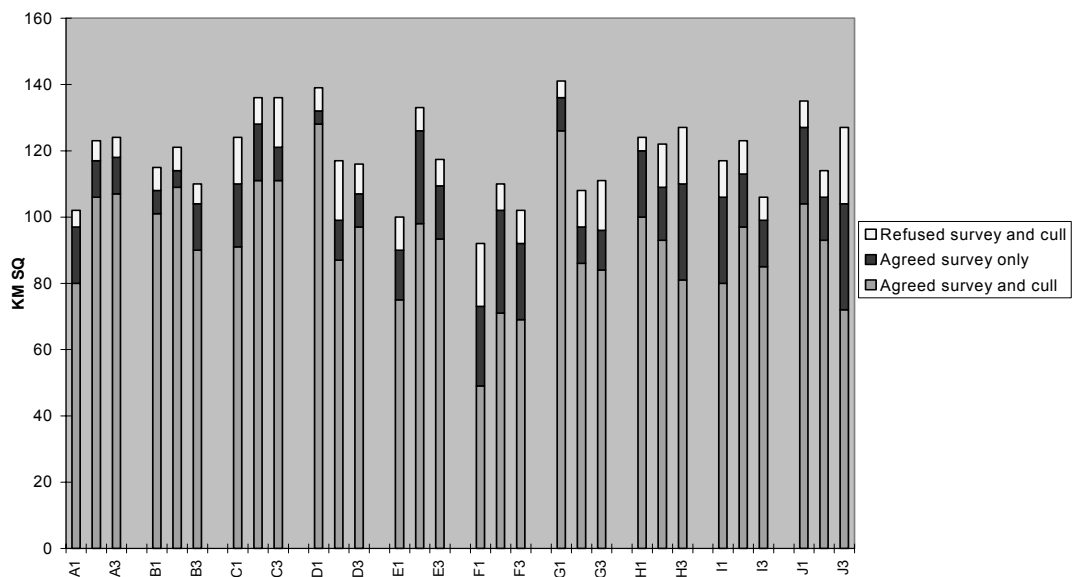

Figure 3.2 Level of co-operation - in treatment areas and inner buffer zones (percentage of available area)
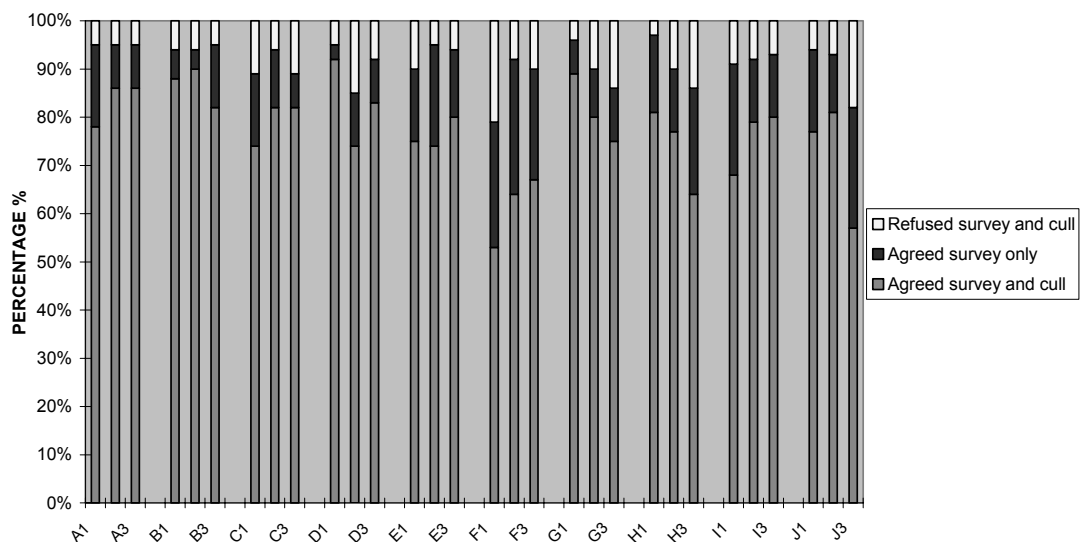
Figure 3.3 Level of co-operation - in treatment areas and inner buffer zones (percentage of all occupiers visited)
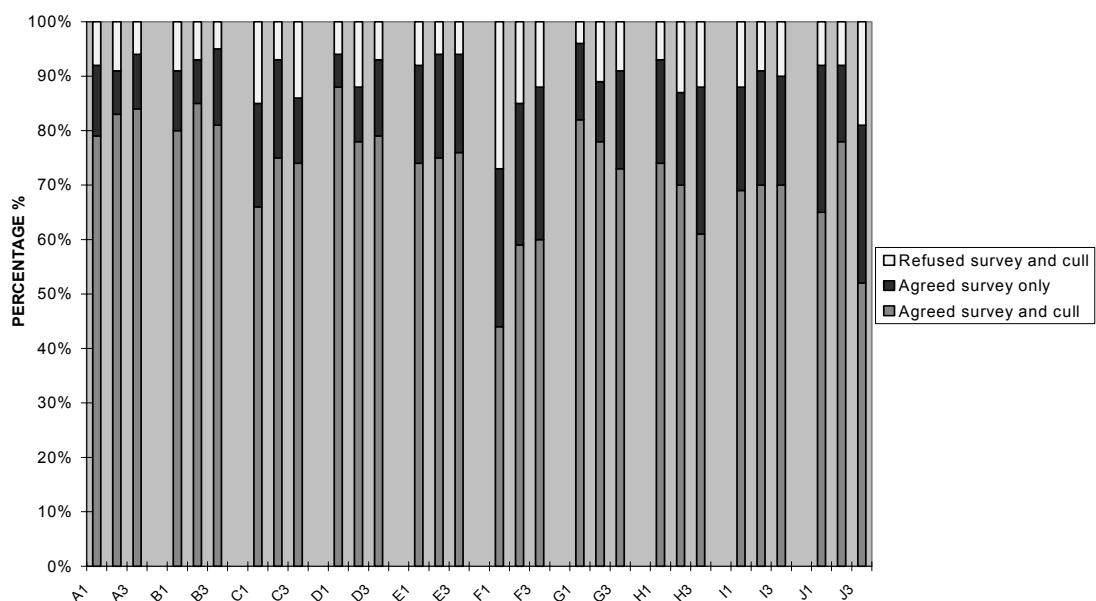
Consequences of the FMD epidemic for the RBCT

3.9   The FMD epidemic commenced on 19 February 2001 and it was not until 28 November 2001 that it was considered to be over. The effects on the trial over this period were threefold: a) the cessation of all field activity as part of the effort to control disease spread; b) the suspension of the programme of routine TB testing on herds; and c) the loss of cattle herds due to the FMD slaughter policy.

3.10   The ISG's initial assessment of the impact of FMD on trial activities was reported to Ministers in May 2003 (Appendix I). 223 farms in trial areas were depopulated as a consequence of FMD, but this represented less than 7% of the farms with cattle in these areas[*]. Thus, the direct effects of herd depopulation were never likely to be substantial. The numbers of herds in all trial areas remain above the minimum of 50 that was specified at the outset as a criterion for an area to be included in the trial (as at July 2004 the range was from 52 to 197, with a median herd number of 99). Therefore, as previously reported, the ISG believes that the loss of herds and cattle from within trial areas was not particularly damaging to the progress of the RBCT. In addition, the FMD epidemic provided a unique opportunity to put in place epidemiological studies on farms, both within and outside trial areas that were depopulated and subsequently restocked. This research is already delivering useful data that would not have been available elsewhere. This is commented on in Chapter 9 of this report.

3.11   The RBCT protocol specifies that regular 'follow-up culls' are undertaken in the proactive areas to maintain reduced badger densities at their established low levels, and these were delayed in all seven of the triplets (A, B, C, E, F, G, H) that were active before the FMD epidemic started (Table 3.1). Triplets A, F, G and H were awaiting their first follow-up cull in 2001, but these were delayed, resulting in a median period of 21 months between initial and first follow-up culls in those triplets compared to a median of only 12 months in triplets B, C and E, prior to FMD. For these three triplets, however, it was their second follow-up culls that were delayed. The remaining three triplets, D, I and J, should have received initial proactive culls in 2001, but the cessation of fieldwork due to FMD meant that these culls were delayed until the following year; they were then subject to their first follow-up culls a median of 10 months later.

3.12   Although this suspension of RBCT culling meant that some triplet years were lost, the seven triplets that had been initiated prior to the FMD epidemic did, of course, continue to accumulate functional data because the badger numbers had already been reduced by the proactive treatment and so the effects of this were ongoing. A statistical assessment of the accruing trial data indicates that (assuming there are no further unanticipated setbacks) the

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[*] based on currently-available data

proactive treatment should now yield a result sufficient to inform policy development in 2006 rather than the previously anticipated 2005. The statistical auditor has seen these calculations and approved[3] the conclusion reached by the ISG.

3.13   Some reactive culling had been conducted in triplets A, B, and C before the FMD epidemic, but reactive culls were then delayed in all seven triplets that were active for two reasons. First, because all field activity was restricted to prevent the spread of FMD, cattle breakdowns that had been identified in reactive areas could not receive culling during the 2001 culling year (which ran from 1 May 2001 to 31 January 2002). When reactive culling recommenced in May 2002, there was a backlog of cases, and in the event, some breakdown farms scheduled to receive culling in 2001 but with lifted TB-related movement restrictions, were not culled because of resource constraints. Some of these farms did receive partial culling under other operations, but in total 16 farms did not receive full culling because of the restrictions on field activity. A further 16 farms with breakdowns outstanding from the period before FMD did receive reactive culling after field activity resumed in 2002, with the long delay potentially weakening the impact that badger culling may have had on future breakdowns.

3.14   Second, when cattle TB tests were resumed there was a large backlog of herds that required testing. As a confirmed herd breakdown triggers a notification and the planning for a cull, the lack of tests delayed the identification of breakdowns that would trigger reactive culling, and thus probably also provided greater opportunities for the spread of TB both within the affected herd and more widely.

Progress with operations in the proactive culling trial areas

3.15   The culling year extends from 1 May to 31 January, with a 'closed season' implemented on welfare grounds to prevent the trapping of lactating female badgers with dependent cubs underground. The first proactive cull in the RBCT was completed in December 1998 in triplet B (see Table 3.1 for geographic locations). Subsequently, proactive culls were undertaken in triplets A and C in the 1999 culling year and four further triplets received initial proactive culls in the 2000 culling year. The initial proactive culls in the final three triplets were planned for the 2001 culling year but delayed until 2002 due to FMD restrictions.

3.16   Standard operating procedures (SOPs) for the proactive treatment specify that the initial cull should be followed 5-9 months later by a "first follow-up cull". Following this, further annual culls seek to maintain badger density at low levels. The suspension of culling activity during the FMD epidemic created the possibility that badger populations in the proactively culled areas might to an extent recover due to immigration and births. Data

from other areas (e.g. Thornbury, Woodchester, North Nibley) suggest that this usually happens only slowly, and on this basis, one might expect that the FMD epidemic would have only a small effect on proactive culling efficiency. Comparison of the numbers of badgers captured on successive culls that either were, or were not, delayed by the FMD epidemic suggests that the FMD-related delays to culling had no detectable effect in five of the seven proactive areas that were active at the time. FMD probably did hinder the effective implementation of the proactive treatment in two triplets that had had inefficient initial culls due to being carried out in winter[17], and under restricted trapping procedures due either to security concerns (triplet A), or extreme weather conditions (triplet H).

3.17   First follow-up culls in proactive areas were undertaken between five and 28 months after the initial proactive culls, with the median time being 13 months. The full list of triplets, the dates of initial and first follow-up proactive culls and the total number of badgers taken up to the end of the 2004 culling year are given in Table 3.1. The table also reflects the extent of delays due to FMD in 2001.

Table 3.1 Details on the timing and extent of proactive culling (in terms of numbers of badgers captured) by triplet.

Triplet identifier and location	Initial proactive cull	First follow-up cull	Number of badgers proactively culled by 31 Jan 2005
A-Gloucestershire/Hereford	Jan 2000	May 2002	314
B- Devon/Cornwall	Dec 1998	Dec 1999	729
C-East Cornwall	Oct 1999	Jan 2001	802
D-Herefordshire	Dec 2002	May 2003	873
E-North Wiltshire	May 2000	Jan 2001	1311
F-West Cornwall	Jul 2000	May 2002	1022
G-Staffordshire/Derbyshire	Nov 2000	Jul 2002	880
H-Somerset/Devon	Dec 2000	Jul 2002	537
I-Gloucestershire	Oct 2002	Oct 2003	487
J- Devon	Oct 2002	Aug 2003	737

3.18   The numbers of badgers caught on initial and follow-up proactive culls are plotted in Figures 3.4-3.6. Information is presented separately for three groups of triplets depending on whether or not they had received their initial cull and/or their first follow-up cull before the FMD epidemic.
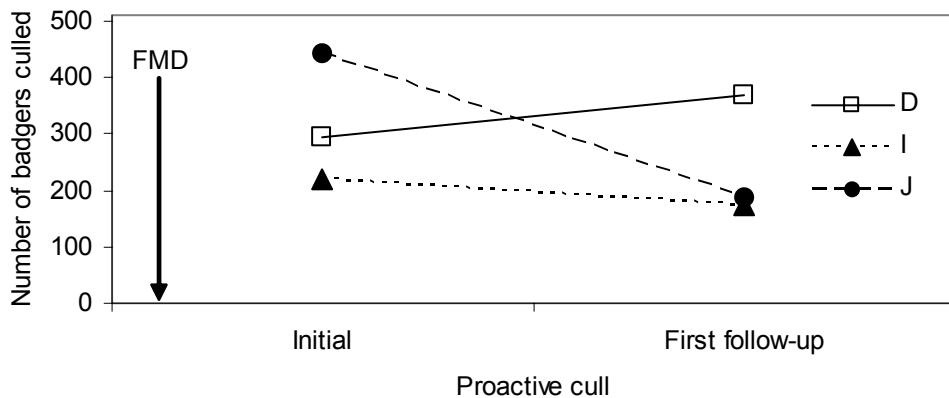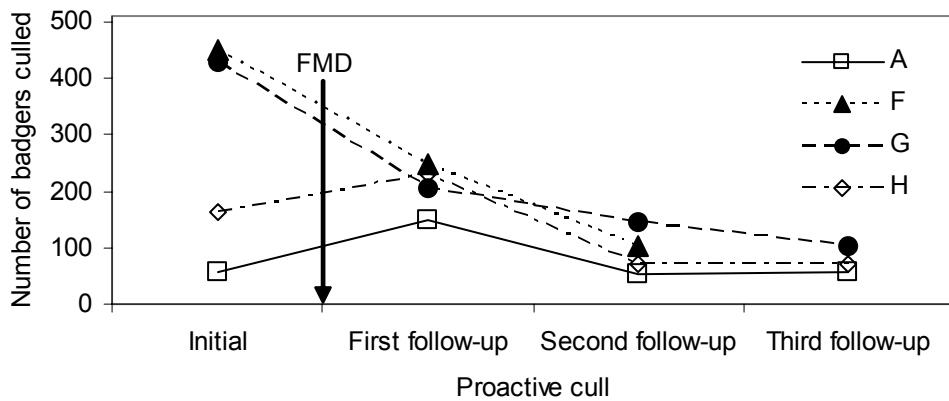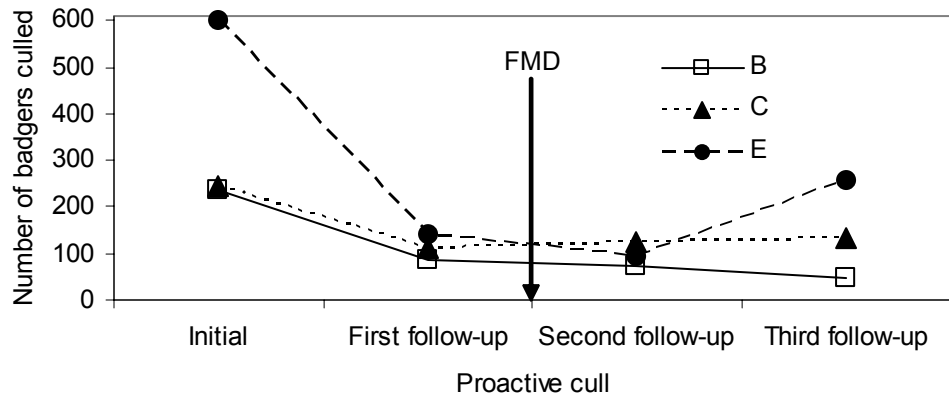
Figures 3.4-3.6 **Numbers of badgers caught at initial and follow-up proactive culls. Triplets are split into three groups, those with initial and first follow-up culls before the FMD epidemic (triplets B, C and E), those with only initial culls before the FMD epidemic (triplets A, F, G, H) and those, which have only been culled following the FMD epidemic (triplets D, I, J). The timing of the 2001 FMD epidemic is shown by the arrow, which indicates that the whole of the epidemic happened between the first and second follow-up culls for B, C and E; between the initial and first follow-up culls for A, F, G and H and before the initial cull for D, I and J.**

3.19   Triplets B, C and E had both initial and first follow-up culls before the FMD epidemic, and in all cases (as expected) fewer badgers were caught at the first follow-up than at the initial cull. Subsequent follow-up culls have seen the numbers of badgers caught increase somewhat but still remained well below the number caught at the initial cull.

3.20   Triplets A, F, G and H received their initial proactive culls in 2000 before the FMD epidemic but their delayed first follow-up culls in 2002 after it was over. In triplets F and G fewer badgers were caught at the first follow-up cull than the initial cull, as was the case with triplets B, C and E. However, in triplets A and H more badgers were caught on the first follow-up than the initial cull. Second follow-up proactive culls resulted in fewer badgers being caught in all these triplets.

3.21   Triplets, D, I and J were not culled until after the FMD epidemic. Fewer badgers were caught at first follow-up culls than in initial proactive culls in triplets I and J. In triplet D, the number of badgers caught in the first follow-up cull was greater than in the initial proactive cull, an outcome that can be explained by the initial proactive cull having been undertaken in winter when trapping success is impaired and the first follow-up cull having been undertaken in May when trapping success is high.

Description of the reactive strategy

3.22   Within reactive trial areas 'breakdown land' (the area of farmland associated with the herd that has suffered a TB breakdown) was identified by the State Veterinary Service (SVS) and formally notified to the national trial manager at the Defra WLU. Notifications were received for breakdowns where cattle were resident at the time of the breakdown or were resident within 30 days of the breakdown in reactive trial areas. Additionally, if land associated with growing forage was inside the trial area, then that land was also subject to notification.

3.23   Trapping in reactive areas was carried out in accordance with trial trapping procedures. The reactive strategy in each triplet operated from the end of the initial proactive cull, from which date all breakdowns in reactive areas should have been notified in order to trigger culling. The period of time between the initial proactive cull and the first reactive cull had a range between six and 25 months depending on the triplet, with a median of nine months.

Table 3.2 Details of the timing of the initiation of proactive and reactive culling by triplet.

Triplet identifier and location	Initial proactive cull	First reactive cull
A-Gloucestershire/Hereford	Jan 2000	Jul 2000
B- Devon/Cornwall	Dec 1998	Jun 1999
C-East Cornwall	Oct 1999	May 2000
D-Herefordshire	Dec 2002	Sep 2003
E-North Wiltshire	May 2000	Jun 2002
F-West Cornwall	Jul 2000	Aug 2002
G-Staffordshire/Derbyshire	Nov 2000	Aug 2002
H-Somerset/Devon	Dec 2000	Jan 2003
I-Gloucestershire	Oct 2002	Oct 2003
J- Devon	Oct 2002	None

3.24   In triplet J, proactive culling had been carried out, but Ministers decided to suspend the reactive treatment before any reactive culling had been done. The median time from the initial proactive cull to the first reactive cull was nine months in the nine triplets that received reactive culling.

3.25   Table 3.3 presents a summary of the number of breakdowns notified to the national trial manager, by triplet and cull status, up to the time that reactive culling was suspended in November 2003. Over 64% of all the notifications received complete (or partial) culling. The reasons for not culling reactive notifications varied from a lack of consent (around 6%), reporting of ineligible notifications (around 6%), abandonment due to the delays associated with FMD (about 4%) to notifications being due for culling at the time of the ministerial announcement (approximately 20% of all notifications).

Table 3.3 Number of reactive notifications by 4 November 2003.

Triplet identifier and location	Culled	Not culled	Total
A- Gloucestershire/Hereford	23	18	41
B- Devon/Cornwall	33	12	45
C-East Cornwall	44	15	59
D- Herefordshire	9	8	17
E-North Wiltshire	20	11	31
F-West Cornwall	23	6	29
G-Staffordshire/Derbyshire	11	10	21
H-Somerset/Devon	8	9	17
I-Gloucestershire	8	3	11
J-Devon	0	11	11
Total	179	103	282

3.26   Because TB breakdowns were frequently detected on adjacent or nearby farms, a single reactive culling operation could relate to multiple notified herd breakdowns. The various reactive operations that took place over the period May 1999 to November 2003 each covered between 1 and 8 breakdown notifications.   This included some cases where the breakdown land corresponding to a notified breakdown was only partially culled. The detailed pattern of culling operations is presented in the table 3.4. The largest numbers of operations were undertaken in triplet C while no operations were conducted in triplet J.

Table 3.4 Number of reactive operations in each triplet carried out by culling year. Shaded regions relate to periods before the initial proactive cull, where triplets had not yet started to contribute information, so no notifications were sought.

Triplet	May 1999-Jan 2000	May 2000- Jan 2001	May 2002- Jan 2003	May 2003- Nov 2003	Total
			Culling Year		
A		4	4	2	10
B	3	2	3	2	10
C		7	8	5	20
D				4	4
E			4	6	10
F			5	5	10
G			5	2	7
H			2	2	4
I				3	3
J				0	0

3.27   The area covered by an individual reactive operation varied in size from 0.65 km^2 to 32.5 km^2 (Figure 3.7). Triplet B had operations that were on average larger than those carried out in other triplets, with the majority of operations in other triplets covering less than 10km^2.
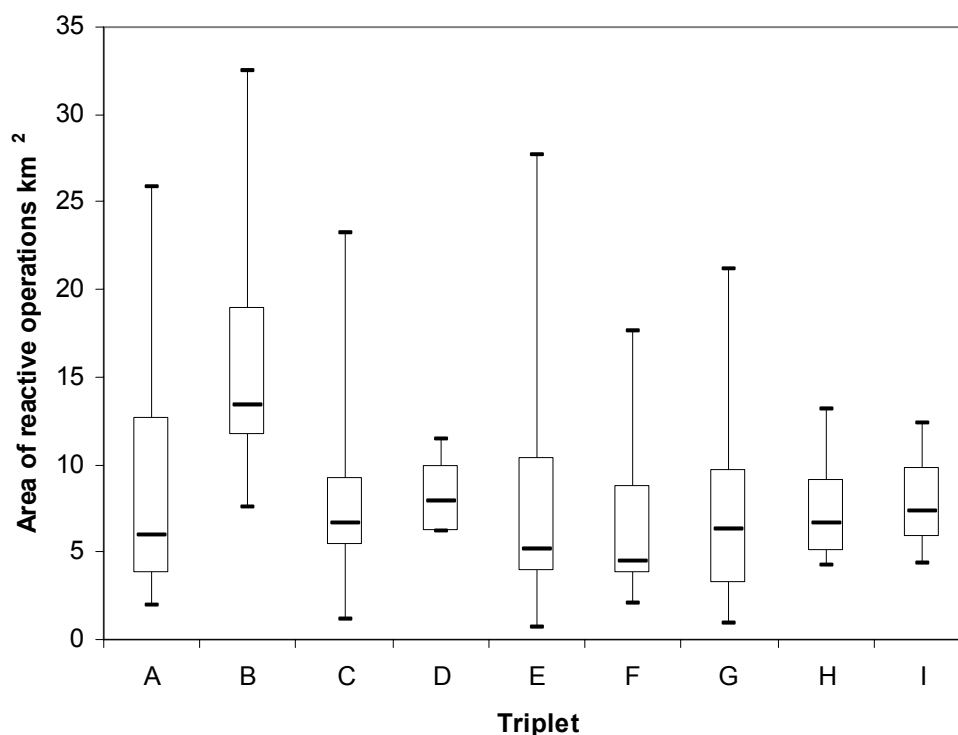
Figure 3.7 Area (km^2) of reactive operations that were culled. Note that the operations included between 1 and 8 breakdown notifications. The box represents the middle 50% of the area or reactive operations; inside the box, the median (the solid line) is the point that 50% of data lie above and 50% below. The minimum and maximum are represented by the lines extending from the box.

3.28   The numbers of badgers culled throughout the trial in reactive areas are shown in Table 3.5. Triplets B, C and F had over 300 badgers taken during operations, together comprising 55% of all the badgers taken in the reactive treatment.

Table 3.5 Number of badgers culled in reactive operations by culling year. Shaded regions relate to periods where triplets had not yet started to contribute information, i.e. they had received no notifications so no reactive operations had yet been carried out.

Triplet	Culling Year				Total
	May 1999-Jan 2000	May 2000-Jan 2001	May 2002-Jan 2003	May 2003-Nov 2003	
A		34	47	36	117
B	73	34	84	110	301
C		179	115	101	395
D				122	122
E			62	126	188
F			145	291	436
G			172	76	248
H			17	143	160
I				94	94
J					0

3.29 As well as the cessation of trapping during the 'closed season' of 1 February to 30 April, the reactive strategy was subject to the same limitations and difficulties that previous strategies such as the "interim strategy" had experienced. Before any field preparations for reactive culling could commence, breakdowns had to be confirmed by laboratory culture of *M bovis* or the presence of visible TB lesions, and then operational staff had to be notified. Staff resources were then timetabled for both field surveys and the subsequent culling. These inevitable delays are a feature of a reactive strategy as it was carried out, though operational improvements were made throughout the implementation of the strategy to try to improve response times.

Effects of culling on badger activity

3.30 It is difficult to measure the effectiveness of badger culling carried out in the course of the RBCT, because there are no techniques currently available that can precisely estimate badger density without intensive monitoring of marked individuals. However, available field data indicate that the levels of badger activity in trial areas are consistent with the treatments applied. Quantification of badger field signs have been shown to give an index of badger density, albeit a somewhat imprecise one.[18] A preliminary analysis of badger survey data from the first three triplets[19] showed that activity was highest in survey-only areas, lowest in proactive areas, and intermediate in reactive areas – exactly as predicted from the treatments implemented. Ongoing analyses of data from three-year surveys carried out in other triplets, and from bait-marking exercises carried out in spring 2004, show identical patterns. Hence, while trapping success was never expected to be total, speculation that illegal culling in survey-only areas might have reduced badger densities below those occurring in culling areas is inconsistent with the available data.

Statistical analysis of treatment comparisons

3.31 From the outset of the RBCT, the ISG agreed that interim analyses of the data emerging from the trial would be undertaken at appropriate intervals, conducted by the two statistician members of the Group, and with the results known only to them and the external statistical auditor (Professor D Mollison of Heriot-Watt University). The method for the interim comparison of outcomes from the three treatments was formulated by the ISG and then approved[9] by the independent statistical auditor in late 2000 at the first interim analysis. Due to the lack of cattle testing during the FMD epidemic, the next analysis was not conducted until 2002. Interim analyses continue to be undertaken and reported to the statistical auditor every six months.

3.32 The analysis of treatment effects compares the number of confirmed cattle herd breakdowns associated with each culling strategy with the number associated with the no-cull survey-only strategy. Breakdowns contribute to the

analysis once the triplet is "active" (from the end of the initial proactive cull). The treatment comparison is adjusted for triplet effects, as well as baseline variables including the number of herds and the historical TB incidence in cattle. In all analyses the standard errors, and therefore all confidence intervals, were adjusted for any overdispersion (that is greater variation in the data than is expected under the assumption of a Poisson model).

3.33 Data relating to each herd breakdown were obtained from the animal health information system VETNET, which holds information on all herds in Great Britain (covering size, type, breakdown history, etc), and their disease management including TB tests conducted by the State Veterinary Service.

3.34 The primary analysis was conducted based on the confirmed breakdowns which had occurred since the end of the initial proactive cull. Additional analyses were conducted using alternative definitions of the time period under study. These included: pre-FMD (breakdowns before 20 February 2001); post-FMD (breakdowns after 28 November 2001); from both the date of the proactive follow-up; and the date of the first reactive cull. For comparison, a second set of analyses were undertaken based on all breakdowns (both confirmed and unconfirmed).

3.35 The baseline number of herds is a measure of the size of the cattle population at risk. Further analyses adjusted for alternative measures of the at-risk population including the baseline number of cattle, the number of whole herd TB tests conducted and the number of cattle tested.

3.36 The primary regression, including the published[20] reactive results, analysed data for all treatments simultaneously. Further analyses were conducted excluding each culling treatment in turn, for all time periods and measures of the size of the population at risk, to examine the robustness of the results.

3.37 If the effectiveness of a culling treatment varies between different triplets as a function of some measured feature of the triplet or of the implementation of the strategy, this would appear (in statistical terms) as an interaction between the treatment comparison and the feature in question. Such effects were investigated as shown in Table 3.6. They included cattle variables, interim badger removal variables, initial badger activity, and time variables.

Table 3.6 Variables tested to examine stability of treatment effects. <u>Counts were log transformed before analysis.</u>

Variable	Description
1. Historical variables	
Number of historical breakdowns	Confirmed herd breakdowns in the three years before the initial proactive cull or before the 2001 UK FMD epidemic for triplets first culled in 2002
Number of badgers culled in badger removal operations	Number of badgers caught during the interim strategy (April 1 1986 to December 12 1998)
Number of badger removal operations	Number of culling operations conducted during the interim strategy (April 1 1986 to December 12 1998)
Badger *M. bovis* prevalence in badger removal operations	Percentage of *M. bovis* positive badgers caught during the interim strategy
2. Time related variables	
Triplet duration	Total number of years since the initial proactive cull in the triplet
Calendar year of breakdown	Analysis conducted on yearly incidence by calendar year and adjusting for the number of days in the year
Year since enrolment	Analysis conducted on yearly incidence by the year since the initial proactive cull
Culling year	Analysis conducted on yearly incidence by culling year May 1 to April 30
3. Trial badger variables	
Number of active main setts	Number of active main setts identified during initial surveys before randomisation
Number of active setts	Number of active setts identified during initial surveys before randomisation
Number of badgers caught in initial and first follow-up proactive culls	
Initial badger prevalence	Percentage of *M bovis* positive badgers caught at initial proactive culls
4. Other trial variables	
Number of baseline herds	Baseline herds must have had a whole herd test in the five years before the initial proactive cull or during the trial and also have been in existence on VETNET
Trap opportunities	Percentage of all cage traps set to catch, which were available to catch badgers, i.e. that were not damaged, and did not catch non-target species etc.
Occupier compliance	Percentage of occupiers agreeing to cull and survey at the time of the analysis
Wildlife unit	The two Defra Wildlife Unit bases, which undertook trial fieldwork including culling operations.

3.38   Additional analyses investigated the effect of treatment on: the number of reactors in completed breakdowns; the time to the end of the breakdown; and the time to a repeat breakdown. A negative binomial distribution was used to analyse the number of reactors in completed breakdowns to allow for the interdependence between cattle in the same herd. The time-to-event variables were investigated using survival analysis methods, and parameters were estimated[21] using the Weibull distribution.

Effect of the reactive treatment

3.39   Statistical analysis of the effect of culling treatments has been undertaken at intervals since 2000 and the findings reported to the independent

statistical auditor. Analyses, based on data on herd breakdowns up to 31 August 2003, revealed[20] that reactive badger culling was associated with an estimated increase of 27% in the incidence of confirmed cattle herd breakdowns (95% overdispersion-adjusted confidence interval (CI): -2.4% decrease to 65% increase). Under its agreed operating procedures the ISG was obliged to bring this information to the attention of Ministers, it being the first time that any clear indications with potential implications for policy had emerged from the trial. However, in its report (copy of report to Minister appendix I), the ISG recommended that culling operations should be continued until the end of the trapping year (31 January 2004) to allow a further analysis of data in March 2004. Our stated judgement was, however, that the position was unlikely to change significantly in the interim. After receiving our report, the Minister decided, in consultation with Defra officials, to suspend reactive culling as from 4 November 2003.

3.40 A further analysis of confirmed breakdowns has subsequently been conducted based on herd breakdowns up to 15 February 2004. These results confirmed the original findings, with the reactive treatment associated with an estimated increase of 28% in confirmed herd breakdowns (overdispersion-adjusted 95% CI: 1.1% to 62% increase) compared to the no-culling survey-only areas.

3.41 We investigated separately the breakdown rates from the initial proactive cull up to the end of the first reactive cull, and from the first reactive cull. Before the first reactive cull 11.9 triplet years had accumulated over all triplets and, as we would expect with not much data, the confidence interval was wide, ranging from a 13% decrease to a 99% increase in herd breakdowns. The overall estimate before reactive culling had occurred was a 30% increase in herd breakdowns in reactive areas compared to survey only areas. Although the point estimate is non-zero, the confidence interval includes zero so there was not a significant increase in herd breakdowns before treatment had commenced. After the first reactive cull, we estimated that the reactive treatment was associated with a 26.2% increase in herd breakdowns compared to survey only areas. These data covered 19.2 triplet years and so the confidence interval is estimated with more precision ranging from a 1.3% decrease to 61% increase. This provides further evidence that reactive culling could not be beneficial in combating TB in cattle.

3.42 The clear conclusion supported by all the analyses undertaken by the ISG is that there is convincing evidence that reactive culling of badgers does not offer a beneficial effect large enough to make it useful as a practical policy option and that there is substantial but not overwhelming evidence of an adverse effect of the reactive strategy. It is not as yet clear how to explain the underlying process that led to this finding; hypotheses relating to 'perturbation' and dispersion of badger populations due to culling have been advanced, but clearly there are complex processes at work within the disease transmission system between cattle and badgers. Nevertheless, the statistical analyses have

been extensive and carefully conducted and the empirical findings are remarkably consistent. One has to add the caveat that the estimated effects refer specifically to the reactive strategy in the form implemented in the RBCT and over the time span considered in the analysis.

Effect of the proactive treatment

3.43   The results on the effect of the proactive treatment remain inconclusive. The treatment continues and the data remain strictly confidential, since premature release could compromise the trial. At the time of the last interim analysis in September 2004, 36 triplet-years had accumulated among the 10 triplets. The initial power calculations suggested[15,16] that 50 triplet-years would be required to detect a difference of 20% in cattle TB incidence associated with either of the culling treatments and this will be reached by February 2006. Subsequent calculations, independently verified[3] by the statistical auditor, have confirmed that we can expect a result to guide policy development by early 2006.

Importance of the scientific results of the trial

3.44   The trial is a key component of the ISG's programme to obtain scientific results to inform the development and implementation of TB policy. There has been some concern expressed that a finding that the proactive culling is associated with only a small, or even no, reduction in TB incidence in cattle would be 'inconclusive'. On the contrary, however, the ISG believes that such a result would be informative in developing future policy with respect to taking action against badgers. Similarly, a finding that proactive culling is associated with a dramatic reduction in TB incidence in cattle would also inform future policy development.

3.45   In view of the possibility that culling policy options trialled in the RBCT are either not sufficiently effective in reducing TB breakdowns, or are too costly to be adopted, the ISG has encouraged Defra to consider alternative TB control strategies. The broad research base that Defra has put in place on ISG advice is specifically designed to scientifically evaluate potential alternative strategies as discussed elsewhere in this report.

Badger Welfare Issues

3.46   Since the inception of the trial, the ISG has been committed to testing the effectiveness of badger culling strategies that would constitute practicable policy options if they were found to be effective. It was considered that if culling strategies had very serious impacts on conservation and animal welfare they would not be sustainable in the long term – not least because they would risk being widely rejected by the public, including landowners in trial areas. Hence, we gave careful consideration to badger welfare in devising culling strategies and Ministers have, since the start of the trial, encouraged and supported this commitment.

3.47   In our First Report[15] we outlined our approaches to two aspects of badger culling that would have implications for badger welfare: the methods used to capture badgers, and the timing of culling in relation to badgers' breeding season. In this section, we use data from the trial to evaluate whether the approaches taken have helped to mitigate the suffering of badgers culled.

3.48   The methods used to kill badgers have been subjected to repeated external and internal audit. Rather than discussing this issue in detail here, we draw readers' attention to the auditors' reports[8, 10, 12], noting simply that the auditors considered badger despatch to be "*humane*", with death occurring instantaneously in "*almost all, if not all, cases*".

Methods of catching badgers – cage trapping

3.49   Badgers culled in the course of the RBCT are captured in cage traps. After a pre-baiting period of up to two weeks, traps are set as late in the day as logistically possible, and checked early the following morning.   Standard operating procedures stipulate that all captured badgers should be despatched before noon; in practice, the majority of badgers are despatched before 10am.

3.50   Krebs *et al.*[2] suggested that snares, rather than cage traps, should be considered to capture badgers as being potentially more effective. In our first report, we gave a detailed explanation of our decision to use cage traps[15]; our reasons included issues of public acceptability, the risk of capturing non-target species that could not easily be released humanely, and a lack of data on the welfare consequences of trapping *vs.* snaring badgers. More recently, one farming lobby group has called for badger gassing (discontinued in 1982 on welfare grounds[22]) to be reinstated [23], and Godfray *et al.*[14] allude to '*more controversial means of culling badgers*' being considered by Defra if the RBCT showed that culling effectively reduced cattle TB.

3.51   Against this background, we present here an evaluation of the injuries sustained by badgers captured in cage traps, and show how these have been influenced by modifications of trap design. A detailed analysis will be published shortly in the peer-reviewed literature[24]. We acknowledge that cage

trapping may have consequences for badger welfare in addition to injuries (particularly stress)[25], however, we argue that measurement of injuries is a useful starting point. We present these data primarily as a basis for comparison with other capture techniques that Defra might consider adopting in future.

3.52   Most badgers (88%) confined to traps since the start of the RBCT in 1998 until 2004 received no detectable injuries as a result of being confined in the trap (Table 3.7). Of those that were injured, most (74%) received only minor skin abrasions. A minority (1.7%) experienced tooth damage likely to have involved serious (albeit short-term) suffering.

3.53   Our analyses indicate that badgers despatched later in the day (and particularly after the noon deadline) are no more likely to receive injuries than those despatched earlier. This is probably because badgers (which are nocturnal) tend to remain fairly inactive in the traps during the day, with most injuries likely occurring in the hours immediately after capture. While trap-related injuries are no more serious if traps are checked late, other forms of suffering (e.g. dehydration) may occur; hence, we have continued to urge WLU staff to check traps as early as possible.

3.54   Two changes were made to the trap design to try to reduce trap-related injury. Untreated wire mesh cages tend to rust quickly, creating an abrasive surface. Hence, following our recommendation in 2001 all traps were coated with a polymer to give a smoother surface, intended to reduce abrasion injuries. Additionally, in November 2002 the door mechanism was modified to try to reduce injuries. This modification involved adding a piece of angle iron to restrict badgers' access to the bottom of the door, a part of the trap that is often a target for biting.

3.55   Coating of traps successfully reduced the proportion of badgers that experienced minor skin abrasions from 12.8% to 7.1%, although it was associated with an increase in the (much smaller) number of animals experiencing more serious abrasions or cuts (from 0.7% to 1.8%). Modification of trap doors reduced the proportion of badgers suffering tooth breakage from 2.9% to 1.1%. While all injuries to trapped badgers are regrettable, we are reassured that the proportions injured have declined in response to trap modification. While additional modifications of trap design and trapping practices (e.g. using a smaller mesh size, possibly checking traps at night) might further reduce the incidence of trap-related injuries, they would probably also have implications for both the humane dispatch of badgers, and the health and safety of field staff. While we shall continue to explore the possibilities for further modifying capture methods to protect badger welfare, we are reassured that the methods currently in use are acceptable. We also note that the same practices are widely used – and licensed by the Home Office – for ecological studies such as Tuttyens et al[17].

Timing of badger capture – the closed season

3.56   As discussed in our first report[15], culling badgers during the late winter and early spring risks leaving unweaned cubs to starve when their mothers are trapped and killed. To avoid this, badger removal operations carried out up to early 1998 released females considered to be lactating. Because these releases have implications for the efficiency of badger culling and TB control, Krebs et al[2] suggested that the practice should be abandoned, as did Dunnet et al[26]. We chose to avoid culling lactating females by instituting a closed season during which all culling was suspended each year.

3.57   The closed season covers the calendar months of February, March and April. These months were selected, on the basis of the best available data on the timing of badger reproduction, to cover the lactation period: we estimated that 92% of cubs should be weaned by 1 May. However, since data on badgers' weaning dates were scarce, we committed to reviewing the performance of the closed season as data became available from the trial. This evaluation will be published shortly in the peer-reviewed literature[27] but it is summarised here.

3.58   We evaluated the efficiency of the closed season by identifying actively lactating females at *post mortem*, and then consulting trapping records to determine whether cubs were caught at the same site (or close by) and, if so, how many were caught. If multiple females were caught at the same sett, we allocated cubs to the most likely mother, based on lactation status, or split cubs equally among mothers. We then compared the litter size captured with published litter sizes, to estimate whether complete litters were likely to have been caught.

3.59   In no cases were lactating females caught immediately prior to the closed season (in January). This may be because very few females give birth so early, or because females with very young cubs are reluctant to enter traps. In either case, this suggests that an earlier start to the closed season would not reduce the number of cubs left to starve.

3.60   By contrast, we estimated that, across four culling years (1999, 2000, 2002, 2003), a total of 36 unweaned cubs (average 9 *p.a.*) may have been missed by trapping operations when their mothers were culled in the month of May, immediately after the end of the closed season. This contrasts with a prediction of 2,300 cubs projected and publicised by the National Federation of Badger Groups (NFBG) for roughly the same period[28], an estimate we always considered to be an unrealistic figure. The difference between the NFBG projection and our estimate possibly relates to the frequency distribution of badger births[29] used by the NFBG, which over-estimates the extremes of unseasonal birth dates, and from the NFBG's assumptions concerning the timing of trapping outside the closed season.

3.61   Adoption of the closed season had some practical disadvantages, since it limited the time available for badger culling, and necessarily delayed responses to TB breakdowns in cattle herds in reactive treatment areas (many of which are disclosed during autumn/winter when cattle are housed and when testing intensity is greatest[16]). Delays to reactive culling imposed by the closed season have been linked to the failure of this experimental treatment to reduce the incidence of cattle TB[14].   While the reactive treatment has now been suspended, the attention paid to aspects of the trial concerned with badger welfare suggests that managers might wish, in future, to modify[14,30] these procedures should badger culling form a component of future TB control policy. It is appropriate, therefore, to consider whether the length of the closed season could or should be altered.

3.62   Trial data cannot be used to evaluate the impact of shortening the closed season, since by definition no information could be gathered when culling was suspended. However, data on the timing of badger reproduction suggest that shortening the closed season would lead to a marked increase in the number of cubs left to starve in the sett.

3.63   The effects of prolonging the closed season are more easily assessed. Extending the closed season back to January would appear to have few benefits as no lactating females were culled in January. Extending the season into May could reduce the number of actively lactating females culled, although it would be impossible to eliminate entirely the risk of missing dependent cubs. Under the existing closed season, the number of unweaned cubs missed by culling operations is low (approximately 9 per year) relative to the total number of badgers culled. Extending the closed season would involve compromises to the effective implementation of badger culling as an experimental treatment and as a candidate TB control policy. We conclude that the length of the closed season is currently appropriate for use in the field trial. However, we propose to continue evaluation of the closed season's performance throughout the course of the field trial, and to modify it in future if necessary. We also recognise that it may be appropriate to reconsider the length of the closed season in future, should trial results indicate that badger culling may form an effective component of TB control policy.

Table 3.7 Injuries sustained by badgers while confined to traps from May 2000 to August 2003

Type of injury	Number (percentage)
TOTAL WITHOUT INJURY	**4,407 (88.4%)**
Abrasion of snout only	181 (3.6%)
Abrasion of limbs only	200 (4.0%)
Abrasion of snout & limbs	46 (0.9%)
TOTAL WITH SKIN ABRASION ONLY	**427 (8.6%)**
Cuts on limb only	13 (0.3%)
Damage to claws only	40 (0.8%)
Cuts on head only	–
Cuts on limb with damage to claw	0 (0%)
TOTAL WITH CUTS ONLY	**43 (0.9%)**
Cuts on limb with abrasion of snout	3 (0.06%)
Cuts on limb with abrasion of limb	2 (0.04%)
Damage to claw with abrasion of snout	2 (0.04%)
Damage to claw with abrasion of limbs	4 (0.08%)
Cuts on head and abrasion of snout	–
Cuts on head and abrasion of limb	–
Cuts on limb with abrasion of snout & limbs	1 (0.02%)
Damage to claw with abrasion of snout & limbs	1 (0.02%)
Cuts on head and abrasion of snout & limb	–
TOTAL WITH CUTS AND ABRASIONS	**13 (0.3%)**
Damage to teeth only	56 (1.1%)
Damage to teeth & jaw only	10 (0.2%)
Damage to teeth with abrasion of snout	4 (0.08%)
Damage to teeth with abrasion of limb	6 (0.1%)
Damage to jaw with abrasion of snout	2 (0.04%)
Damage to teeth with cuts on limb	1 (0.02%)
Damage to teeth & claws	6 (0.1%)
Damage to teeth & claws and cuts on limb	0 (0%)
TOTAL WITH TOOTH BREAKAGE OR JAW DAMAGE	**85 (1.7%)**
TOTAL INJURED	**578 (11.6%)**

4.   TB99 EPIDEMIOLOGICAL SURVEY

Background

4.1   With the initiation of the Randomised Badger Culling Trial (RBCT) in 1998, the ISG recognised the need for the collection of comprehensive epidemiological data that would describe the distribution of TB breakdowns, provide husbandry advice relating to more effective on-farm biosecurity and, through analysis, identify testable hypotheses about those factors that could influence disease outbreaks.

4.2   Several risk factors, particularly in relation to cattle husbandry and environmental practices, have been suggested as predisposing farms to TB breakdowns.   Such risk factors are not amenable to being investigated by designed experiments with controls, because of the large number of variable factors, the impracticality of conducting controlled experiments on commercial livestock farms, and the need for data from a large number of representative TB breakdowns.   In such circumstances, a 'case-control' study provides the appropriate approach and this was the method we adopted to identify and quantify risk factors in the TB99 study.   This epidemiological study is of fundamental importance to the TB research programme, and was designed to provide data to complement that from the RBCT.   Its objectives were addressed through the implementation of the specially constructed TB99 epidemiological questionnaire, which was designed to collect epidemiological data on risk factors, as well as assisting the State Veterinary Service (SVS) to manage the TB breakdown.

Case-control approach

4.3   The data collected using the TB99 epidemiological survey allow investigations into the wide range of factors potentially associated with an increased (or decreased) risk of TB in cattle.   These include herd size and composition, environmental factors such as land cover and soil type, and husbandry factors such as grazing system and housing.   One strength of the case-control approach is that a relatively large number of factors may be investigated simultaneously within the framework of such a large-scale survey.

4.4   A case-control study involves the collection of data from TB affected farms, the 'cases' and equivalent data from similar farms without TB, the 'controls'.   Structured comparisons between the two datasets can provide evidence of associations between TB breakdowns and risk factors. Due to the relative infrequency of TB breakdowns, the case-control method represents the most economical study design to search for associations with TB breakdowns, and yields estimates of relative risk of various factors, which can be prioritised.

4.5   Ideally, the two groups of farms should differ only in their case-control status and prior exposure to a risk factor. To address this, and also to take account of potential spatial associations, the objective in the TB99 study was to collect data from three control farms (one contiguous and two non-contiguous) for every case breakdown farm in trial areas. The use of three controls per case increases the sensitivity of the study, whereby risk factors associated with breakdowns on farms can be detected.

Survey developments 1998-2004

4.6   The ISG's original recommendation in 1998 was to focus TB99 data collection initially in trial areas. On this basis, it was expected that after two years there would be sufficient data for meaningful analyses to be undertaken. However, at MAFF's insistence, the TB99 questionnaire was, from the outset, also applied outside trial areas as a disease management tool, and as a means of describing the epidemiology of TB breakdowns nationally; however in those areas no comparative control data were to be collected.

4.7   The ISG had undertaken to carry out an initial analysis of TB99 data when 100 complete datasets (i.e. 100 cases each with three matched controls) were available from the trial areas. The purpose of this was to provide insights to inform any modifications of the questionnaire that might improve data collection, and to determine if strong associations of risk could be identified at that early stage. It was anticipated that this point would have been reached by the end of the 2000-culling season (January 2001), when, as stated in reports, the Group also planned to redesign the TB99 questionnaire.

4.8   As early as 1999 the ISG was advised by MAFF that data for control farms in trial areas were not being collected to match breakdown data, despite being required by the case-control design. Of 43 breakdowns in 1999, 41 appeared in the database, and only 11 had the requisite 3 controls, 8 had 2 controls and 7 had 1 control; i.e. data for only 56 controls overall were obtained out of a total of 123 controls that should have been collected. Also, 15 of the 41 completed questionnaires were cases only, with no accompanying control data. MAFF gave assurances that this issue was being addressed.

4.9   The Classical Swine Fever (CSF) epidemic in 2000, and the FMD epidemic in 2001, intervened to divert the SVS and reduce seriously its capacity to carry out tuberculin testing and to collect the data required. It became apparent, however, that after SVS field operations resumed in late 2001, data collection for TB99 was still not receiving high priority. As a result of the ISG expressing its concerns, extra resources were directed to this part of the work programme. In addition, at the request of Defra, the ISG agreed to changes in the structure of the TB99 questionnaire, so that Part 1 specifically addressed the management of the incident, and Part 2 the collection of data on risk factors for scientific evaluation.

4.10   To address the backlog that had developed by the end of 2002, the SVS identified 3 categories of TB99 questionnaires to be considered: 1) cases in trial areas, 2) controls in trial areas, and 3) cases outside trial areas. The SVS gave priority to breakdown management sections (Part 1) of TB99 for cases inside and outside trial areas. Only then were risk factor data collected (Part 2 of TB99) for cases inside and outside trial areas. Collection of risk factor data for controls was given the lowest priority. In response to this the ISG recommended that priority be given to completion of both breakdown management and risk factor data sections for cases inside trial areas, followed by risk factor data for controls and finally to breakdown management sections for cases outside trial areas. This approach was accepted for implementation. Additionally, at the start of 2003 Defra took the decision to cease collecting risk factor data (Part 2) for cases outside trial areas because of SVS resource constraints. This decision was regrettable but it was at least consistent with the ISG's wishes that TB99 effort in the trial areas should not be compromised.

4.11   In 2002 Defra engaged the services of ADAS to assist the SVS with the backlog of TB99 questionnaire completion in trial areas, and in particular with the completion of appropriate time-matched controls for each of the TB99 case reports. The ISG expressed the wish that the SVS should continue to collect data in order to avoid potential inconsistencies in the way questionnaires were completed. However, the Group agreed to ADAS input on the basis that cases collected by ADAS would have their associated matched controls also collected by ADAS, and similarly cases collected by the SVS would continue to have their associated matched controls collected by the SVS. With ADAS assistance an increased proportion of TB99 controls have been collected since 2002. However in 2002 alone, there were 340 cases collected by the SVS of which they only managed to collect an associated 20 controls, the remaining matched controls for these cases being collected by ADAS. Clearly, a large number of cases have had their matched controls collected by a different organisation. This shortcoming is of major concern to the ISG as it poses a threat to the validity and appropriateness of the data for scientific analysis. The table shows the number of case and control reports collected up to the first week of November 2004.

Table 4.1 Number of case and control reports collected up to the first week of November 2004

Year	Triplets included at end of year[a]	Case Reports		Control Reports		Cases with at least 1 control	No. of cases with:		
		Expected[b]	Received[c]	Expected[d]	Received[e]		1 control	2 controls	3 controls
1998	1	2	2	6	0	0	0	0	0
1999	2	43	41	123	56	26	7	8	11
2000	7	198	156	468	112	52	14	16	22
2001	7	125	45	135	10	6	3	2	1
2002	10	492	443	1329	361	219	101	94	24
2003	10	527	457	1371	273	179	100	64	15
2004	3	109	92	132	76	76	27	42	7
Total		1496	1236	3564	888	558	252	226	80

[a] *Number of Triplets operational at the end of that year reflecting enrolment to the RBCT. For 2004 collection of cases and controls was limited to triplets B, D and E only.*
[b] *A TB99 is expected for any unconfirmed or confirmed breakdown in a trial area since the end date proactive cull for that Triplet.*
[c] *Does not include any TB99s received that cannot be attributed to a breakdown or appear invalid i.e. unconfirmed outside a trial area.*
[d] *Expected controls for the TB99s received - 3 times the number of TB99s received.*
[e] *An additional 2 controls do not link to any cases.*

4.12   Although the situation ultimately improved, it remains that, despite repeated emphasis by the ISG, implementation of the TB99 has been inadequate for such an important element of the TB research effort. Although over 1400 TB cases have been reported since the start of the trial in 1998, insufficient controls have yet to be collected to provide 100 complete data sets, originally conceived by the ISG as the benchmark for an initial analysis; furthermore, the opportunity to collect some data has been irretrievably lost. With the increase in herd breakdown rates in recent years and all ten triplets in the RBCT becoming active, the number of cases in each of the years 2002 and 2003 has been more than originally anticipated. However, the number of controls obtained has been many fewer than planned due to lack of attention to the collection of control farm data and in some triplets the difficulties of finding herds which have been TB-free for 12 months prior to the case breakdown (the criterion for eligibility to serve as a control).

Analysis of data

4.13   The Third Report[1] of the ISG provided some preliminary analyses of the TB99 questionnaire but this was limited to farms outside trial areas between 1998 and early 2001. Descriptive statistics were reported on herd sizes, cattle age and location, environment and human TB infection. In addition, these summary data were used to assess the performance of the tuberculin skin test in identifying TB-infected animals.

4.14   In view of the disruption to TB testing arising from the FMD epidemic in 2001 and consequently the small number of TB99 case reports for that year, it was recognised that the TB99 case and control data for the pre-FMD period provided a clearly defined set of data for analysis. Although the number of cases before 1 January 2001 exceeded 100, the requirement for 3 matched controls had not been met and so the principal analysis approach was unable to take satisfactory account of herd matching. Nonetheless data for a total of 117 contiguous and non-contiguous control herds were available for comparison with 151 case herds from the three trial triplets A, B and C, which were active before 2001. It is recognised that the control farms choosing to take part may be atypical, although such checks as are possible are reassuring.

4.15   A large number of explanatory factors from the TB99 questionnaire were screened for association with the risk of a herd breakdown. Using logistic regression analysis, with triplet, treatment and herd size as forced covariates, in the final regression model four factors were identified as being associated with an increased risk of a TB breakdown and two factors as being associated with a decreased risk. In particular, cattle brought on to the farm from markets or from farm sales, the use of covered yard housing and use of 'other' housing types, and a cattle farm operating two or more farm premises were associated with an increased risk of a breakdown. The highest odds ratio to be associated with an increased risk was 4.22 (95% CI: 1.41 to 12.65) for the use of covered yard housing. (This odds ratio means that a TB breakdown was observed to be 4.22 times more likely on farms where covered yard housing was used than on farms where this did not occur.) The lowest odds ratio associated with an increased risk was 1.79 (95% CI 0.97 to 3.32) for use of two or more premises. In contrast, use of artificial fertiliser or farmyard manure were associated with a *decreased* risk of a breakdown with odds ratios 0.21 (95% CI 0.07 to 0.63) and 0.42 (95% CI 0.20 to 0.85), respectively.

4.16   The findings of factors associated with increased risk are all relatively plausible, but it is less easy to explain the apparent risk-reducing factors. These results from the analysis of the first tranche of the TB99 data have identified herd-level risk factors associated with TB breakdowns. Because of potential biases and the possibility that some explanatory factors are surrogates for other more biologically relevant variables, the findings must be treated cautiously.   At this stage, they cannot be regarded as causes, but as associations; drawing specific conclusions will require further proof and in particular the further evidence to be gained from TB99 data collected after the FMD epidemic.

4.17   More extensive discussion of the methods of analysis and of the findings from the pre-FMD TB99 analyses has been prepared for peer-review and publication. These will appear[31] early in 2005. Similar work is in hand to identify risk factors associated with herd breakdowns for 2002, when sufficient data from seven triplets were available for analysis (the last three triplets

became active in October and December 2002, too late in the year for sufficient TB99 data to be accrued) and the dataset therefore more broadly based. In view of changes made to the TB99 questionnaire before its relaunch in 2002 after FMD, this more extended analysis will provide an opportunity for the pre-FMD results to be further assessed and for additional factors to be considered with greater precision using data from over 400 case and 300 control herds. Analyses of the 2003 and 2004 data will also be possible once all case and control data have been entered into the TB99 database maintained by the VLA.

Future developments and strategy

4.18   Clearly an immediate consequence of MAFF/Defra's failure to manage the collection of adequate and appropriate TB99 case and control data has been an unfortunate waste of resource and, significantly, a delayed opportunity not only to conduct the initial analyses but also the lost possibility for the ISG to carry out a robust enough analysis to more usefully inform interim control policies.

4.19   The House of Commons Environment, Food and Rural Affairs Committee Review of Badgers and Bovine TB noted[6] that the TB99 form was complex and time-consuming for farmers and veterinarians to complete. The TB99 programme was audited[4] in 2003 by Dr Martine Wahl of Clinical Research & Communication, Basel, who was specifically appointed for the purpose. Key recommendations made were that (1) the questionnaire should be made simpler and easier to complete - a stated objective of the ISG that the Group expected to meet in 2001; (2) that mechanisms should be put in place to ensure the quality of the data; and (3) that TB99 data collection should be run by a Project Manager with a small dedicated team.

4.20   In view of the large numbers of TB breakdowns during 2002 and 2003 in the RBCT triplets, the ISG has advised focusing effort to collect control data and to complete as many of the outstanding data sets as possible for this period. For 2004, it has recommended that subject to unhindered progress being made with the TB99 survey in 2003, TB99 data collection should no longer be applied across all triplets. Instead, sentinel data collection should take place in three of the ten triplets (nominated to be triplets B, D and E) to provide completed questionnaires on approximately 100 cases and associated controls. This reduced effort will result in substantial savings while focusing resources on the collection of three controls per case.

4.21   As the end of 2004 approaches, it is likely that the target of 100 cases will be achieved, but not the 300 controls. For some cases it has been difficult to allocate suitable controls but there still remain difficulties in obtaining farmer consent and completing the questionnaire. Consequently it will be difficult for Defra to obtain even 100 controls. The ISG has given advice that effort should focus on controls if the 2004 TB99 information is to be useful.

4.22   In keeping with the recommendations of the TB99 auditor and other stakeholders, the TB99 questionnaire is undergoing substantial revision to provide a new simpler and much shorter form for 2005. A working group with members from the ISG, Defra, VLA and SVS is undertaking the redesign of the TB99 form and its implementation.   In view of VLA's competent database provision for handling existing TB99 case and control records, it is the wish of the ISG that this should continue for the new form and allow for interaction with the SVS VETNET database. The new questionnaire format will make use of existing databases, which will improve its accuracy and consistency while requiring considerably less information to be collected at the farm level.   In addition, it will provide an opportunity for improving the clarity of the questions and removing ambiguity.   The new form has been piloted and it is planned to introduce it in 2005, to replace the TB99 questionnaire. This will provide continued collection of risk factor information from a sample of triplets during the final stages of the RBCT and provide valuable information from outside the triplets.

4.23   The ISG continues to stress that the collection and analysis of TB99 epidemiological survey data is of central importance to contribute to the understanding of the epidemiology of TB in cattle herds, and hence is an essential element in the scientific information base needed for the design and implementation of more effective TB control strategies. The approach is broad and part of a process to identify risk factors for breakdowns at herd level, which has to be balanced against the appropriateness of the questionnaire, the quality of the data collection and further corroborative evidence. As the risk factors become more clearly identified, it will be important for the findings to contribute to TB control through informed policy initiatives on improved and better directed on-farm husbandry and cattle management practices.

5.   ROAD TRAFFIC ACCIDENT (RTA) SURVEY

5.1   The Krebs report[2] recommended a survey to collect badgers found dead on roadsides and to identify what proportion of these showed evidence of *M. bovis* infection. It was thought that this would allow an additional analysis of the link between herd breakdowns and the prevalence of *M. bovis* infection in badgers over time and space. The ISG supported the Krebs recommendation as an important means of collecting data on the prevalence of TB in badgers within and outside trial areas, recognising that future control policy options may require data on badger prevalence on a wider basis than that which is otherwise available only for trial areas. In the absence of a reliable test, or range of tests, to diagnose the infection in live badgers, the RTA was seen as the only practical and acceptable way of estimating the prevalence of *M.bovis* infection in the wildlife population.

5.2   In line with the Krebs recommendation, the ISG decided to target areas with high or increasing herd breakdown rates (including those in the RBCT) and areas nearby with low breakdown rates. We recognised that the ability of the RTA survey to provide prevalence data required validation that could be obtained only by comparison with the accurate measured prevalence data obtained within the RBCT.

5.3   The ISG originally proposed that RTA survey data should be collected from areas within and adjacent to trial areas and not specifically on the basis of whole counties. Subsequently, the choice of counties for data collection was made to enable the publicity of badger collection to be targeted at recognisable areas. Seven counties were chosen for the RTA survey: Cornwall, Devon, Gloucestershire, Herefordshire and Worcestershire were selected as high risk areas and Shropshire and Dorset were selected as nearby counties with low breakdown rates. In these counties the existence of the survey was publicised and members of the public invited to inform Defra of any badgers seen dead by the roadside. These were collected and sent to VLA laboratories for post mortem and culture of the *M. bovis* organism.

5.4   Data collected on infection prevalence in badgers will initially be used to estimate regional (county-level) prevalence. As sample sizes increase, the data will be used to estimate local (within-county) trends and prevalence.

5.5   The validation of prevalence of *M. bovis* infection in badgers derived from the RTA survey data, by comparing it with RBCT data collected nearby in space and time, is the first step of the analysis. If no significant divergence is found, then the RTA data can be interpreted as providing a dependable estimate of the infection prevalence in the badger population from which they were collected. If a bias were found (for example, if RTA badgers were many times more likely to be infected than comparable RBCT badgers), it would

have to be determined whether an estimated calibration factor could be applied to the RTA data to give suitable prevalence estimates and comparisons.

5.6   To achieve these goals, the ISG indicated at the outset the need for a sample size of 1200 badger carcasses a year for post mortem examination and diagnosis. However, only in 2003 was this goal, near to being achieved- Table 5.1.

5.7   The ability of the RTA to inform policy decisions will depend on the reliability with which the level and trends in prevalence of *M. bovis* infection in badger populations in RTA surveyed areas can be estimated.

5.8   Farming groups and others have urged Defra to extend the geographic scope of the RTA survey with the expectancy that it would usefully inform decisions on policy to improve control of the disease in cattle. The ISG has advised that until it has been demonstrated that the RTA survey can provide prevalence data of sufficient sensitivity to detect major spatial and temporal changes, (and there is doubt about that), an extended survey will add little scientific information to inform disease control policies.   The ISG has emphasised this point in correspondence with the CVO, which relates to a Defra proposal for a limited RTA survey in the Furness Peninsula (Appendix I - letter dated 10 November 2003).

Table 5.1: Number of badger carcases collected and post mortemed in the RTA survey in each calendar year up to September 2004

Years	Number of carcases collected	Number of badgers post-mortemed
Nov 2000 – Feb 2001	233	197
2002	787	662
2003	1057	849
2004 (as at 30 Sept 2004)	962	802

6.   VACCINE DEVELOPMENT

6.1   The Krebs Committee[2] considered vaccination of either cattle or wildlife to be a potential long term policy option for TB control. It recommended that a research programme should be initiated to develop a vaccine against TB in cattle, but it also stated that the opportunity of developing a vaccine for use in badgers should not be overlooked. The latter vaccine would not be required to protect individual animals against TB, but rather its use would be to reduce transmission to cattle, assuming badger infection to be a major source of herd breakdowns. Thus, a vaccine which lessened the excretion of bacteria could have a beneficial effect in reducing transmission.

6.2   MAFF started in 1998, and Defra has continued, a research programme to develop bovine TB vaccines, spending between £1-2 million each year. Research at the VLA, Weybridge and at the IAH, Compton, is taking place to produce candidate vaccines and to evaluate these in the target species. The candidates include a range of live attenuated vaccines and sub-unit vaccines. Vaccine delivery systems are also being developed.

6.3   A Vaccine Scoping Study Sub-Committee (VSSSC) of the ISG has completed a study[5] to examine and report on the feasibility for pursuing a TB vaccination strategy for either cattle or wildlife and has considered future research requirements to complement those already in place. The Scoping Study was presented to Ministers in July 2003 and its membership and an executive summary are reproduced as Appendices F and G.

6.4   Vaccines are often spoken about simplistically and this reflects a presumption that a vaccine for either cattle or badgers is scientifically, technically and operationally easy to put in place. Such a view ignores both the scientific difficulties to overcome in developing, testing and implementing a successful vaccine, and the financial and time frame requirements to validate the vaccine in the field. The Scoping Study advised that there was currently no suitable vaccine available that could be considered for use in cattle although the use of the human vaccine, BCG (Bacillus Calmette and Guerin), might be considered for use in badgers. The VSSSC recommended nonetheless that both vaccine options should be pursued, since it was recognised that the generic enabling research would be applicable for both cattle and badger vaccines and would greatly benefit from the ongoing international collaborations with workers trying to develop an improved human vaccine against *M. tuberculosis*. However, it is also quite clear that improved diagnostics for cattle must be developed as an essential complement to any vaccine control strategy.

6.5   Previous studies on a number of species in laboratory tests have demonstrated[5] a usually beneficial but variable degree of protection to experimental challenge with *M. bovis* following parenteral vaccination with

BCG. Some of this beneficial effect has been revealed in badgers. However, quantification of the effectiveness of BCG under field conditions is essential before any assessment can be made of its use as a practical disease control policy, and such analysis would necessitate setting up a scientifically designed trial with clear objectives. The Scoping Study advised that such a trial should be guided by the outcome of the RBCT, which is expected to be completed by 2006, since the impact of culling badgers on cattle herd TB breakdowns would then be known, and this could assist in making an estimate of the likely impact of badger vaccination on the disease in cattle. The Scoping Study further advised that if a badger vaccination trial was thought to be justified, it would have to be conducted on a very large scale to include an appropriate number of cattle herds if the effect of vaccination on herd breakdown rates was to yield a statistically meaningful measure. It would have to be similar in size to the ongoing RBCT and conducted over the same time scale or longer. Having to conduct a trial on this scale would, for logistical reasons alone, discount the use of parenteral vaccination of trapped badgers; it would also prohibit the subsequent implementation of this delivery method as a practical control policy option. The need would therefore be for the use of non-parenteral vaccination, possibly using an oral bait.

6.6   In view of the obvious cost and scale of the trials outlined above, enthusiasm has, perhaps understandably, been redirected to the possibility of conducting a small, quick, trial based on badgers alone, using parenteral vaccination of BCG. It has been assumed this could provide an indicator for the potential policy value of badger vaccination to control cattle TB, by measuring its impact solely on the disease in badgers with no reference to associated herd breakdowns. The ISG has looked closely at field trial protocols based on a number of assumptions with respect to vaccine efficacy, *M.bovis* prevalence in badgers and predicted mortality of badgers among others (Appendix H). On the basis of this, it has to advise that such an approach to measure the impact of BCG vaccination on bovine TB in badgers (rather than its impact on the disease incidence in cattle, the ultimate target species) is unrealistic; even a small scale trial would inevitably have to include a very large number of badgers to be statistically meaningful. Moreover we believe it would need to be guided by the outcome of the RBCT, not on its validity, but on its value, since culling badgers (unless accompanied by massive perturbation) would be expected to be more effective at controlling cattle TB than BCG vaccination of badgers.

6.7   An added difficulty of assessing the impact of badger vaccination on other than the ultimate target, cattle TB herd breakdowns, is how to measure effectively the impact on TB in badgers, since badgers protected by BCG will receive only partial protection, and will develop pathology when exposed to infection from whatever source.

7.   DIAGNOSIS OF TUBERCULOSIS IN CATTLE

7.1   A critical requirement of a disease eradication programme is accurate and sensitive disease diagnosis. The low levels and intermittent nature of excretion of *M. bovis* by infected cattle preclude the use of culture and antigen detection systems for diagnosis in the live animal. For similar reasons newer DNA technologies, including the polymerase chain reaction (PCR), are also inadequate. Diagnosis must therefore be based on detection of a specific immune response to *M. bovis*. Because antibody responses in cattle are variable in magnitude and onset, diagnosis has relied on the detection of cell mediated immune responses to the TB organism by using the tuberculin skin test.

Tuberculin skin test

7.2   The background to the development and use of this test is described in the ISG's Second Report[16] (appendix C) where its advantages and disadvantages are documented. The main shortcomings of the test are: 1) difficulties of quality control, which relate to batch-to-batch variation of the diagnostic protein (purified protein derivative - PPD) and the subjectivity of applying and reading the test; 2) difficulties in interpretation of the test due to complications of immunological cross-reactivity between *M. bovis* and other Mycobacteria, which are detected in the test by comparison of responses to *M. bovis* and *M. avium* PPD. The criteria that define a positive reading are set to give high specificity (i.e. to avoid giving positive readings in TB–free herds) but in so doing compromise the sensitivity of the test; and 3) the requirement for a repeat farm visit to complete the test. Despite these limitations, use of the tuberculin test to identify test-positive cattle for slaughter, plus imposition of restrictions on the movement of animals from breakdown farms, have contributed to the successful control of TB in many countries and in parts of Great Britain. However, use of these control procedures has not prevented spread of the disease to farms in previously relatively disease-free areas of Great Britain over the past two decades. There has also been a year on year increase in the number of herd breakdowns in traditionally high incidence areas.

7.3   The latter has been widely interpreted as indicative of a continuing, and geographically extending, source of infection from wildlife, specifically the badger, leading to the notion that control strategies should focus primarily on elimination of the wildlife source of infection, coupled with current herd testing procedures. The higher frequency of testing in high incidence regions coupled with the prevailing belief that the testing protocols are effective in clearing herds of infection, would, it is claimed, minimise the possibility of cattle to cattle transmission.

7.4   We have questioned this dogma, since we believe that higher levels of infection, irrespective of the source of disease, may place greater demands on the diagnostic test, whose sensitivity may not be sufficiently high to deal with a situation where there is repeated introduction of infection. The manner in which the disease has spread to new areas would support this view.

7.5   The tuberculin skin test was developed and, in initial TB control programmes, used as a whole herd test to identify and eliminate infected herds, or groups of animals within a herd. This type of application is now relatively rare however, and the tuberculin test is now used almost exclusively as a test to detect individual TB-infected animals, in order to identify and remove them from the herd. This is emphasised by the fact that testing reveals only one tuberculin–positive animal in almost 50% of confirmed herd breakdowns. Meeting such a focused objective places a great demand on the test with respect to its sensitivity.

7.6   The sensitivity of the tuberculin test has been estimated in a number of field studies, which have yielded values ranging from 68% to 83% (ISG second report[16] Appendix C Table Cvii). However, many of these studies involved relatively small numbers of animals and in some cases the level of interpretation of the tuberculin test (standard or severe) used to define the reactor animals was not specified. Thus, dependable figures on the sensitivity in practice of the tuberculin test in Great Britain are lacking. Sensitivity probably falls within the above wide range, although it may well differ across the country due to the complicating effect of other species of Mycobacteria and the varying levels of infection with *M. bovis* in the local cattle populations. However, the failure of the test to detect a significant proportion (perhaps one quarter or more) of TB infected animals, some of which would be expected to have the potential to transmit the disease, has obvious practical relevance. There is a strong likelihood of the prolongation of herd restrictions due to previously undiagnosed animals being subsequently correctly diagnosed at follow up tests, and of cattle-to-cattle spread of the disease within and between herds. The worrying finding of such a high proportion of herd breakdowns in herds re-stocked following FMD, as a consequence of cattle movement, is commented on in Chapter 9.

7.7   Experimental and field studies on the pathogenesis of TB in cattle as part of the on-going programme of Defra-funded research, have demonstrated opportunities for disease transmission from infected animals in the very early as well as later stages of the disease process. Some of the infected animals were not diagnosed by the tuberculin test but were diagnosed by the IFN assay test.

Gamma interferon assay test

7.8   The recognised shortcomings of the tuberculin test, including the limitation in its sensitivity, have encouraged the development of alternative *in vitro* tests. A test involving the culture of whole blood with *M. bovis* antigen and measurement of interferon (IFN) production by responding T-lymphocytes after 16-24 hours has been developed in Australia[32, 33]. It is claimed that this test offers an additional tool that can be used strategically in TB control programmes[34]. Being laboratory based, the IFN assay test can be subjected to quality control more easily than the tuberculin test, requires one farm visit only, and does not result in interference of responses during the post-injection period, allowing testing to be repeated more frequently than the skin test without compromising test results.

7.9   It is claimed [34] that the high sensitivity of the IFN test makes it ideal for use in situations where the prevalence of TB is high or where disease is spreading into new areas, where detection of as many animals as possible is desired.

7.10   Stated values for specificity of the IFN test, as for the tuberculin test, vary widely and for both tests these must be viewed cautiously, since they depend on how the test is read and on local environmental factors. Results of field trials carried out in Australia, Northern Ireland and the Republic of Ireland (see our Second Report, Appendix C [16]) indicate higher sensitivity than the tuberculin test; however, a reduced specificity compared to the tuberculin test implies it is more prone to falsely identifying cattle as TB positive although Italian trials[35] claim that the specificity of the IFN test is higher than that of the skin test. This underpins the need for the collection of comparable data under conditions pertaining to Great Britain (see below).

7.11   Neither the tuberculin test nor the IFN assay test, as currently used, detects all animals that have been exposed to *M. bovis*. However, each test identifies a mainly overlapping but different cohort of infected animals, so that by using the tests in combination, it is possible to enhance the overall sensitivity of diagnosis. In view of the possible limitation in specificity of the IFN test, it is claimed that, in its current form, it would not be practical or cost-effective as an alternative test to the tuberculin test. On the other hand, it is an empirical matter (and one that has not yet been examined) as to whether, in a situation where infection appears to be spreading widely and rapidly, it might still be economically worthwhile employing the IFN test, despite its likelihood of identifying more animals for slaughter. Nevertheless, we consider that there are circumstances where complementary use of the IFN test along with the tuberculin test would be justified to provide for more effective control of TB in cattle.

7.12   We strongly emphasise that more effective control of the disease must depend on improved disease diagnosis and advise that urgent action be taken. The amount of cattle-to-cattle transmission depends on the length of time an infectious animal remains undetected. Even with a perfect test procedure i.e. 100% sensitivity, this period could be up to one year for areas subjected to annual testing. With an imperfect test, the period of exposure, during which there is potential for disease transmission, could be up to two years or even much longer. An annual test with a sensitivity of 66% (i.e. with a chance of 1 in 3 of failing to detect an infectious animal) can be shown, by simple modelling, to be approximately equivalent to a perfect test when the latter is applied at a two year interval. An increase in sensitivity from 66% to the range of 80-90% would lead to a noticeable improvement in the effective exposure, reducing this to roughly 1.2 years on average. This provides a strong argument that an appreciable improvement in test sensitivity would have a noticeable impact on reducing disease prevalence. Previous ISG reports have highlighted the critical importance of this and strongly supported work, in the laboratory and the field, to further refine diagnostic tests, particularly the IFN assay test, and gain experience of its use in the field. We have encouraged the setting up of a scientifically designed field trial to assess the currently available IFN test as a necessary step. We believe that it is essential that data be obtained on the IFN test under epidemiological conditions that prevail in Great Britain and particularly to compare its performance with that of the tuberculin test. The collection of these data is necessary for informed strategic decisions to be taken on the most effective use of IFN in a range of control options.

7.13   The ISG designed and recommended the implementation of, in the first instance, a small scale field trial, as part of adaptive management of the disease, to provide maximal scientific data in the most economic and practical way in order that the two tests could be compared and economically evaluated for a range of potential future control options. It is of extreme concern to the Group that following presentation of these proposals, Defra nevertheless implemented a pilot study of limited scope, and without any genuine attempt to consult the ISG or provide a sound scientific protocol for the study. The ISG concerns expressed in a letter to Ministers at the time (Appendix I –7 November 2002) remain. The ISG recognises its responsibility to advise on the provision of a science base to underpin a range of potential policy options. We are also conscious of the need to respond to the increasing incidence of the disease nationally and for Defra to develop new initiatives that will have an impact on disease control. We firmly believe that strategic use of the IFN will be an essential feature of future control options and that Government will ultimately be obliged to provide scientifically valid information on the performance of the test.

7.14   The ongoing pilot study of the use of IFN in problem herds received the encouragement and endorsement of the ISG (Appendix I - 13 August 2002) with the expectancy that it would be designed with scientific rigour to

maximise the capture of scientific data that can be interrogated to inform a range of potential future control options. Unfortunately, we believe that the ongoing pilot study has a number of deficiencies of both scientific rigour and in providing information for designing possible policy measures; in this respect we consider it to be a misuse of valuable resource and a lost opportunity to make more speedy progress to find effective ways of controlling bovine TB. We advise and would expect Defra to ensure that scientific opportunities for this strategically important diagnostic assay are maximised.

Future needs

7.15 For the future, the ISG supports the stated intention of Defra to put in place quality control of the tuberculin test, which will inevitably remain an important diagnostic tool. In addition, we advocate work on improving and refining the IFN test. There must be increased effort of research in this area and provision of the necessary resources for an appropriately scientifically designed field trial to maximise data on the performance of the IFN test to enable it to be evaluated for use in a range of potential policy options; the opportunity must also be taken to test new diagnostic antigens. Ultimately it is likely that the IFN test using a cocktail of defined antigens will have wide applicability in the field, and should be considered as the future primary diagnostic tool. To achieve this objective we believe that Defra should refocus its diagnostic research, from merely providing tools for future vaccine use to a clear strategic drive which accepts the central importance of improved diagnosis to achieve effective control of this disease.

8. ECONOMIC ASPECTS OF CONTROL POLICIES

8.1   The RBCT and its associated research programme are directed towards establishing the technical information needed to design potential strategies for controlling the spread of TB among cattle herds and lowering its incidence over time. The failure of past policies to achieve this objective, despite continual veterinary effort and high levels of public expenditure over several decades, highlights how crucial it is now to develop new understandings of the TB complex and new scientific knowledge concerning its immunology and epidemiology in cattle and wildlife. Dependable scientific data will enable not only new thinking on possible disease control interventions, but is also essential to assess the potential effectiveness of different actions, the field conditions to which they are sensitive and the implementation framework necessary for them to achieve their required effects.

8.2   But technical effectiveness is not itself a sufficient criterion for the selection of a control policy. Disease management, whether for cattle TB or any other condition affecting farm animals, is in the last analysis subject also to economic criteria.   Disease causes obvious economic losses in livestock production, directly to farmers, frequently to the public purse, and elsewhere in the economy more widely; and so disease reduction (or elimination where possible) is clearly a highly desirable objective. But that objective cannot be pursued regardless of the costs incurred in control. If the economic gain from disease reduction does not exceed the economic cost it requires, then that control policy is not adequately justified (the 'clean ring' badger culling strategy of the early 1980s was curtailed partly on these grounds[26]).

8.3   Once the RBCT results and other research findings are available, this should permit an assessment of control options (whether involving wildlife culling, different diagnostic procedures and testing regimes, regional zoning, cattle movement restrictions, on-farm husbandry adaptations, etc) so as to enable, in principle, a ranking of policies in terms of technical effectiveness – i.e. their predicted success in lowering/preventing herd breakdowns. Given this, the next essential step is to undertake comparative economic assessments so as to identify which policies are worth adopting, and then, which appear to be most worth adopting (and it is conceivable that the technically best policy is not the best economically). Even such economic analysis is not itself the final arbiter, because there may well be wider operational, institutional, political and social equity considerations which influence policy choice as well. The ISG has consistently stressed that it sees its role as establishing the information framework that will best assist Ministers in confronting this complex choice of policy.

8.4   In its first report[15] the ISG set out the elements of a programme of research that were needed if such economic assessments of policy options were to be made. That programme was put in place by MAFF/Defra and some of its results are now emerging. A fundamental component of the information that is required, regardless of whatever control option is being assessed, is the cost that bovine TB imposes on the economy – for this, by the same token, is a measure of the benefit to be gained from controlling the disease. These costs arise from the on-farm, laboratory and administrative costs of animal testing, the destruction of productive capital resources (the slaughter of reactor cattle), reductions in the flow of output from affected dairy and beef farms, and the extra costs due to the disruption of farming processes as cattle are held on farms and movements restricted until breakdowns are cleared.

8.5   A major study[36] conducted by the University of Reading has for the first time derived reliable estimates, for farms in England, of the costs incurred at farm level resulting from a TB breakdown. Its findings show that the typical costs of a herd breakdown vary widely across farms depending on a range of factors, but do provide a sound basis on which to estimate the economic benefits that could be expected from any specified technical option for controlling cattle TB. It is a separate issue of policy as to how the cost of TB breakdowns – i.e. the benefits to be gained from better control – are shared out between different involved parties. At present the bulk of the costs are carried by the public purse, either through government provision of TB diagnostic services or the payment to farmers of financial compensation for slaughtered reactors. However, a distinct element in the construction and appraisal of control options is the implied distribution of costs and benefits between public and private interests, and a determining consideration in the choice of policy might be how the costs are borne.

8.6   As well as its technical effectiveness, a more specific characterisation of any TB control option is what it costs to implement. Policies involving badger culling, for example, would be expensive if welfare and wildlife conservation considerations, as implemented in the RBCT, continued to be required. Other methods of badger culling could be proposed which are cheaper and probably more functionally effective, e.g. snaring or gassing; but to countenance such methods would be to ignore widespread public sensitivities about the conservation and welfare of wildlife, and place the interest of farmers and the control of localised TB above all other considerations.

8.7   By contrast, policies based on biosecurity and on-farm husbandry practice are likely to be relatively low-cost; possibly also low in the incremental disease control benefits they offer, but perhaps yielding a high benefit-cost ratio for all that. Other control options which involve relatively low economic costs are zoning and movement restrictions, which, while perhaps imposing harshly on the trading freedom of affected farmers, should

have little economic impact on the overall efficiency of cattle farming compared to their potential disease-limiting effects.

8.8   The ultimate cost-effective control policy is probably one of cattle vaccination.   The implementation of regular vaccination is unlikely to be expensive as an annual expenditure, and the research investment cost in immunological science, vaccine development and testing, while very substantial, when amortised over the indefinite future, might amount to a tolerable annual charge[*]. All these general propositions are empirical issues in the last analysis, of course, and it requires continued economic research and data analysis to accompany the scientific research to underpin the evaluation and choice of policy options.

8.9   Two further points should be borne in mind.   First, the costs of any control policy are not necessarily expressed solely in terms of the financial expenditures and resources used in its implementation.   One of the costs associated with culling badgers to lower the risks of cattle infection is the loss of economic value represented by the badgers that are killed.   There is no 'market' for badgers and so they do not get assigned a conventional money price by the everyday workings of the economy, as is the case with the traded commodities with which we are familiar. But this is no different from countless other things from which we derive value and so would experience a sense of loss ('cost') if they were not available.   One of the projects in the ISG's proposed agenda for economic research is pursuing the question of how the value that society places on changes in the badger population may be estimated so as to offer an informational input into the economic evaluation of TB control policy.

8.10   Second, caution must be exercised to ensure that 'economic analysis' does not become just simple static accounting.   This would happen by assuming that the cost of bovine TB, or the benefits of its control, are captured simply by multiplying the average cost of a breakdown by the total number that occur. The reason is that not all herd breakdowns carry the same cost implications for the cattle economy, and the economic assessment of control policy options needs to explicitly recognise this fact.   For example, a breakdown within an already high-incidence region would impose a cost that, in aggregate terms, may not be all that great; it would simply be a duplication of an economic event that occurs fairly regularly and, while highly undesirable in itself, does not represent a substantial economic effect beyond the 'normal' average cost.   By contrast, the same breakdown occurring in a previously TB-free area could represent the nucleus from which a whole series of subsequent and related herd breakdowns develop, becoming responsible for a new hotspot

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[1] It might be argued that the cost of pasteurising milk and slaughterhouse carcasses inspections should be included as an element in the cost of TB control, since these are the means by which the potential zoonotic impact of the disease is largely prevented. However, these procedures are implemented as part of a wider framework of food biosecurity and so cannot validly be attributed solely to the problem of bovine TB.

and the imposition of a substantial cost burden on many associated cattle herds. In a dynamic setting, therefore, the benefits (and hence the justifiable costs) of a policy designed to prevent the occurrence of such 'focal point' breakdowns are of a totally different order of magnitude from an equivalent policy which simply prevents the occurrence of yet another TB event that is not atypical of its area. The assessment of any control option has therefore to consider the dynamic setting in which it operates as well as its effect on the established chain of events.

8.11 While a formal economic evaluation of alternative TB control options must await the required technical information on the link between badger culling and herd breakdowns, a certain amount of useful economic 'scenario exploring' could be undertaken as a research exercise. Using information now available on the cost of TB breakdowns measured at the farm level, and combining it with data on the public sector costs of testing and disease management, a series of estimates could be constructed as to the potential economic benefits from reducing breakdowns on cattle herds of different sizes and types, of different durations and in different regions of the country (the estimated cost associated with breakdowns being the benefits to be gained from avoiding them). Next, a number of potential policy interventions ranging from adjusted TB testing regimes, different methods and levels of badger culling, various constraints on inter- and intra-regional cattle movements, through to vaccination and possible farm level biosecurity restrictions and management practices could be set out in detail. This would then allow estimates of the costs of implementation of each defined policy to be constructed. Then, by a process of relatively simple computation and comparison - in the form of what might be termed a "cost/required benefit analysis" - it is possible to calculate the number of herd breakdowns that each policy would need to prevent in order to cover its cost, and therefore to be considered a candidate policy on economic grounds. Although such break-even analysis may not identify any actual policies to implement (because the field performance of the policies in practice are not necessarily known), it would represent a reliable first pass through the options and permit some prior judgments to be made about which approaches might possibly meet the criterion of economic acceptability, and which options look likely to be not worth pursuing further.

9. CONSIDERATION OF OPTIONS FOR TB CONTROL

9.1   In the light of the evident complexity of the problem of cattle TB, the ISG had already recognised in previous reports that effective control of the disease in the future would require a multi-dimensional approach. This would be based on explicit recognition that *M. bovis* infection exists in badgers, the major wildlife host, and also on the fact that, despite the continuing programme of herd testing, infected cattle remain undetected in the national herd. In addition, it has been recognised that infection is sometimes present in other wildlife species. So, this complex disease system involves a web of transmission between wildlife, between cattle, and between wildlife and cattle.

9.2   The options for control therefore include a wildlife control element, a cattle control element and a general farm management plan for improved biosecurity.

9.3   Wildlife-based control would aim to reduce the threat of TB from badgers (and other wildlife?) by culling, vaccination or wildlife management practices.

9.4   Cattle-based control would build on the assumption that many infected cattle are currently undetected in herds, either because they have not been recently tested or because the test fails to detect them. Its central feature would be more effective diagnosis of the disease in individual cattle, to identify and remove from the herd those animals exposed to TB and which are potential disease transmitters. It would also involve much more rigorous restriction of movement of cattle from herds that have had TB in an attempt to eliminate the transmission of disease through movement of infected cattle to TB-free herds and would advisedly include both pre- and post-movement testing and appropriate restocking policies. Consideration would need to be given as to whether this could be achieved through voluntary codes of practice or be legally enforced, as was done in the past by attestation schemes.

9.5   The implementation of appropriate on-farm husbandry and cattle and wildlife management practices may also reduce the risk of TB but the recommended management practices for this are not yet clear.

Wildlife control – culling

9.6   Since the inception of the RBCT, the culling of badgers has been allowed to take place only within a clearly defined framework, which has been sensitive to public concerns relating to animal welfare and, recognising the

protected status of the badger, has avoided total elimination of badgers over large areas of the countryside. These are the essential characteristics that any badger culling programme would have to satisfy if it were to represent a sustainable element of TB control. The contribution that any such sustainable culling of badgers can make to reducing the incidence of TB in cattle will be known when the trial delivers conclusive results, which we calculate will be by early to mid-2006. At present, there is insufficient scientific evidence upon which to design a possible badger culling strategy due to remaining uncertainty concerning the impact of proactive badger culling on TB incidence in cattle.

9.7   Despite the fact that this scientific information is not yet available, pressure has been put on government and on the ISG from the outset of our work to sanction the culling of badgers outside trial areas, based on the preconceived view that localised badger culling had previously contributed significantly to the control of the disease. This view is not, however, supported by evidence or indeed by the logic of the Krebs report, which recommended initiating a trial specifically because the value of badger culling in controlling cattle TB was unknown. The ISG response to proposals for culling outside trial areas was embodied in our letter to Ministers (Second ISG Report[16], Appendix E) and reasserted clearly that the scientific evidence needed to consider any such approach was being investigated by the ongoing RBCT and it was not appropriate to consider the culling of badgers outside trial areas until that study had been completed. Subsequently the results and analysis presented to the Minister in October 2003, and strengthened by further analysis in April 2004, have shown that reactive, localised culling, as conducted in the trial is at best ineffective and more likely counterproductive (see detailed discussion in Chapter 3). This finding has fully justified the considered scientific approach that we have consistently advised should be adopted, with action based on carefully collected data and rigorous statistical analysis. Whether more extensive, proactive culling has a role to play in the control of cattle TB has yet to be demonstrated but the question of culling badgers outside trial areas as a component of short term disease control must be put to one side until further trial results are forthcoming. Future policy development could also be informed by findings from the ongoing field trials in the Republic of Ireland when they are peer-reviewed and published, although consideration of these data must take into account the different environmental and ecological features in the Republic of Ireland compared to those prevailing in Great Britain.

Cattle control element

9.8   Regardless of the role of wildlife intervention as a component of future TB control, we believe it essential in both the longer term and in the short term that more effective disease control measures directed at cattle should be put in place without further delay.

9.9   Available data suggest that bovine TB in both cattle and badgers is a low incidence infectious disease with what appears to be a relatively low, but variable, transmission rate. Given that TB is not generally highly contagious and is most effectively transmitted through intimate contact, it may be argued that opportunities for the disease to be transmitted from cattle to cattle are actually greater than those for the transfer of infection from badgers to cattle; this implies that, notwithstanding widespread presumptions to the contrary, transmission of infection between cattle and dissemination through cattle movements could be important contributory factors to the rising incidence of herd breakdowns. If this were in fact the case, then focussing aggressively on cattle factors alone, ignoring the wildlife component, could lead to markedly improved control of the disease - although such a view does not take into account the claim that severely clinically diseased badgers ("super excretors") could make a disproportionate contribution to disease spread, a hypothesis on which little empirical evidence is available. The RBCT cannot directly address the specific details of transmission routes.   However data from the trial, including detailed post mortem examination and the diagnosis of *M. bovis* infection in badgers, plus molecular epidemiological data and pathogenesis studies in cattle, taken together, can be expected to lead to a better understanding of the complex disease transmission system.

9.10   The ISG has always been clear of its role to elucidate and advise on the implementation of longer term strategies for TB control, this advice being dependent in part upon the outcome of the RBCT and on other ongoing scientific investigations.   But it has also emphasised the need to develop effective short-term control options to reverse, or at least contain, the current escalating disease incidence in traditionally high incidence areas and halt the geographic spread of the disease, which carries such damaging consequences.

Cattle to Cattle Transmission of TB

9.11   The ISG has commented in earlier reports on the obvious potential for TB to be spread directly from cattle to cattle, independent of any contribution that badgers or any other wildlife might make. Because of the incomplete sensitivity of the tuberculin test, which fails to accurately identify all infected animals, there is a real prospect that infection continues to exist in ostensibly TB-free herds, and in these circumstances the movement of cattle carries a clear risk of the disease being spread to new herds. The lack of restriction of cattle movements, other than from currently known TB-infected herds therefore provides a clear opportunity for disease spread.   Geographic spread was heightened by the predictable increase in cattle movements, and its associated disease risk, that followed the lifting of restrictions imposed during the FMD epidemic. Our concern at the increased potential for the spread of TB that this represented, particularly into relatively unaffected areas of the country, as a result of inadequate biosecurity (movement of infected cattle), was forcibly expressed at the time to Government representatives and the farming

community. Sadly, these warnings went unheeded and we are now seeing the consequences of this lack of caution.

9.12   In order to better inform Ministers on what action might be taken, both outside and within trial areas, and to gain some control of the TB problem the ISG developed a number of initiatives (ISG 977 - appendix I) which included the consideration of new and emerging data from the research programme.

9.13   Molecular epidemiological data demonstrate that distinct genotypes of *M. bovis* predominate in different localities, being found in both cattle and badgers, and associated with local herd breakdowns.   A number of distinct clusters involving different strain types occur across the main infected regions and these clusters have increased in size locally over time.   New breakdowns occurring in geographically separate and previously TB-free regions of the country can be linked by genotyping back to one or other of these specific *M. bovis* strains.   It is likely that this appearance of TB strain types in new and distant geographic locations is a result of the movement of TB-infected cattle. Involvement of badgers as a source of infection for these breakdowns is much less likely, since both behavioural and genetic evidence indicate that badgers tend not to make very long-range movements.   Irrespective of the source of infection, there is a risk that such breakdowns will go on to develop into new endemic clusters if infected animals remain undetected.

TB Clusters

9.14   The local persistence and spread of the disease in cattle, which has resulted in clusters of infected herds, has typically been ascribed to wildlife and the existence of local wildlife reservoirs of infection.   The part that cattle play in the local dissemination and persistence of TB in cattle herds is unknown and heretofore has not been seriously considered.   Cattle movement data, which are now becoming available for analysis, highlight the extent of local cattle movements that typically take place as a result of normal farm trading practice and suggest that this represents a considerable risk of spreading disease. Preliminary analysis of TB99 epidemiological risk analysis data also points to the importance of cattle movement at farm level as a risk factor for herd TB infection (see Chapter 4).   Cattle tracing data show that there are high levels of cattle movement between farms in high TB risk areas, although this may be to some extent simply a reflection of the high cattle and herd density in these areas.   However, it is also obvious that bringing fresh animals onto a farm to replace reactor cattle, and the sale of animals off farms when they finally become free of restrictions following a breakdown, creates its own momentum of animal movement in addition to normal practice.   As discussed above, because of the poor sensitivity of the TB skin test, a proportion of these transferred animals can be expected to be TB-infected.

9.15   Data from the ongoing IFN pilot study being conducted by Defra give some indication of the extent of this problem. These early data show that, on 27 farms involved in the initial stage of the study, 402 cattle which had tested negative at the disclosing tuberculin skin test in problem herds were subsequently diagnosed positive by the IFN test.   More than 50 of these animals were shown at subsequent post mortem examination to be diseased; while it might be expected that some of these animals would be identified and eliminated by adopting a super severe interpretation of the tuberculin test and by further short interval testing, the strong likelihood remains that a proportion of infected animals are undiagnosed. The quantitative significance of this is unknown but would be amenable to quantitative analysis/ modelling if comparative data on the performance of the two tests were available.

9.16   Further evidence on the disease risks implicit in cattle movement is emerging from an ongoing epidemiological study being carried out in trial areas and in parts of the country with low TB incidence, which is studying farms that were destocked as a result of FMD and subsequently restocked. The study combines molecular strain typing of *M. bovis* isolates with collection of animal movement and other epidemiological data. Preliminary findings show that cattle movement has introduced onto farms *M. bovis* strain types that have a geographic distribution previously remote to these areas, resulting in cattle herd breakdowns that can be directly attributed to the movement of TB-infected cattle from the remote region from herds that have had TB in the past. This study is in its early stage but emerging data suggest that some of the restocked farms that finally test clear of the disease are then breaking down again. Whether this is due to previously infected animals being mis-diagnosed by the initial tuberculin test, to amplification of infection within the herd due to undiagnosed animals, to re-infection from wildlife, or to a novel source of infection, is not yet known. Irrespective of how infection is being maintained, these preliminary findings highlight the dangers of moving undiagnosed infected animals around the countryside. It is of serious concern that Defra reports that 60% of herd breakdowns in Cumbria, post FMD, are associated with the movement of infected cattle onto breakdown farms.

9.17   The data that are emerging, albeit preliminary, from these independent but coordinated studies reinforce the view that infected but undiagnosed cattle can carry the disease to new areas of the country. The question arises whether failure to adequately identify and control the disease results not only in transmission of infection to other herds in the locality, but whether this is not also a means whereby infection becomes introduced to, and established in, the local wildlife.

Reservoirs of Infection

9.18   The prevailing concept of wildlife as a "reservoir" of infection supposes that TB pre-exists as an endemic disease in the badger population, spilling into

cattle when badger numbers in a particular area grow to a critical level or when there is a change in other circumstances that favour transmission to cattle. This view may represent an over-simplified picture of the epidemiology. Rather than challenge to cattle from wildlife being due entirely to an inherent reservoir of TB in badgers which constantly reinfects cattle, failure to control the cattle disease may result in a parallel cattle 'reservoir'. Thus, a dual source of infection is created, and it is this that explains the persistence of the disease in cattle and the maintenance of cattle hotspots. Cattle infection can persist partly because of the inadequate implementation of control measures, but many of the features associated with the origin and maintenance of a wildlife reservoir of infection are unknown.

9.19 The data supporting the above concepts are preliminary, but nonetheless suggest that, unless appropriate steps are taken to prevent this cycle of events, there is every likelihood that national disease incidence will continue to increase and the spread of TB into new areas of the country will continue and possibly gain pace. The seriousness of this and its potential magnitude, can be observed by reference to maps (Fig. 9.1) of TB breakdowns in Great Britain in 1986 and 2002. These demonstrate clearly the inexorable spread of infection over this twenty year period and the failure of past TB control policies to contain the disease.
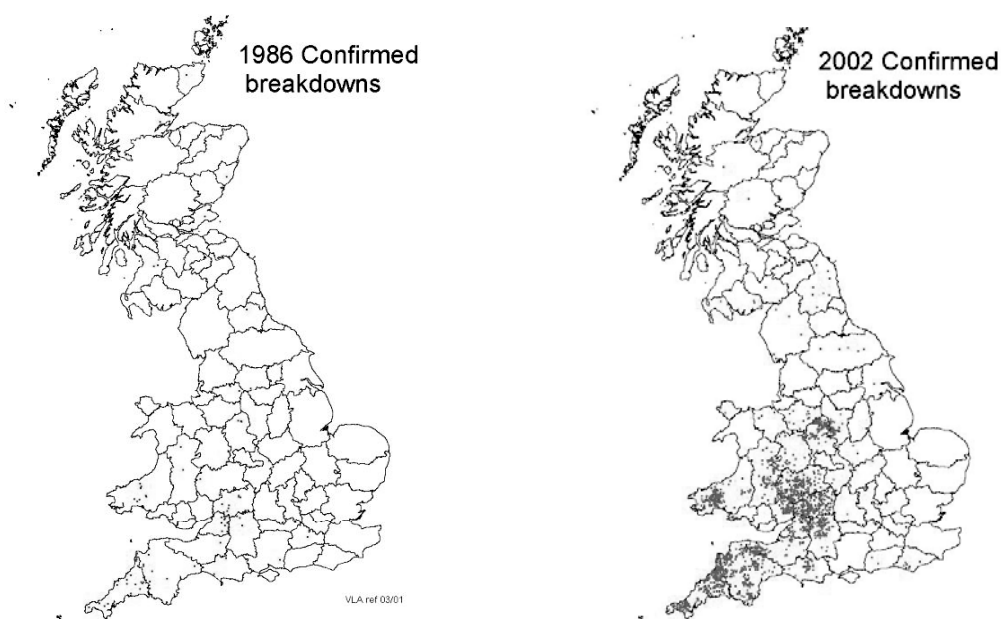
Figure 9.1 TB incidence in GB in 1986 and 2002

CREDIT: VLA

Improved diagnosis

9.20   As we have stated, the prospects for control measures that might be adopted with respect to sustainable wildlife culling will depend on the outcome of the ongoing RBCT.

9.21   Nonetheless, we believe that in both high and low risk areas, improved and strategically applied diagnostic tests for the disease in cattle, along with heightened cattle herd biosecurity including in particular more rigid cattle movement controls, must be a central component of future control measures.

9.22   A critical feature of disease biosecurity is accurate diagnosis.   As discussed in chapter 7, research has shown that the tuberculin test, while effective when applied as a herd test, when used to detect individual infected animals has a high probability of failing to detect every diseased animal in an infected herd. The frequency of testing and the sensitivity of the diagnostic test has also been commented on in chapter 7, but pathogenesis studies, in both experimental and field situations, have confirmed the limitations of the tuberculin test and highlighted the potential value of a complementary IFN test. Experimental studies have also demonstrated the potential for bacterial shedding and transmission in the early as well as later stages of the disease and that some of the infected animals that evade diagnosis by the tuberculin test have well developed pathological lesions. These animals were diagnosed by the IFN test, indicating the potential of the IFN test to detect at least some of the tuberculin negative animals in infected herds. We advise that irrespective of the measures that might be adopted to prevent incursion of the disease from wildlife to cattle, improved diagnosis of the disease in cattle is essential and must be built in as an integral component of the options for future disease control.

Vaccines

9.23   Vaccines have the potential for disease management and might seem to offer the ultimate approach in situations where complete elimination of the disease organism cannot be achieved. However, while one of the potential elements of a TB control policy (whether for cattle or for badgers), vaccines can still only be regarded as a long term and uncertain option and would need to be complemented by other control measures.

Overview

9.24   It is to some extent reassuring that Defra is now consulting with stakeholders on future TB control options, since it is obvious that more effective control will require a new and collaborative effort between many interested parties. However, it is also essential that Defra create the flexibility

to exploit scientific developments, both in the shorter and longer term. We remain concerned at the apparent lack of urgency to attempt to implement what we believe to be necessary control measures. In the shorter term there are three interrelated but distinct challenges: 1) measures to reduce the disease incidence in areas where TB is firmly established; 2) prevention of disease spread adjacent to these areas; and 3) prevention of spread, and its persistence, to areas of the country that are currently relatively free of the disease.

9.25   For all three challenges, the same principles of cattle disease control apply and should be rigorously reinforced. Improved and suitably applied and monitored diagnosis can be expected to play a crucial role; detection and speed of response are likely to be especially important. The frequency of testing and the test, or combination of tests, used is particularly critical in high disease incidence areas and while it would be important not to overreact to individual breakdowns in low incidence areas, disease surveillance must be more rigorously structured and the advisability of four yearly testing questioned. The empirical data to address these questions have not been thoroughly interrogated. More disciplined control of the movement of animals is essential and improvements in biosecurity on farms are likely to be important. Results from TB99 may give some more specific guidance on this.

9.26   It is clear to us, however, that sustainable and effective control measures cannot be applied by Defra without the full cooperation and goodwill of the livestock industry. Farmers need to share ownership of the problem of TB and accept some responsibility to protect themselves against introduction and spread of the disease. We therefore urge Defra and the cattle industry to work together, closely and effectively, to put in place and implement the control measures that we believe are necessary, including appropriate guidelines on restocking[37]. Such measures are, after all, no more than sensible, implementable, biosecurity measures that would be expected to be applied to control the spread of any infectious disease. There is no guarantee that these measures will prevent spread of disease, but they can be expected to reduce the extent of transmission between herds and thus contain the disease. Ongoing research, assuming that its momentum is maintained, can be expected to lead to a refinement of these control measures as new findings emerge and thinking develops.

9.27   The foregoing discussion has focussed on short-term control options in order to gain a measure of control on the escalating cattle TB problem. For the longer term, measures may include some or all of the short-term options but will also be guided by further findings from the ongoing research programme. Potential control interventions have to meet acceptability criteria not only in relation to their technical effectiveness in controlling cattle TB, but also in terms of their economic benefit and sustainability.

10. RECOMMENDATIONS FOR FUTURE ACTION

10.1 Diagnosis

a) It is necessary for Defra to implement immediately an appropriately designed study to determine the sensitivity and specificity of the IFN test in the field, to make comparisons with the tuberculin skin test, and to inform on their combined use in a range of control options.

b) The opportunity should be taken also to secure data on the use in the IFN test of new diagnostic antigens.

c) A major strategic drive should give greater urgency to refining the IFN test.

d) Longitudinal pathogenesis studies in cattle are necessary to add to our understanding of disease dynamics and development in the longer term. This should include obtaining further information on latency, of diagnostic capability at different stages of the disease and potential for disease transmission.

e) A quality control study of the application and use of the skin test in the field should be undertaken.

10.2 Data Interrogation

a) More intensive interrogation of herd testing data should be an integral part of TB surveillance.

b) Molecular epidemiological data and the cattle movement database is a valuable resource. An in-depth analysis of the cattle movement database linked to molecular epidemiological data should be given high priority, recognising their scientific and strategic value, and can be expected to provide valuable insights into the spread, development and control of cattle TB and will reinforce and inform other epidemiological studies.

c) The ISG advises Defra to urgently reconsider aspects of its control and surveillance strategies, particularly in low disease incidence areas in order to refine its testing and surveillance strategies.

10.3 Vaccine Research

The momentum of the vaccine development programme should be continued to ensure that the high scientific standing, and the international collaborations of the VLA TB Vaccine Research Group is maintained. This should ensure that

findings from the International Human TB programme, from which any major development is likely to emerge, can be capitalised on.

10.4   TB99/Case Control Study (CCS) epidemiological risk analysis

(a) Priority should be given to ensuring the adequate and timely collection of case and control data.

(b) For the future we recognise that methods for the collection of TB epidemiological farm data are undergoing change and increasingly a large proportion of such information will be available remotely through the integration of improved national databases. Further research is required on the best use of modern information handling methods for the rapid assimilation and analysis of TB99/CCS and other farm management data.

10.5. Economic research

(a) Defra needs to get into the position where it can undertake detailed evaluation of the economic implications of alternative control actions as part of the process of constructing a multifaceted TB control strategy. Meaningful cost/benefit analyses of alternative control options cannot yet be undertaken because the essential economic relationships reflecting the wider impacts of bovine TB in the local/regional/national economy, and necessary information on the benefits of alternative control interventions, are not sufficiently known.

(b) There is a major requirement to undertake research to discern the benefit side of TB control options. The primary component of this is technical data relating to the effectiveness (in terms of reducing breakdowns) of different TB testing regimes, different testing methods (skin test versus IFN test), different strategies of badger culling, different programmes of restriction or zoning of cattle movement, of alternative on-farm biosecurity and management practices, of local or area-wide vaccination for badgers or cattle, etc.

(c) In addition, information is needed on the distributional aspects of TB breakdowns on farms of different sizes and types, and on the 'external' economic effects on associated commercial businesses (markets, farm suppliers, veterinary practices, neighbouring but unaffected farms) and on the local economy.

(d) It is plausible to assume that the costs of different control strategies can be reasonably estimated (although this information has yet to be assembled). Costs need to be considered not only in terms of expenditures (public or private financial outlays) but also on the disease effect on production, the efficiency and distribution effects of restricted cattle trading, and of the conservation and wildlife values that may be involved.

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MEMBERSHIP OF THE INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

Professor John Bourne CBE, MRCVS (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.

Professor Christl Donnelly (Deputy Chair)

Professor of Statistical Epidemiology, Department of Infectious Disease Epidemiology, Imperial College Faculty of Medicine. A specialist in infectious disease modelling and statistical analysis.

Sir David Cox, FRS

Honorary Fellow of Nuffield College, University of Oxford since 1994. A statistician with considerable experience in developing and applying statistical methods of analysis and design.

Professor George Gettinby FRSE

Professor in the Department of Statistics and Modelling Science at the University of Strathclyde. An applied statistician and modeller and a specialist in experiment design for the evaluation of veterinary products.

Professor John McInerney OBE, FRSA, FRASE

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

Professor Ivan Morrison FRSE

Professor of Immunology, Centre for Veterinary Tropical Medicine, University of Edinburgh. A veterinarian and specialist in bovine immunology and disease pathogenesis with practical experience of field experiments.

Dr Rosie Woodroffe

Assistant Professor and Conservation Biologist, Department of Wildlife, Fish and Conservation Biology, University of California, Davis. A specialist in wildlife disease and badger ecology and behaviour.

TERMS OF REFERENCE OF THE INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

The Terms of Reference of Independent Scientific Group on Cattle TB (ISG) are:

"To advise Ministers on implementation of the Krebs Report on bovine TB in cattle and badgers by:
- overseeing the design and analysis of the randomised trial to test the effectiveness of badger culling as a means of controlling bovine TB;
- regularly monitoring the progress of, and outputs from, the trial and assessing any important differences in results between the treatments;
- monitoring data on the *Mycobacterium bovis* situation in areas and species outside the trial;
- reporting to Ministers on progress; and
- advising, as requested, on related issues."

REGISTER OF MEMBERS' INTERESTS

Professor John Bourne CBE, MRCVS (Chairman)

Honorary Professorship of Animal Health from the University of Bristol from 1988 onwards.

Honorary Research Fellow of the Edward Jenner Institute for Vaccine Research from January 2002 onwards.

Consultant to the Meat and Livestock Commission on pig disease research from November 2001 onwards

Professor Christl Donnelly (Deputy Chair)

Current main employment is as Professor of Statistical Epidemiology in the Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College London.

One area of research is transmissible spongiform encephalopathies, including BSE, CJD and scrapie. Joint contractor on two grants relating to this area of research: "Predicting the future course of the vCJD epidemic in Great Britain" sponsored by the Department of Health and "Epidemiological assessment of the potential risk to human health in GB posed by possible entry of bovine spongiform encephalopathy infection into the national sheep flock" sponsored by the Food Standards Agency. Royalties received as an author of the BSE and vCJD: Models for Epidemics by C A Donnelly and N M Ferguson, published in 1999.

Principal supervisor of two Defra-funded epidemiological / statistical research assistants analysing data on bovine TB in cattle and badgers, in association with the ISG.

BBSRC-funded Ph.D. studentship awarded on "Modelling and analysis of the spatiotemporal dynamics and control of foot-and-mouth epidemics" jointly supervised with N M Ferguson.

Sir David Cox, FRS

None relevant

Professor George Gettinby FRSE

Research contracts held in the area of sea lice epidemiology on salmon farms funded by Defra, and endopthalmitis in cataract patients funded by the European Society of Cataract and Refractive Surgeons.

Member of the Defra Veterinary Fellowship Review Panel and, until 2003, member of the UK Veterinary Products Committee.

Scientific adviser to Waltham Centre for Pet Nutrition, Novartis Animal Health, Intervet and Organon Medical Research Laboratories

Professor John McInerney OBE, FRSA, FRASE

Member of the Farm Animal Welfare Council and service on the Economics Advisory Panel of the South West of England Regional Development Agency.

Visiting Professorship at the Royal Agricultural College.

Land owner within the buffer zone of one of the Triplets (Cadbury) of the Devon (J) Trial area.

Sometimes asked by public sector or commercial interests to undertake analyses in the area of agricultural production and policy, for which a fee may be paid.

Fellow of the Royal Agricultural Society of England.

Professor Ivan Morrison FRSE

Visiting Professorship held at Bristol University.

Horserace Betting Levy Veterinary Advisory Committee (1997-present).

Wellcome Trust Veterinary Medicine Interest Group (1998-present).

The Moredun Research Institute, External Strategy Group (2001-present).

Dr Rosie Woodroffe

Grant support from Defra ("Ecological correlates of TB incidence in cattle").

Member of the World Conservation Union's Veterinary Specialist Group, joint co-ordinator of the Canid Specialist Group's working group on infectious disease, and a member of the Society for Conservation Biology, the Association for the Study of Animal Behaviour, and the Mammal Society.

HISTORICAL AND CURRENT SUMMARY DATA ON TRIPLETS RECRUITED TO THE RBCT

1. Triplet name	Gloucestershire / Herefordshire		
2. Trial area	Blaisdon A1	Dymock A2	Broadway A3
3. Number of cattle herds in Trial area	135	91	74
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1995 – 1997) 12 month (1997) annual incidence[*]: 3 year (1995 - 1997) 12 month (1997)	 54 17 0.13 0.13	 37 14 0.14 0.15	 39 12 0.18 0.16
5. Total surface area (trial area and inner buffer zone) km^{2†}	163	165	155
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	115	144	140
7. Total number of land occupiers visited in trial area and inner buffer zone	250	299	179
8. Treatment	Reactive	Survey-only	Proactive
9. Number of badgers culled (to 31 January 2005)	117	0	314
10. 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	 300 36%	 165 49%	 86 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.)

1. Triplet name	Cornwall / Devon		
2. Trial area	Hartland B1	Putford B2	Bude B3
3. Number of cattle herds in Trial area	90	153	129
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1995 – 1997) 12 month (1997) annual incidence[*]: 3 year (1995 – 1997) 12 month (1997)	 37 16 0.14 0.18	 48 26 0.10 0.17	 35 11 0.09 0.09
5. Total surface area (trial area and inner buffer zone) $km^{2\dagger}$	119	143	130
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	114	125	120
7. Total number of land occupiers visited in trial area and inner buffer zone	164	270	232
8. Treatment	Reactive	Proactive	Survey-only
9. Number of badgers culled (to 31 January 2005)	301	729	0
10. 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	 306 32%	 377 20%	 331 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.)

1. Triplet name	East Cornwall		
2. Trial area	Otterham C1	Launceston C2	Lanreath C3
3. Number of cattle herds in Trial area	151	180	107
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1996 – 1998) 12 month (1998) annual incidence[*]: 3 year (1996 – 1998) 12 month (1998)	 21 7 0.05 0.05	 16 9 0.03 0.05	 14 5 0.04 0.05
5. Total surface area (trial area and inner buffer zone) km^{2}[†]	145	157	151
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	137	154	140
7. Total number of land occupiers visited in trial area and inner buffer zone	259	315	237
8. Treatment	Reactive	Survey-only	Proactive
9. Number of badgers culled (to 31 January 2005)	394	0	802
10. 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	 162 19%	 360 24%	 257 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.)

1. Triplet name	Hereford		
2. Trial area	Pudlestone D1	Withington D2	Bosbury D3
3. Number of cattle herds in trial area	107	115	96
4. Historical incidence of TB in cattle in herds in trial area: breakdowns: 3 year (1997 – 1999) 12 month (1999) annual incidence[*]: 3 year (1997 – 1999) 12 month (1999)	9 1 0.08 0.01	27 12 0.23 0.10	19 7 0.20 0.07
5. Total surface area (trial area and inner buffer zone) $km^{2\dagger}$	154	147	147
6. Total area for which permission for trial operations was sought (trial area and inner buffer zone) km^2	139	118	115
7. Total number of land occupiers visited in trial area and inner buffer zone	233	206	251
8. Treatment	Reactive	Survey-only	Proactive
9. Number of badgers culled (to 31 January 2005)	122	0	873
10. 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	64 51%	14 14%	67 46%

* - 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.)

1. Triplet name	North Wiltshire		
2. Trial area	Cold Ashton E1	Charlcott E2	Poulshott E3
3. Number of cattle herds in Trial area	96	104	123
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1996 – 1998) 12 month (1998) annual incidence[*]: 3 year (1996 – 1998) 12 month (1998)	 18 7 0.06 0.07	 14 5 0.04 0.05	 24 10 0.07 0.08
5. Total surface area (trial area and inner buffer zone) $km^{2†}$	149	156	152
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	113	147	118
7. Total number of land occupiers visited in trial area and inner buffer zone	205	211	207
8. Treatment	Reactive	Survey-only	Proactive
9. Number of badgers culled (to 31 January 2005)	188	0	1311
10. 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	 479 24%	 240 30%	 140 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.)

1. Triplet name	West Cornwall		
2. Trial area	Madron F1	Godolphin F2	Stithians F3
3. Number of cattle herds in Trial area	137	206	253
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1997 – 1999) 12 month (1999) annual incidence*: 3 year (1997 – 1999) 12 month (1999)	 20 6 0.05 0.04	 25 19 0.04 0.09	 17 8 0.02 0.03
5. Total surface area (trial area and inner buffer zone) $km^{2\dagger}$	145	149	164
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	90	112	100
7. Total number of land occupiers visited in trial area and inner buffer zone	252	527	658
8. Treatment	Proactive	Survey-only	Reactive
9. Number of badgers culled (to 31 January 2005)	1022	0	435
10. 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	 447 13%	 246 13%	 441 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.)

1. Triplet name	Derbyshire / Staffordshire		
2. Trial area	Nettly Knowe G1	Lady Edge G2	Cubley Brook G3
3. Number of cattle herds in Trial area	114	241	132
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1/7/96 – 30/6/99) 12 month (1/7/98 – 30/6/99) annual incidence[*]: 3 year (1998 – 2000) 12 month (2000)	 18 11 0.13 0.08	 19 9 0.06 0.03	 14 9 0.08 0.06
5. Total surface area (trial area and inner buffer zone) $km^{2[\dagger]}$	156	151	154
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	138	109	124
7. Total number of land occupiers visited in trial area and inner buffer zone	263	299	247
8. Treatment	Reactive	Proactive	Survey-only
9. Number of badgers culled (to 31 January 2005)	256	880	0
10. 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	 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.)

1. Triplet name	Devon / Somerset		
2. Trial area	Brendon Hills H1	Tarr Steps H2	Huntsham H3
3. Number of cattle herds in Trial area	80	68	136
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1/7/96 – 30/6/99) 12 month (1/7/98 – 30/6/99) annual incidence[*]: 3 year (1998 – 2000) 12 month (2000)	 11 7 0.12 0.09	 15 8 0.17 0.11	 17 6 0.11 0.04
5. Total surface area (trial area and inner buffer zone) km^2[†]	145	146	149
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	122	122	125
7. Total number of land occupiers visited in trial area and inner buffer zone	176	224	317
8. Treatment	Reactive	Proactive	Survey-only
9. Number of badgers culled (to 31 January 2005)	159	537	0
10. 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	 61 23%	 49 37%	 31 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.)

1. Triplet name	Gloucestershire		
2. Trial area	Alderton I1	Wetmoor I2	Apperley Grove I3
3. Number of cattle herds in trial area	78	99	103
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1998 – 2000) 12 month (2000) annual incidence[*]: 3 year (1998 – 2000) 12 month (2000)	 31 12 0.40 0.15	 23 15 0.23 0.15	 20 7 0.19 0.07
5. Total surface area (trial area and inner buffer zone) km^{2}[†]	155	145	137
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	117	123	106
7. Total number of land occupiers visited in trial area and inner buffer zone	172	259	217
8. Treatment	Reactive	Proactive	Survey Only
9. Number of badgers culled (to 31 January 2005)	94	487	0
10. 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	 15 0%	 358 35%	 28 57%

* - 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.)

1. Triplet name	Devon		
2. Trial area	Luffincott J1	Cadbury J2	Northlew J3
3. Number of cattle herds in Trial area	116	133	129
4. Historical incidence of TB in cattle in herds in Trial areas: breakdowns: 3 year (1998 – 2000) 12 month (2000) annual incidence[*]: 3 year (1998 – 2000) 12 month (2000)	 19 11 0.16 0.09	 21 18 0.16 0.14	 15 14 0.12 0.11
5. Total surface area (trial area and inner buffer zone) $km^{2\dagger}$	152	132	145
6. Total area for which permission for Trial operation was sought (trial area and inner buffer zone) km^2	135	114	126
7. Total number of land occupiers visited in trial area and inner buffer zone	286	317	341
8. Treatment	Proactive	Reactive	Survey Only
9. Number of badgers culled (to 31 January 2005)	737	0	0
10. 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	 75 0%	 94 25%	 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.)

AUDITS OF RBCT AND TB99 EXERCISES

Completed audits with Defra responses

REPORT	AUDITOR	REPORT DATE	REF. NO.*	SUMMARY OF FINDINGS AND ACTION TAKEN
Humaneness of despatch procedures (1st audit)	James Kirkwood	October 2000	PB 5325	Shot recording started; SOP redrafted to reflect auditor's comments; extra staff training; bullet trajectory study undertaken; closed season and recording of records kept under review; ensure early trap visits; recommendation on firearm not accepted and current firearm retained.
Statistical design of trial (1st audit)	Denis Mollison	November 2000	PB 5385	Once sufficient data are available, ISG should give a more refined estimate of the expected duration and precision of the RBCT and the ISG should clarify the circumstances when the RBCT would be stopped early or prolonged beyond its original projected duration.
Effectiveness of surveying and of social group delineation (1st audit)	Cresswell Associates	February 2001	PB 5497	More accurate system started for field location identification and less fragmented approach to surveying; bait marking use reviewed; tessellation now staged in conjunction with re-surveying; further staff training adopted; Auditor recommended more complex sett classification - not adopted.
Humaneness of despatch procedures (2nd audit)	Roger Ewbank	June 2003	PB 8253	SOP redrafted to reflect auditor's comments; more emphasis placed on checking training and internal audit; staff reminded that audit is directed towards the system, not individuals; firearm recommendation not accepted and current firearm retained.
Post mortem examination procedures used in the RBCT	Graham Hall	May 2004	PB 9702	Post mortem SOP redrafted to reflect auditor's comments; post mortem recording forms modified; changes to procedures of assessing tooth wear to distinguish a badger cub from adult; trial of Haematoxylin & Eosin staining underway.
TB99 (1st audit)	Martine Wahl	July 2004	PB 9839	The Department has accepted and is acting on the recommendations. The questionnaire to be re-designed for use in 2005.
Humaneness of despatch procedures (3rd audit)	Roger Ewbank	July 2004	PB 9957	The Department has accepted and is acting on the recommendations. These relate to minor revision of the SOP and better control of copies, and minor improvements in staff training procedures.

Bacteriological culture procedures	Mike Corbel	September 2004	PB 10204	The Department has accepted in full and is acting on the seven recommendations of the auditor. These relate to the carrying out of a larger measure of quality control analysis and additional diagnostic tests, minor revisions in laboratory procedures and improved badger TB diagnosis feedback to Defra staff.

* Full report obtainable from Defra Publications, Admail 6000, London, SW1A 2XX or can be found on the Defra Internet site (www.defra.gov.uk/animalh/tb).

Audits in progress or with response under consideration

OPERATION TO BE AUDITED	AUDITOR	OBJECTIVES	COMMENT
Effectiveness of trapping procedures	Cresswell Associates	Part of the evaluation of the RBCT, to assess, on a sample basis, the effectiveness of trapping operations in accordance with the SOP. This work links with the audit on effectiveness of survey and social group delineation published in 2001.	Report delivered. Defra response in preparation. Report and response will be published in 2005.
Repeat audit of the Surveying SOP	Cresswell Associates	This repeats certain elements of the previous audit published in February 2001 (PB 5497) in order to evaluate any improvements in the application of the SOPs and the effectiveness of revised procedures.	Report delivered. Defra response in preparation. Report and response will be published in 2005.
Statistical design of trial (2nd audit)	Denis Mollison	Auditor commented on the March/April 2004 RBCT Interim Analysis, recommendations of the Godfray Report and the future duration of the RBCT.	Report published on the Defra website.
TB99 (2nd audit)	Martine Wahl	To further assess the TB99 process.	In progress
Humaneness of despatch procedures (4th audit)	James Anderson	To ensure that in the culling process in 2004-5 trapping season humane standards have been maintained.	In progress
RBCT administrative data	Martine Wahl	To assess the handling and storage of RBCT data.	In progress

MEMBERSHIP OF THE VACCINE SCOPING SUB-COMMITTEE OF THE ISG

Chairman:

Professor F J Bourne	ISG

Members:

Dr C L Cheeseman	Defra Central Science Laboratory, Woodchester Park
Dr M J Colston	National Institute of Medical Research, London
Professor C A Donnelly	ISG
Miss S M Eades	Defra Animal Disease Control Division
Professor P Fine	London University, School of Hygiene & Tropical Medicine
Dr B Grenfell	Cambridge University
Dr R G Hewinson	Defra Veterinary Laboratories Agency, Weybridge
Mr S Houghton	Hoechst Roussel Ltd., Milton Keynes
Professor W I Morrison	ISG
Dr J Pollock	Queens University, Belfast
Mr A G Simmons	Veterinary Endemic Animal Diseases & Zoonoses Division
Dr R Woodroffe	ISG
Professor D B Young	London University, Imperial College

Adviser:

Miss F A Stuart	Defra Science Directorate

Visiting Speakers:

Dr L Corner	Massey University, New Zealand
Dr E Gormley	University College, Dublin, Eire
Mr W Nash	Industrial Consultant

Secretariat:

Dr A L Patey	Defra Animal Disease Control Division
Mr J W Pitchford	Defra Animal Disease Control Division
Mr T K Matthews	Defra Animal Disease Control Division
Ms S Shah	Defra Animal Disease Control Division

EXECUTIVE SUMMARY OF THE REPORT OF THE ISG VACCINE SCOPING SUB-COMMITTEE

1. Introduction

1.1 Vaccination of either cattle or badgers should be retained as a potential policy option for the control of cattle TB. Success however cannot be guaranteed and the likely time frame required to develop and field trial a vaccine suggests that vaccines can only be regarded as at best a medium-term option and more likely a longer-term option. Other control measures for cattle TB will have to be adopted in the short-term and even if a successful vaccine becomes available, it is likely that it will need to be complemented by other control measures.

1.2 The research needed to identify vaccine candidates is common to humans, cattle and wildlife. A well-funded and effectively co-ordinated international TB vaccine research programme has been in place for some time, but thus far no vaccine has been developed that is superior to, or as good as, the BCG (Bacillus Calmette and Guerin) vaccine developed in the early part of the last century. This is a live, attenuated strain of *M. bovis* and has been used to protect humans against tuberculosis since the 1920s. In vaccine trials in various parts of the world, it has been shown to provide very variable protection ranging between 0% to 80%. The reason for this variability is unclear. BCG is the only candidate vaccine that could currently be considered for use in cattle or wildlife.

2. Cattle Vaccines

2.1 From an operational perspective, the field use of a cattle vaccine should present few problems since cattle can be directly vaccinated. There are however serious scientific questions that must be addressed before a vaccine could be considered since an acceptable vaccine would need to largely prevent disease transmission and markedly reduce or eliminate the development of visible pathological lesions to avoid carcass condemnation at post mortem slaughterhouse inspection. In laboratory challenge experiments BCG has been shown to provide between 0% and 70% protection against the development of macroscopic tuberculous lesions in cattle; but even in protected animals disease can persist and animals remain culture positive. Field trial results have generally given disappointing results.

2.2 A further requirement for a cattle vaccine would be for it not to interfere with the tuberculin, or any other immunological test, that might be used to identify diseased animals. Technically it would be feasible to develop a diagnostic test to differentiate vaccinated from non-vaccinated animals but a

more serious complication is a vaccinated animal that is subsequently challenged by exposure to TB from infected wildlife which would be present in the environment. It would be technically very difficult to distinguish a vaccinated protected animal from a vaccinated, or non-vaccinated, non-protected animal. This would invalidate the use of the tuberculin, or any other currently available immunological diagnostic test, and would necessitate a change from the current TB control policy.

2.3   Based on currently available evidence therefore BCG is not considered to be a suitable candidate vaccine for cattle although it is advised that work on vaccine development be continued along with work on the development of new diagnostic tests.

3.   Badger Vaccines

3.1   The demands of a badger vaccine would be less than for cattle since the aim would be not the protection of the individual badger, but to reduce the transmission of the disease to cattle. Such a vaccine would however only be effective in reducing cattle TB if most infection is derived from badgers. This question is in doubt and is currently being addressed by the RBCT.

3.2   Before serious consideration could be given to using a badger vaccine in the field, it would be necessary to establish that the vaccine will influence the course of the disease in badgers. Preliminary studies on a small number of badgers have previously indicated that some degree of protection is achieved following vaccination. More information has been obtained from BCG vaccination of possums in New Zealand; vaccination by a variety of routes, including oral, gave some protection against experimental challenge with *M. bovis*. Protection was also claimed from a field study, but the results of the study are difficult to interpret because of the experimental design. The impact on cattle TB was not determined.

3.3   Studies have recently started in the Republic of Ireland (RoI), with collaborative links to Defra scientists, on a small group of captive badgers. These are designed to provide information on the protection afforded by BCG to experimental challenge with *M. bovis*. The results of this study are likely to become available at the same time as those from the RBCT.

3.4   One of the problems of designing a field trial and developing a vaccine strategy for badger vaccination is the limited knowledge of the epidemiology and dynamics of TB in badgers. Some new epidemiological data will be forthcoming from the RBCT and other research which will indicate how vaccines in the field could be best used. Only when the RoI protection studies and the RBCT are completed can a field trial of BCG as a badger vaccine be considered.

3.5   Regulatory requirements for use of BCG as a wildlife vaccine would have to be considered, but logistically a badger vaccine field trial in itself presents a major challenge and it must be kept in mind that the ultimate aim of the trial would be to measure the effect of badger vaccination on cattle TB. To have a significant and measurable impact this would have to be conducted on a very large scale, similar in size to the RBCT, to include an appropriate number of cattle herds, and for a prolonged time-scale, as long as or possibly longer than the RBCT. This scale of operation would probably necessitate the use of non-parental vaccination of badgers, possibly using an oral bait vaccine. This in turn presents its own set of problems with respect to bait formulation, its delivery and uptake by badgers and the possible avoidance of uptake by other species.

3.6   While trapping and parenteral vaccination of badgers might be considered a simpler practical option it would present serious logistical difficulties since it would also have to take into account the statistical requirement to include an appropriate number of cattle herds, which would involve a treatment area similar in total size to the above requirement for oral baiting. This would be very labour intensive and costly, and would present a number of other difficulties.

4   Recommendations

4.1   BCG may be of value to protect badgers but before a field trial of BCG can be put in place it is essential to await the outcome of vaccine protection studies that are currently being carried out on a population of housed wild badgers in the RoI. It is advised that even if a degree of protection is shown in these studies, success in the field cannot be guaranteed and that a field trial would inevitably have to be put in place and designed on a large scale and continue for an extended time period, in order to demonstrate its effect on the incidence of TB in cattle.

4.2   It will also be necessary to await the outcome of the RBCT in order to obtain essential epidemiological data on TB in the badger and the impact of badger culling on cattle TB before deciding on whether or not to proceed with a field trial.

4.3   A field vaccine for badgers will need to be delivered as an oral bait. Priority needs to be given to development of oral/respiratory delivery systems that are effective in stimulating protective immune responses without capture of badgers.

4.4   There is additional preparatory work that could be undertaken in order to enable a field trial to be in place as soon as badger vaccine protection and field trial data become available. It is recommended that oral bait formulation studies be continued, and that field studies be initiated on bait uptake and bait

targeting in badgers and the level of bait uptake by non-target species including cattle.

4.5   BCG is the only currently available vaccine candidate that could be considered for practical use. Experimental challenge of vaccinated cattle has demonstrated very variable protection of up to 70%, as judged by reduction in pathology, but lower levels of protection against establishment of infection. Field trials have generally provided poor protection. It is the view of the Scoping Study Committee that BCG in its present form would not provide an effective cattle vaccine and that cattle vaccination could only be considered when an improved vaccine is available.

4.6   It will be imperative to maintain the current effort on development and testing of vaccines, which relates to both cattle, including neonates, and badgers, with emphasis on testing in the target species (cattle). The well-developed and effective international collaborations with scientists working on vaccines for both animal and human TB must be maintained and built on.

4.7   It is recommended that studies take place on the oral sensitisation of cattle with BCG and on the effect of vaccinating already infected animals particularly with respect to lesion development.

4.8   It is also recommended that greater priority be given to developing improved diagnostic tests for both cattle and badgers.

4.9   A large body of data on BCG safety in a number of wildlife species, based on laboratory experimentation, already exists. It is further recommended that an extensive literature search is carried out to collate these data.

BADGER VACCINE TRIAL DESIGN CONSIDERATIONS

1.1 This paper discusses the sample sizes that would be required for a vaccine trial conducted in badgers aimed at reducing the prevalence of *M. bovis* infection in badgers. It is not aimed at arriving at a recommended study design but to demonstrate the magnitude of study that would be required to obtain informative results under particular assumptions. Assumptions are, by definition, required, because if the impact of a vaccine candidate on badgers was already known, then the study would not be necessary. A serious difficulty is the absence of a validated accurate (highly sensitive and highly specific) live test for *M. bovis* infection in badgers. The impact such a test could make on the size of the study is examined.

STUDY DESIGN

2.1 It is assumed that within a single population of badgers, individual badgers are trapped and marked. Among those considered eligible for vaccination (discussed later in detail), half are chosen at random for vaccination prior to release. The other half of the eligible badgers are hereafter referred to as controls. One year later badgers are retrapped. Both vaccinated and control badgers are culled, subject to post-mortem examination and cultured to confirm disease status.

2.2 A 25% per annum death rate among badgers has been assumed. Furthermore, uninfected badgers of any age are assumed equally susceptible to infection. Vaccine efficacy was assumed to be constant over the timescale of the study (i.e. the effect was immediate and did not diminish over time). Finally, the force of infection of *M. bovis* infection was constant.

SAMPLE SIZES FOR STUDY WITHOUT ANY LIVE TEST

3.1 In the absence of a live test, all trapped badgers are considered eligible for vaccination. A number of the badgers (both vaccinated and control) would have been infected prior to enrolment in the study, complicating the detection of vaccine efficacy and making sample sizes larger.

3.2 Table 1 presents the prevalence of infection that would be found in the vaccinated badgers one year after vaccination - as a function of the endemic 'standing' prevalence in the badger population (taken to be between 5% and 30%, prior to the study) and the efficacy of the vaccine (taken to be between 20% and 100%). Even if the vaccine were completely effective (100% efficacy), the prevalence in vaccinated badgers would not be zero due to the infections that happened prior to vaccination.

Table 1. Expected prevalence in vaccinated badgers one year after vaccination. The end of this document details how these expected values were obtained.

		Vaccine efficacy				
Standing		20%	40%	60%	80%	100%
Prevalence	5% (6.4%)	6.1%	5.8%	5.5%	5.2%	4.9%
of Infection	10% (12.8%)	12.2%	11.7%	11.1%	10.5%	9.9%
	15% (19.2%)	18.3%	17.5%	16.6%	15.7%	14.9%
(Prevalence in	20% (25.5%)	24.4%	23.3%	22.2%	21.0%	19.8%
control group	25% (31.8%)	30.5%	29.1%	27.7%	26.3%	24.8%
after 1 year)	30% (38.1%)	36.5%	34.9%	33.2%	31.5%	29.8%

[Note: A fully (100%) effective vaccine yields an infection prevalence slightly lower than the standing prevalence because the oldest group of vaccinated badgers are the most likely to be infected (simply due to the length of their exposure) and are assumed not to survive the full year following vaccination.]

3.3 The sample sizes (of post-mortemed badgers) required to achieve 80% power (at the standard 5% significance level) to detect the impact of the vaccine are presented in Table 2. Since not all trapped badgers will be alive (or indeed re-trapped) one year later, it is necessary to consider the number of badgers to be recruited into each group (the vaccinated and the unvaccinated controls). Table 3 presents the sample sizes needed in each group to achieve the appropriate numbers of badgers for post-mortem examination one year later, taking into account the 25% death rate. In other words Table 2 sample sizes are 75% of those in Table 3. (Note that incomplete re-trapping due to reasons other than mortality has not been allowed for. However, this will inevitably occur and the study sample size should be correspondingly increased.)

Table 2. The sample sizes (of post-mortemed badgers) needed <u>in each group</u> (the vaccinated and unvaccinated controls) to detect the impact of the vaccine with 80% power (in the absence of a live test). The software package nQuery Advisor (Statistical Solutions http://www.statsol.ie/nquery/nquery.htm) was used to obtain these sample sizes.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing	5%	102656*	25968	11150	6090	3791
Prevalence	10%	51178	12540	5395	2952	1841
of Infection	15%	33133	8041	3467	1901	1177
	20%	24311	5878	2525	1371	850
	25%	18474	4494	1933	1050	648
	30%	14893	3597	1537	835	514

*This number was obtained as the sample size required in each group to obtain 80% power to detect a difference between 6.4% and 6.1% prevalence. Other sample sizes were obtained similarly based on the expected prevalences given in Table 1.

Table 3. The sample sizes needed <u>in each group</u> (the vaccinated and unvaccinated controls) to achieve the appropriate numbers of badgers for post-mortem examination one year later taking into account the 25% death rate. Thus, twice this number of badgers would need to be trapped in total.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing	5%	136875	34624	14867	8120	5055
Prevalence	10%	68237	16720	7193	3936	2455
of Infection	15%	44177	10721	4623	2535	1569
	20%	32415	7837	3367	1828	1133
	25%	24632	5992	2577	1400	864
	30%	19857	4796	2049	1113	685

SAMPLE SIZES FOR STUDY WITH AN IMPERFECT LIVE TEST

4.1 Even an imperfect live test could reduce the number of badgers needing to be trapped as well as the number needing to be subjected to post-mortem examination. The following assumes a test with 44% sensitivity and 95% specificity (assumptions based on results recently obtained by VLA of a trap-side antibody-based test). It is assumed that trapped badgers are subjected to the live test and only those testing negative are considered eligible for vaccination (half of these being vaccinated and half being controls). Since such a test would leave 56% of the positive badgers unidentified, the prevalence in vaccinated badgers would be reduced compared to the badger population as a whole but non-zero due to the infections that happened prior to vaccination that were undetected by the live test.

4.2 Table 4 presents the prevalence of infection that would be found in the vaccinated badgers one year after vaccination - as a function of the endemic 'standing' prevalence in the badger population (taken to be between 5% and 30%, prior to the study) and the efficacy of the vaccine (taken to be between 20% and 100%).

Table 4. Prevalence in vaccinated and control badgers one year after vaccination.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (4.3%)	4.0%	3.7%	3.4%	3.1%	2.8%
	10% (8.6%)	8.0%	7.4%	6.8%	6.2%	5.5%
	15% (13.0%)	12.1%	11.2%	10.2%	9.3%	8.3%
	20% (17.4%)	16.2%	15.0%	13.7%	12.4%	11.1%
	25% (21.9%)	20.4%	18.8%	17.2%	15.6%	13.9%
	30% (26.5%)	24.6%	22.7%	20.8%	18.8%	16.7%

4.3 The sample sizes (of post-mortemed badgers) required to achieve 80% power (at the standard 5% significance level) to detect the impact of the vaccine are presented in Table 5. Since not all trapped badgers will be alive (or indeed re-trapped) one year later, it is necessary to consider the number of badgers to be recruited into each group (the vaccinated and the unvaccinated

controls). Table 6 presents the sample sizes needed in each group to achieve the appropriate numbers of badgers for post-mortem examination one year later taking into account the 25% death rate. In other words, Table 5 sample sizes are 75% of those in Table 6. (Note that incomplete re-trapping due to reasons other than mortality has not been allowed for.)

Table 5. The sample sizes (of post-mortemed badgers) needed in each group (the vaccinated and unvaccinated controls) to detect the impact of the vaccine. The software package nQuery Advisor (Statistical Solutions http://www.statsol.ie/nquery/nquery.htm) was used to obtain these sample sizes.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (4.3%)	69060	16663	7138	3795	2341
	10% (8.6%)	33224	7895	3329	1788	1094
	15% (13.0%)	20783	4920	2098	1128	685
	20% (17.4%)	14513	3491	1474	790	480
	25% (21.9%)	11042	2615	1108	591	357
	30% (26.5%)	8637	2038	859	457	275

Table 6. The sample sizes needed in each group (the vaccinated and unvaccinated controls) to achieve the appropriate numbers of badgers for post-mortem one year later taking into account the 25% death rate.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (4.3%)	92080	22217	9517	5060	3121
	10% (8.6%)	44299	10527	4439	2384	1459
	15% (13.0%)	27711	6560	2797	1504	913
	20% (17.4%)	19351	4655	1965	1053	640
	25% (21.9%)	14723	3487	1477	788	476
	30% (26.5%)	11516	2717	1145	609	367

4.4 Table 7 presents the number of badgers needed to be trapped to obtain the per-group sample sizes presented in Table 6. (The numbers in Table 7 are, of course, greater than twice the sample sizes in Table 6, since they also include badgers that tested positive when first trapped.)

Table 7. The total number of badgers needed to be trapped (including those that tested positive when first trapped, the vaccinated badgers and the unvaccinated controls).

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (4.3%)	197915	47754	20456	10876	6709
	10% (8.6%)	97253	23110	9745	5234	3202
	15% (13.0%)	62166	14717	6276	3374	2049
	20% (17.4%)	44382	10676	4508	2416	1468
	25% (21.9%)	34540	8180	3466	1849	1117
	30% (26.5%)	27649	6524	2750	1463	880

SAMPLE SIZES FOR STUDY WITH AN AS-YET-UNAVAILABLE PERFECT LIVE TEST

5**.**1   Similar calculations were performed assuming a live test with 100% sensitivity and 100% specificity. The comparable numbers are given in Tables 8-11.

Table 8. Prevalence in vaccinated and control badgers one year after vaccination.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (1.6%)	1.2%	0.9%	0.6%	0.3%	0%
	10% (3.2%)	2.6%	2.0%	1.3%	0.7%	0%
	15% (5.1%)	4.1%	3.1%	2.1%	1.0%	0%
	20% (7.1%)	5.7%	4.3%	2.9%	1.5%	0%
	25% (9.3%)	7.5%	5.7%	3.8%	1.9%	0%
	30% (11.8%)	9.5%	7.2%	4.9%	2.5%	0%

Table 9. The sample sizes (of post-mortemed badgers) needed <u>in each group</u> (the vaccinated and unvaccinated controls) to detect the impact of the vaccine. The software package nQuery Advisor (Statistical Solutions http://www.statsol.ie/nquery/nquery.htm) was used to obtain these sample sizes.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (1.6%)	22627	5040	1965	930	499
	10% (3.2%)	10899	2393	929	448	237
	15% (5.1%)	6874	1539	593	284	150
	20% (7.1%)	4952	1095	423	201	106
	25% (9.3%)	3739	832	320	152	80
	30% (11.8%)	2979	658	252	119	62

Table 10. The sample sizes needed <u>in each group</u> (the vaccinated and unvaccinated controls) to achieve the appropriate numbers of badgers for post-mortem examination one year later taking into account the 25% death rate.

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (1.6%)	30169	6720	2620	1240	665
	10% (3.2%)	14532	3191	1239	597	316
	15% (5.1%)	9165	2052	791	379	200
	20% (7.1%)	6603	1460	564	268	141
	25% (9.3%)	4985	1109	427	203	107
	30% (11.8%)	3972	877	336	159	83

Table 11. The total number of badgers needed to be trapped (including those which test positive, the vaccinated badgers and the unvaccinated controls).

		Vaccine efficacy				
		20%	40%	60%	80%	100%
Standing Prevalence of Infection (Prevalence in control group after 1 year)	5% (1.6%)	63514	14147	5516	2611	1401
	10% (3.2%)	32293	7090	2753	1327	702
	15% (5.1%)	21565	4828	1860	891	471
	20% (7.1%)	16507	3650	1410	670	353
	25% (9.3%)	13294	2958	1138	540	284
	30% (11.8%)	11349	2507	960	453	236

DISCUSSION

6.1 This document demonstrates the large sample sizes required to detect an effect of the vaccine and that the use of even an imperfect live test can considerably reduce the sample sizes required.   A 44%-sensitivity-95%-specificity test yields a 28-36% reduction in the number of badgers trapped and a 33-46% reduction in the number of badgers culled and subjected to post-mortem. A more sensitive test could improve the situation further (at least 71% fewer badgers trapped and at least 78% fewer badgers culled and post-mortemed with a perfect live test), but sample sizes remain large.   A laboratory-based test (e.g. IFN gamma) with a validated higher sensitivity and specificity could be used retrospectively to identify uninfected badgers following trapping, marking and vaccination (for half of the badgers, randomly chosen).   This process, carried out between the initial trapping/vaccination operation and the follow-up trapping operation, would reduce the number of badgers that would need to be culled and subjected to post mortem.

6.2 It should be noted that all these calculations assume that post mortems are completely sensitive and specific for recent infections although in reality vaccinated "protected" badgers could show varying pathology and bacteriological culture.

6.3 Vaccine efficiency of 60-80% is very optimistic. Based on a standing prevalence of 20% and using the imperfect live test, this study design would necessitate the capture of 2400 to 4500 badgers and the ultimate culling of 1600 to 3000 badgers. Clearly, such an endeavour is costly in terms of animals culled as well as other resources.

6.4 Waiting longer, say two years after vaccination before recapture, would increase the difference in prevalence between vaccinated and control group, assuming protection persisted at the same level, but more badgers would die or move elsewhere. Thus, further calculations would be required for studies of longer duration.

6.5 A final point regarding statistical power is that many studies are based on 90% rather than 80% power with sample sizes correspondingly increased. Those funding and carrying out the experiment should be aware that a study with 80% power means there is a 1 in 5 chance that the effect (as defined in the sample size calculations) will be found to be non-significant.

PRECISION RATHER THAN SIGNIFICANCE

7.1 An alternative, and in many ways preferable, basis for the calculation of sample size is the precision of estimates to be obtained (as opposed to statistical significance). This is in line with a general preference for estimation (i.e. how big is the impact of the vaccine?) over significance testing (i.e. did the vaccine have an effect?). Clearly, the precision of the estimate of vaccine efficacy will be of key interest. Thus, while the calculations presented here should be helpful in considering some aspects of trial design, further detailed statistical consideration of sample sizes and precision should be undertaken before the trial design and size is finalised.

7.2 The variance of the estimated vaccine efficacy can be approximated by the following:

$$Var(\text{Vaccine Efficacy}) = \frac{p_V^2}{p_U^2} \frac{p_U(1-p_U)}{n} + \frac{1}{p_U^2} \frac{p_V(1-p_V)}{n}$$

where p_V and p_U are the infection prevalences (obtained at the end of the experiment) in the vaccinated and unvaccinated control groups, respectively, and n is the sample size in each group.

7.3 Consider, for example, a situation with background prevalence of 30% and vaccine efficacy of 80%; then we would expect variances and confidence intervals of the magnitude presented in Table 12 as a function of the sample size n.

Table 12. Expected variances and confidence intervals assuming a background prevalence of 30% and a vaccine efficacy of 80% (and assuming the use of a perfect test).

n (the sample size in each group)	Expected variance of the estimated vaccine efficacy	Corresponding 95% confidence interval if the estimate were 80%
119 (as in Table 9)	0.017	(54% - nearly 100%)
150	0.014	(57% - nearly 100%)
250	0.0083	(62% - 98%)
500	0.0042	(67% - 93%)
1000	0.0021	(71% - 89%)

7.4 These calculations demonstrate the cost, in terms of sample size, of gaining precision in the estimate of vaccine efficacy.

ILLUSTRATIVE CALCULATIONS USED TO OBTAIN TABLE 1

8.1 As stated previously a 25% per annum death rate was assumed for the badgers. Furthermore, it is assumed that no badgers survive to 16 years of age. Thus the age distribution (in one-year age groups) of the population is:

Table A

Age Group (years)	Percentage of population in this age group
0	25.3
1	18.9
2	14.2
3	10.7
4	8.0
5	6.0
6	4.5
7	3.4
8	2.5
9	1.9
10	1.4
11	1.1
12	0.8
13	0.6
14	0.4
15	0.3
Total	100

8.2 Assuming that the force of infection is constant (i.e. each susceptible badger is at the same risk of infection in the following year), then a annual force of infection of 0.07372 yields in a population of this age structure an overall infection prevalence of 20%. Where for each age group, the infection prevalence was calculated as $1-\exp(0.7372*A)$ where A is the average age in that age group. The overall infection prevalence was the weighted average of these age-specific infection prevalences, with weights as given in Table A.

Table B

Age Group (years)	Average age in this group (years)	Infection Prevalence (percentage)
0	0.5	3.6
1	1.5	10.5
2	2.5	16.8
3	3.5	22.7
4	4.5	28.2
5	5.5	33.3
6	6.5	38.1
7	7.5	42.5
8	8.5	46.6
9	9.5	50.4
10	10.5	53.9
11	11.5	57.2
12	12.5	60.2
13	13.5	63.0
14	14.5	65.7
15	15.5	68.1
Total		20

8.3 One year later the age distribution (in one-year age groups) of the badgers under study (vaccinated and unvaccinated controls) will be given by:

Table C

Age Group (years)	Percent of population in the age group
0	0.0
1	25.3
2	19.0
3	14.3
4	10.7
5	8.0
6	6.0
7	4.5
8	3.4
9	2.5
10	1.9
11	1.4
12	1.1
13	0.8
14	0.6
15	0.5
Total	**100**

8.4 Assuming the same force of infection, the age-specific prevalence in the vaccinated group (with 100% efficacy) is:

Table D

Age Group (years)	Infection Prevalence (Percent)
0	-
1	3.6
2	10.5
3	16.8
4	22.7
5	28.2
6	33.3
7	38.1
8	42.5
9	46.6
10	50.4
11	53.9
12	57.2
13	60.2
14	63.0
15	65.7
Total	**19.8**

The overall infection prevalence (19.8) was the weighted average of these age-specific infection prevalences (weights as given in Table C).

8.5 Assuming the same force of infection, the overall infection prevalence in the unvaccinated group (or a vaccinated group with 0% efficacy) was the weighted average of the age-specific infection prevalences (Table B) with weights as given in Table C: 25.5%.

INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

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Mr Alick Simmons
DEFRA
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File Ref: TBX 135

13 August 2002

Dear Alick

Proposed Pilot Field Trial Gamma Interferon (γ-IFN)

Many thanks for copying me your paper on the pilot field trial.

It is reassuring that this trial is about to get underway given the now clearly recognised limitations of the tuberculin test, and the need to improve diagnosis in individually infected animals. We agree with you, as you will know from ISG discussions, it is paramount that the trial should be structured to maximise data to satisfy both strategic and scientific needs. One major objective would be to determine whether application of the γ-IFN test in conjunction with the tuberculin test is cost effective in problem herds, and a second to provide information that will allow more meaningful interpretation of the test and how it might influence future control policies.

Rather than comment on the third draft of your paper, which is much improved on the draft presented in June, we thought that it would be more useful if we presented you with our own paper on data requirements and trial design from a scientific perspective, for you then to consider and incorporate in trial protocols. This exercise, which is now advanced, will take a further short time. In the meantime, however we would agree that an initial pilot trial could reasonably be based, as you propose, on multiple reactor problem farms.

We shall comment in detail on the scope and scale of the trial, and the appropriate analysis of the data. Meanwhile, since you wish to get the ball rolling as soon as possible, problem farms could be enrolled immediately.

We fully agree with your sensible proposal to work in Wales and the need also to include problem farms in England, but should wish to ensure that farms in trial areas are not included in this pilot study.

I shall be sending a copy of this letter to Sue Eades.

Yours sincerely,

JOHN BOURNE

INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

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Elliot Morley MP
Parliamentary Under Secretary (Commons)
Department for Environment, Food and Rural Affairs
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Our reference TBX 135

7 November 2002

Dear Mr Morley,

I was grateful for the opportunity that you gave me last month to bring you up to date on a number of aspects of the TB research programme. I was particularly pleased at your suggestion that we meet more regularly on an informal basis, and look forward to doing so in the future.

It was also a pleasure to support you at the press conference where you launched the Autumn Package of TB control measures. The full value of the IFN test may not be apparent for some time, of course; however, if it does provide better identification of infected cattle then your announcement of its use as a policy initiative could well represent a significant step in the control of bovine TB in Great Britain.

As you know, the ISG has long recognised the critical need for an improved diagnostic test for TB. Indeed, if there is ever to be a strategy to control TB without the culling of wildlife then it <u>must</u> be underpinned by a better diagnostic test in cattle. Only in this way will it be possible to identify and remove infected cattle faster than the rate of reinfection. For these reasons we have strongly advocated work on refining the IFN test, and have supported plans for a field trial to provide the detailed data necessary to both fully assess its merits and to determine how it could best be applied in practice. However, the Group believes that, as with all work directed towards resolving the TB problem, this requires a framework of scientific rigour. It is in this context that we have serious concerns about the proposed Defra INF field trial which I feel it is my responsibility to draw to your attention.

The Group recognises the practical need for Defra to respond to increasing TB incidence and has encouraged a number of initiatives outside trial areas in an attempt to provide information that will lead to improved control of the disease.

These included evaluating the IFN test as a policy option. In the light of this, therefore, we were most disappointed to learn that Defra has apparently decided to proceed with plans for an IFN field trial without a meaningful attempt to discuss with the Group a number of aspects on which we had previously expressed concern to officials. We consider that Defra's trial design has a number of deficiencies from a scientific point of view and so have suggested modifications which we believe would significantly enhance its value - some involving little requirement for additional resource. These suggestions have been rejected by Defra without any discussion.

Given the urgent need to develop new policy options, which would incorporate an improved diagnostic test for the disease in cattle, we consider that a more appropriate use of scarce resources in the limited time available, would be to invest in a pilot field trial that will provide more detailed and useful scientific data that can be expected to inform on the development of new candidate policy options. Consequently we are unable to give our unqualified endorsement to the Defra field trial as proposed.

We remain committed to providing the scientific underpinning for future TB control policy options. In order to stimulate what we would hope to be constructive dialogue with Defra officials we will prepare a paper outlining our major concerns about their proposal. We would then expect to consider with Defra how ongoing and planned research initiatives, including the IFN field trial, can be drawn together to provide the essential data that we believe is needed to develop future policy options.

Looking ahead we very much hope that the close collaboration that we had always enjoyed with your officials in the past will again become a central feature in consideration of issues of such importance.

Finally, may I thank you for the encouragement and support that you continue to give to the work of the Group.

Yours sincerely,

John Bourne

F J Bourne

INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

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Elliot Morley MP
Parliamentary Under Secretary (Commons)
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May 2003

Dear Mr Morley

I append an update of progress during the past year on the trial and on related research, following the resumption of work after the Foot and Mouth Disease (FMD) outbreak. A detailed assessment on each of the major components of our work is provided in the accompanying papers.

Field work in the trial areas recommenced in December 2001, just prior to the trapping closed season (February – April 2002), with preparations being made for the subsequent 2002 culling season. We are able to report that the initial proactive culls in the three triplets that were outstanding at that time have now been completed, and that the amended programme of proactive repeat trapping has also been met by the Wildlife Unit (WLU); this aspect of the field work is therefore now back on course.

Proactive strategy

As we reported in March 2002, the outbreak of FMD resulted in effectively a year's delay in completing trapping operations. However, because 7 out of the 10 triplets had already been initiated, 70% of the overall proactive study area was accumulating data during the FMD crisis. We had previously advised that the quality of these data could be assessed only when a better picture of badger abundance in the trial areas had been established, by analysing data from the repeat culling operations. These data now indicate that in five of the proactively culled triplets, badger populations stayed very low throughout the FMD outbreak and were probably not markedly higher than they would have been had culling not been suspended; this is an important finding in providing confidence that the trial has remained robust in these areas despite the suspension of direct activity. In the other two active trial areas, badger populations following initial culls remained high. This was probably due to inefficient initial culling that could be ascribed to seasonal

factors, and implies some weakness in the data provided by these two triplets during 2001. Furthermore, the delays caused by FMD to the repeat culling that would otherwise have taken place would have compounded this. We have estimated that, overall, the data lost during this period and prior to repeat culling is equivalent to the loss of 4 triplet years.

The three triplets in which initial culling had not taken place at the time of the FMD outbreak were not affected, of course, as they had not become active.

The loss of triplet years means that the time of delivering 50 proactive trial years will be extended beyond the end of 2005 which was predicted in our Third Report. An optimistic assessment is, assuming that there are no further unanticipated setbacks, that this point will be reached by mid 2006.

Reactive Strategy

The reactive strategy has been more seriously interrupted by FMD. A reactive response is triggered by a positive herd tuberculin test, so the suspension of TB testing for one year and subsequent delays in the herd testing programme have therefore resulted in inevitable delays. This has been compounded by delays in the SVS reporting herd breakdowns to the WLU, adding to their difficulties in forward planning their reactive culling operations. Regrettably, these delays have resulted in an irretrievable loss of time and resulted in the situation whereby it is now not worth culling some of the long outstanding reactive breakdown farms.

Following discussions with Defra, a number of operational procedures has been agreed to improve the reaction time and to bring the programme of reactive culling back on track. Further delays are inevitable, however, due to the still outstanding testing backlog. We anticipate that the WLU may have caught up the backlog of reactive culling by the end of the present culling year, but we must advise that the situation will require close monitoring. It is not possible at this stage to assess when 50 reactive triplet years will be reached, although we are optimistic that it may coincide with that assessed for the proactive treatment.

Other major initiatives complementing the field trial include the TB99 epidemiological Risk Analysis Survey and the Road Traffic Accident (RTA) Survey. Again, we regret to report that there is a serious shortfall in the data flow that we had expected from both of these major research projects.

TB99 Risk Analysis Epidemiological Questionnaire

A critical feature of the TB 99 survey is the collection of linked case and contemporary control data. It is unfortunate that a significant amount of data expected from this survey has either not been collected, or has been compromised because control data is not adequate or has not been collected contemporaneously with case data. Furthermore, we feel this failure on the part of the SVS to collect data cannot be ascribed solely to the demands of FMD and CSF. It is reassuring that extra resource, post FMD, has now been directed to the TB99 survey to

improve the situation with outside contractors recruited to complete the farm questionnaires; however, it is only now that we are we reaching the point where we can carry out a targeted initial analysis of the first 100 completed data sets – something we had originally expected to be able to do some 2 years ago. As stated in the accompanying report we strongly advise that resource is directed to complete full sets of data (case plus associated controls) for all breakdowns in trial areas during the current year. This would provide a substantial number of data sets for analysis in 2004.

Road Traffic Accident Survey (RTA)

The RTA survey was designed to provide information on whether reliable data on the prevalence of TB in badgers could be obtained without recourse to actively killing badgers. A target of 1200 badger carcasses per year, collected from traffic accident cases in seven counties around trial areas, was proposed for initial analytical purposes. Thus far, too few badgers have been collected to support any meaningful analysis, as prior to June 2002 only 252 badger carcasses had been collected and post mortemed. Responsibility for this programme of work since then has been transferred to CSL and we are optimistic that the annual target of 1200 post mortemed badger carcasses will be reached for the first time by the end of this year.

Taken together, these delays in the epidemiological and the RTA surveys have resulted in a serious loss in opportunities which would have given the potential to provide early advice to Ministers on improved control of the disease in cattle.

There are remaining issues that also cause concern, but also some more positive developments where research opportunities presented by the FMD outbreak have been taken, and also others where good progress is being made.

Tissue Culture

M. bovis culture of tissue samples from field cases is an important component of the diagnostic process and, in addition, the bacteria grown in culture provide essential material for molecular epidemiological studies conducted by scientists at VLA. Prior to FMD, a limit was imposed on the number of slaughtered tuberculin positive animals submitted for culture from breakdown herds. This limit was judged to be consistent with the requirement to ensure that a clear diagnosis could be made, but it was inevitable that molecular epidemiological studies would be compromised to some extent by this limitation on the availability of material they required. However, the increase in the number of herd breakdowns post FMD has overwhelmed the available laboratory culture facilities and the number of animals from a breakdown subjected to culture, and therefore epidemiological data available for future analysis, has been limited still further. It is more reassuring however that a full complement of tissues are being collected from breakdown herds in trial areas.

Post FMD study

A unique opportunity was presented by FMD to study farms, both within trial areas and outside, where herds had been slaughtered and subsequently restocked, and which subsequently suffered a TB breakdown. We pressed strongly for this research opportunity to be taken up, and were glad that Defra took our advice and provided the funding. The resultant study, which has been ongoing for about a year now, has been designed to provide a range of epidemiological information including the relevance of cattle movements to TB breakdowns. This study is complemented by the VLA molecular epidemiological study mentioned above. At the outset it was unfortunate that the required full complement of tissue samples was not collected from breakdown farms outside trial areas, thereby resulting in the loss of some research material; however the SVS has now been instructed to collect this material. Early molecular epidemiological results from breakdown farms in notionally TB-free areas of GB are indicating that *M.bovis* types, associated previously with a geographic distribution remote from the breakdown farm, are being isolated from some of these outbreaks and can be directly attributed to the movement of TB infected cattle from the remote region. The Group is considering the relevance of this, and other data, to short term policy options.

Improved TB Diagnosis

These and other issues serve to underscore the necessity for the holistic approach that we have taken in an attempt to better understand the epidemiology of this troubling disease and also emphasise the central importance of an early and accurate diagnosis. We have continually stressed the crucial importance of an effective and reliable diagnostic test for cattle if the spread of TB is to be brought under strict control. In this respect it is disappointing that Defra has still not responded to ISG proposals to collect what we believe to be essential data from their ongoing pilot study of the gamma interferon test; this would allow an objective assessment to be made of the use of this test in a range of potential policy options and could create the opportunity for a major advance in the strategy for TB control.

I look forward to discussing these and other issues with you when we meet next week.

F J BOURNE

SHORT-TERM POLICY OPTIONS FOR DEALING WITH BOVINE TB

1. The attached paper lists short term policy options for dealing with bovine TB, which can be expected to slow down disease progression, and buy time for Defra and the livestock industry for new, improved disease control measures to be developed and implemented.

2. The Group is invited to comment and advise on the short-term policy options.

SECRETARIAT
May 2003

SHORT TERM POLICY OPTIONS FOR DEALING WITH BOVINE TB

ISG Response to TBF 79

The ISG has commented (Minutes ISG 59th meeting April 2003) that the options outlined in this paper are a common sense application of disease control principles which have been understood for some time, and which should have been put in place many years ago. The paper appears, however, not to have taken into consideration recent scientific research findings which had it done so would have strengthened the proposals.

In order to better inform the ongoing debate on action that might be taken outside trial areas to combat the escalating problem of bovine TB, the ISG has developed a number of initiatives (ISG--), these included proposals relating to the use of the IFN gamma diagnostic test, analysis of data on inconclusive reactors and an analysis of data from emerging hot spots outside the trial areas (Cluster Studies).

Cluster Studies

The data obtained from hotspots (which were discussed at Defra in Sept 2002 and at TB Forum in Oct 2002), albeit not specifically collected for the purpose of an epidemiological analysis, were not consistent with wildlife being the sole source of infection, and suggested that cattle to cattle transmission played a role. We recognised a need for supportive molecular epidemiological data, based on *M. bovis* typing and cattle movement data, from breakdown farms in relatively TB free areas of the country. A proposed study centred around selected breakdown herds in 2000 in low TB incidence areas, was not funded. However, the opportunity to carry out a similar study presented itself as a consequence of the Foot and Mouth Disease (FMD) outbreak that resulted in a number of farms, in both high and low incidence areas, being de-stocked and, subsequently, re-stocked with purchased cattle, in some instances involving entire herd purchases.

A study was initiated to study re-stocked TB breakdown farms, prospectively and retrospectively, the former within trial areas and the latter outside trial areas, to provide epidemiological data relating to these breakdowns. This study was complemented by an ongoing molecular typing study based at VLA to provide molecular epidemiological data. A recognised limitation of these studies outside trial areas is a lack of wildlife data but, in spite of this, invaluable information on the relevance of cattle movements on TB breakdowns could be obtained.

Early results from breakdown farms in notionally TB-free areas of GB show that *M. bovis* types, associated previously with a geographic distribution remote to the breakdown farm, have been isolated from some of these outbreaks and can be directly attributed to the movement of TB infected cattle from the remote region. This study is in its early stages, and no data is available to demonstrate within herd

transmission from immigrant animals, but even so we believe that these findings, which highlight the dangers associated with moving TB infected cattle, cannot be ignored.

Pathogenesis Studies

Laboratory based experiments with infection models of TB in cattle has confirmed the shedding of organisms in the early stages of the disease process, with a potential for disease transmission, and the failure of the tuberculin test to detect all infected animals, including some with well developed pathological lesions.

Complementary field studies have shown that tuberculin test-negative animals in contact with tuberculin test-positive animals from multiple breakdown herds, are infected and therefore being missed by the disclosing tuberculin test. Shedding of *M. bovis* from these animals has not been detected but there is a clear potential for disease transmission. It is likely that some of these infected, disclosing test negative, animals would have been detected at subsequent short interval tuberculin tests, nonetheless while the risk of disease transmission would have been further reduced, the risk would remain.

The pathogenesis studies are also at an early stage but experimental findings have been consistent, and support the view that the tuberculin test which, in the past, has been used very effectively as a herd test, has serious limitations in identifying individual infected animals in a herd, and is also unable to differentiate between infected animals showing varying degrees of infection and pathology.

The IFN test, using the same pool of antigens as used in the tuberculin test, identified all infected animals, but no data are available on the specificity of the IFN test or its performance relative to the tuberculin test in this country. Detailed trial proposals have been submitted to Defra to obtain this information.

Other Relevant Considerations

• Wherever, globally, a wildlife reservoir has been associated with TB in cattle, control measures relying on the use of the tuberculin test alone have failed to control the disease.

• In Australia bovine TB has been controlled. Control measures involved the elimination of a wildlife reservoir (Water Buffalo) but the role of the wildlife as a source of infection was far from clear and they were eliminated as a precautionary measure. The Water Buffalo was present in only a small part of the country and other control measures were the implementation of strict cattle movement controls and improved diagnosis.

• It has been claimed, and still is claimed, that judicious use of the tuberculin test has resulted in most of GB remaining TB free. A comparison of TB incidence maps of 1986 and 2002 clearly shows that this is a delusion.

Translating Research Findings into Policy

Notwithstanding that bovine TB is a disease of relatively low infectivity, the movement of infected cattle from herds of undisclosed infection, particularly to non infected farms in TB free areas of GB, is dangerous and the potential trigger for the development of new hot spots

The tuberculin test, however strategically applied, will fail to detect some diseased animals that are potential transmitters of disease to other cattle and to wildlife

Detection of diseased animals will be improved, and achieved earlier in the disease process, by complementary use of the IFN test with the tuberculin test.

Molecular typing data suggests a regionalisation of subtypes of *M. bovis*. This indicates that most infection is not spreading as a result of infected cattle moving around the countryside. However molecular typing data taken into consideration with other data suggests that a small but significant component may be due to cattle movement, and this presents a serious risk of establishing new hotspots of infection, involving the infection of wildlife.

Many of the factors associated with the development and maintenance of a wildlife reservoir are unknown but it can be predicted that unless appropriate steps are taken to prevent this cycle of events there is every likelihood that the spread of the disease experienced in the last 15 to 20 years will continue and possibly gain pace.
It is our view that short term policy options should focus primarily on restricting the spread of TB into those areas of UK that are currently relatively free of the disease. Scientific findings give credibility to this approach while the measures that need to be taken to address the situation in high incidence areas are more speculative and dependant on the outcome of ongoing research.

SHORT TERM POLICY OPTIONS:

High incidence areas (Hot spots)

Badger removal-field trial
Complementary use of IFN test-field trial (ISG proposals)
Routine herd testing – one to two year intervals or more frequent
Restrict animal movements to equivalent disease status farms, ban movement to higher health status farms i.e. introduce concept of zoning (this could be refined to encompass a number of options – as highlighted by BCVA)
AWAIT FURTHER RESEARCH FINDINGS.

Low incidence TB areas

The primary objective must be to avoid infection of wildlife, which can be assumed to be the precursor to the development of a wildlife reservoir, and a contribution to the maintenance of the disease in cattle.

Pre-movement

Ban animal movement from high incidence areas of the country to low incidence areas. A compromise would be to ban animal movement from high-risk TB status farms to low risk disease status farms.

Animals moved to farms of equal or lower risk disease status to be subjected to pre-movement testing with the tuberculin test and the IFN test

Post-movement

In addition to pre-movement testing purchased animals should be quarantined, re-tested by the tuberculin test and IFN test 60 days after arrival on a farm and subsequently at 60 day intervals by tuberculin test until negative. The whole herd tested one year following clear test prior to being considered for routine testing.

It is not appropriate at this stage to be too prescriptive about fine details of policy but it must be accepted that cattle movements create a dynamic disease state that should be closely monitored. This demands more frequent testing than at 4 yearly intervals. It is recognised that testing resources are limited and it is important therefore that the effort available is deployed rationally, and that this may require some changes from current procedures.

Other relevant factors such as rapid removal of reactors from a herd are considered in TBF 78.

An overriding consideration of any TB control policy must be the clear recognition that TB is an infectious disease of cattle and wildlife. Infected animals are a danger to other animals and past experience shows that when a wildlife reservoir develops the difficulties and cost of controlling the disease in cattle increase significantly.

Farmers in relatively TB free areas must be advised of the dangers of bringing TB infected animals onto their farms, how to avoid doing so, or at least minimising the risk using the best technology available. They should clearly understand that by not taking precautions they are exposing not only themselves but also their neighbours to disease risk and that optimum risk avoidance is achieved by not moving animals.

There is no guarantee that these measures will prevent new hotspots developing, but they can be expected to slow down disease progression and at least buy time for

Defra and the livestock industry for new, improved disease control measures to be developed and implemented.

**REACTIVE TREATMENT - ADVICE FROM THE INDEPENDENT
SCIENTIFIC GROUP ON CATTLE TB (ISG) TO DEFRA MINISTERS**

The Independent Scientific Group on Cattle TB (ISG) designed and oversees a large-scale trial aimed at evaluating badger culling as a means to reduce the incidence of cattle TB. The trial involves three experimental treatments: (i) proactive culling, which aims to reduce badger densities to very low levels across entire trial areas, (ii) reactive culling, which seeks to remove only those badgers geographically close to recent cattle TB outbreaks on particular premises, and (iii) no culling (survey only).

Triplets (sets of three trial areas) were recruited sequentially, with the initial proactive culls completed in the first triplet in November 1998, and in the tenth and final triplet in December 2002. Interim analyses have been undertaken periodically by two ISG members (statisticians Sir David Cox and Prof Christl Donnelly) with the rest of the ISG remaining unaware of the trial results to maintain the strictest confidentiality. The independent statistical auditor, Prof Denis Mollison, has met the ISG statisticians and has endorsed the trial design and the methods used in the interim analyses.

Earlier this month the ISG statisticians, after consultation with Professor Mollison, informed the group that the analysis of the data on TB incidence in cattle within the trial revealed significant results which required consideration by the ISG as a whole. The ISG has now carefully considered the results of the analyses. The information from the trial on the proactive treatment remains inconclusive, and the remainder of this note focuses on the reactive treatment.

The results reveal that, after appropriate statistical adjustments, the incidence of herd breakdowns in reactively culled areas has been consistently greater than expected. This increase was estimated to be 27%, though it could be as small as 4.3% or as large as 53%. This increase was consistent in all nine triplets that had received reactive culls by the time of analysis (triplet J has not yet been reactively culled). While the larger adverse effects may be implausible on general grounds, even a 10% deterioration, if it persisted, would clearly be of major concern.

The ISG has already documented (Second Report, paragraph 4.1.2) its intention to continue the trial until all areas had been enrolled for at least a year, a milestone not achieved until December 2003. To continue the reactive culling until the end of the trapping season rather than terminating it sooner would involve culling in November, December and January (except during the Christmas break) and would ensure that all triplets had been enrolled for at least one full year . It would mean that an interim analysis in March 2004 would have substantial further information. The ISG recommends that reactive culling continues through the end of the current culling season (the end of January). Unless some major changes were to develop,

however, it seems likely that the ISG would then recommend terminating the reactive strategy on the grounds that it was not a viable base for a future policy option. Following such termination collection of breakdown data should, however, continue.

The ISG recognizes the difficulties involved in making such a recommendation and indeed the pressures faced by the Minister in making a decision based on these findings and recommendations.

29 October 2003

INDEPENDENT SCIENTIFIC GROUP ON CATTLE TB

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10 November 2003

Dear Jim

BOVINE TUBERCULOSIS IN THE FURNESS PENINSULA: SURVEY OF WILDLIFE

Thank you for making the ISG aware of plans to carry out a limited RTA survey of badgers found dead on roads in SW Cumbria and a survey of deer in the same area, and also for inviting the ISG to comment.

I have to say at the outset however, that we see little purpose in conducting such an exercise. While it could provide some useful epidemiological data, this must be in doubt, and is unlikely to add anything worthwhile from a disease control point of view, and could even be disadvantageous by diverting resources that are better used in the more coherently targeted RTA survey that is currently in progress.

In saying this we are well aware of the concerns about the increasing incidence of bovine TB, and particularly the prospect of the disease developing in what have traditionally been relatively TB free areas. As you know, the ISG addressed this very issue in the short term policy option discussion paper we prepared earlier in the year. In this we discussed the key priorities for action to prevent new 'hotspots' developing, and many of the measures we advocate could be applied immediately in the Furness Peninsula.

We are also aware of the pressures that Government have been under to extend the RTA survey beyond the ISG recommended area, where it is currently being carried out to complement the randomised badger culling trial.   The assumption seems to be that an extended survey would provide a clear picture of the prevalence of TB in the badger population across the country.

However, one has to accept that the ability of the RTA to provide reliable and useful prevalence data has yet to be established. Our advice to restrict it to the regions where the trial is taking place will at least allow the approach to be validated against badger prevalence data collected directly in the trial itself. It is our view that extending the RTA outside those areas at this time has limited scientific purpose because it would have no relevant benchmark data. Furthermore it would be likely to add to the considerable problems that Defra has already experienced in properly resourcing the RTA survey – the progress of which, as you know, until recently has been woeful.

All these wider concerns apply to your proposal for the Furness RTA survey, and are encapsulated in your own document, in Appendix 2 paragraph 17 accompanying your letter. The ISG recently agreed to the release to DVMs of the location of TB infected RTA badgers to help them decide on testing frequency in areas that have a low level of TB; but in the Furness peninsula you have already recognised the need to increase testing frequency, so what would you expect to achieve by instituting an RTA survey? If you were to find a TB infected badger questions would immediately arise about what it meant, how you could interpret the finding and what further cattle disease control measures could be put in place that should not already have been adopted.

It is true that typing data from badger TB culture material coupled to cattle typing data could be useful, but as the numbers from an RTA survey in the Furness peninsula would be small and provide only very limited scientific information, it is unlikely to clarify any issues relating to the role of wildlife in cattle TB or to assist the implementation of TB policy in that area. I note that you expect a 30% recovery rate of RTA badgers in the Furness Peninsula; this is much higher than the estimated figure for the seven counties RTA, which has been estimated at most 10% and is probably less than this.

Your paper refers to some 500 deer culled each year from neighbouring areas by the local deer management group. If coordinated this number of culled animals could provide some useful epidemiological data and be linked to the study on TB in wildlife, other than the badger, being carried out by CSL from Woodchester park.

The ISG would emphasise the need to collect scientifically meaningful data from the trial related RTA and suggest that extra resource could be used to increase the proportion of badgers collected and the number of badgers that are subsequently post mortemed.

Yours sincerely,

F J BOURNE

FINANCIAL STATEMENT

The total expenditure per financial year for the ISG since 1998 is as follows:

1998/1999   £81,426

1999/2000   £76,837

2000/2001   £78,000

2001/2002   £76,100

2002/2003   £89,886

2003/2004   £135,181

These figures include fees, travelling expenses, subsistence, catering and room hire.

In line with Cabinet Office guidance, members' fees were increased by 2.8% from 1 April 2004 as follows:

The daily and hourly rates for the Chairman increased from £185.00 to £190.20 and £25.70 to £26.45 respectively. The rates for other Members increased from £153 to £157.30 and £21.25 to £21.85 respectively.

OPEN MEETING

The Independent Scientific Group on Cattle TB (ISG) met at One Great George Street in London on 19 November 2003. The meeting was the first that the Group had conducted in public, and following advance publicity, Members were pleased to welcome around 70 attendees.

The audience observed the Group discuss presentations on 'Strain Typing of *M.bovis* in Great Britain', 'Bovine TB Pathogenesis', and 'Diagnosis of Infection with *M.bovis'*.

Apart from observing the Group deliberate, the audience participated in a Question and Answer session during which were discussed issues such as the cessation of reactive culling, vaccines to control bovine tuberculosis, and pre- and post-movement cattle testing. Informal discussions also took place over lunch and provided attendees with the opportunity to ask further questions.

The Chairman thanked those present for attending the meeting and hoped it had demonstrated the broad-spectrum scientific approach taken by the ISG to advise on the control of bovine tuberculosis.

The attendees were asked for feedback on the meeting; 97% found the meeting informative and 91% indicated that they would like to attend future meetings. The Group intends to hold an annual open meeting in the future.

DISCUSSIONS WITH INTERESTED PARTIES AND PARTICIPATION IN MEETINGS AND CONFERENCE (JUNE 2001-OCTOBER 2004)

1. Environment, Food and Rural Affairs Committee evidence sessions
    *   10 February 2003
    *   24 February 2003
    *   10 December 2003
    *   26 May 2004

2. Selected individual Members of Parliament by request

3. Organisations met

    British Cattle Veterinary Association
    British Veterinary Association
    Countryside Council for Wales
    Country Land and Business Association
    English Nature
    Farmers Union of Wales
    National Beef Association
    National Federation of Badger Groups
    National Farmers' Union
    National Farmers' Union (Wales)
    Royal College of Veterinary Surgeons
    Royal Society for the Prevention of Cruelty to Animals
    Tenant Farmers' Association
    Women's Farming Union

4. Public meetings and conferences attended

    Regular meetings of the TB Forum
    Farmers' Union of Wales Annual Conference
    National Federation of Badger Groups Annual Meeting
    Spotlight Forum at Annual Dairy Event
    NBA Animal Health TB Committee

5. Individuals by request

SUMMARY OF CURRENT DEFRA FUNDED BOVINE TB RESEARCH PROJECTS

Code	Title	Start Date	End Date	Contractor	Cost (£) 2004/2005
A	Genome sequence analysis of *M.bovis*.	01/01/99	31/03/05	VLA	44,732
B	Ecological consequences of removing badgers from an eco-system	01/02/99	31/03/05	CSL	222,178
C	Detection and enumeration of *M.bovis* from clinical and environmental samples.	01/04/99	31/12/04	VLA	61,087
D	Develop innovative methods to estimate badger population density.	01/04/99	31/03/05	CSL	88,361
E	Testing TB vaccines in cattle.	01/04/99	31/03/05	VLA	273,328
F	Generation of vaccine candidates against *M.bovis*.	01/04/99	31/03/05	VLA	78,300
G	Multivariate analysis of risk factors affecting TB incidence in cattle herds.	01/05/99	31/08/04	VLA	28,277
H	Testing of vaccine candidates for bovine TB using a low dose aerosol challenge guinea pig model.	01/07/99	30/06/04	VLA	60,133
I	Development and evaluation of strain typing methods for *M.bovis*.	01/09/99	31/03/05	VLA	30,344
J	Molecular genetic analysis of badgers social structure and bovine TB.	01/01/00	31/03/06	CSL	184,064
K	Pathogenesis and diagnosis of TB in cattle – complementary field studies.	01/10/00	31/03/05	VLA	400,000
L	Application of postgenomics to reveal the basis of virulence, pathogenesis and transmissibility of *M.bovis*.	01/04/01	31/03/06	VLA	791,767
M	Development of improved tests for diagnosis of *M.bovis* infection in cattle.	01/04/02	31/03/05	VLA	149,024
N	Development and testing of vaccines against badger TB.	01/04/02	31/03/05	VLA	199,871
O	Development of immunological assays for detection of *M.bovis* infection in badgers.	01/04/02	31/03/05	VLA	158,966
P	Pathogenesis and immunology of *M.bovis* infection in cattle.	01/04/02	31/03/05	IAH	430,290
Q	Bovine TB transmission in restocked herds: risk factors and dynamics.	01/06/02	30/03/06	WU	349,560
R	Low dose TB infection in cattle: disease dynamics and diagnostic strategies.	01/10/02	30/09/06	QUB VLA	711,516
S	Investigation of potential badger/cattle interactions and how cattle husbandry methods may limit these.	01/01/03	31/12/05	CSL	184,799

T	Long term intensive ecological and epidemiological investigation of a badger population naturally infected with *M.bovis*.	01/04/03	31/03/05	CSL	591,263
U	Economic value of changes in badger populations.	01/06/03	30/11/04	RU	45,437
V	Housing of naturally infected cattle (field reactors) at VLA for immunological and bacteriological analysis	01/04/04	30/09/07	VLA	167,794
W	Kinetics of skin test response in bovine TB	01/04/04	31/03/05	IAH	252,100
				Total	**5,503,191**

Key

CSL = Central Science Laboratory
IAH = Institute of Animal Health, Compton
QUB = Queens University Belfast
RU = Reading University
VLA = Veterinary Laboratories Agency
WU = Warwick University

GLOSSARY OF TERMS

BRO: BADGER REMOVAL OPERATION
The culling (killing) of badgers in a specific countryside area.

BCG: BACILLUS CALMETTE GUERIN
A modified strain of *M. bovis* used for human vaccination.

BOVINE TB/TUBERCULOSIS
A disease caused by the mycobacterium *M. bovis*.

BREAKDOWN
A cow or herd of cattle found to suffer from TB

CULTURE
The generation of living cells.

DIAGNOSIS
The identification of an illness or disease by clinical signs or response to a surveillance or laboratory test.

DNA
Deoxyribonucleic acid – a genetic structural unit, unique to the individual

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 risk.

FMD: FOOT AND MOUTH DISEASE
A highly infectious viral disease affecting cloven-hoofed animals.

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

GENOTYPE
The distinctive DNA identifier distinguishing one individual from another.

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

INTERIM STRATEGY
The GB badger control policy of the Government in 1986-1997 (see *Krebs et al*, p143)

LESION
An injury, wound or discontinuity of (i.e. disease) tissue.

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

PARENTERAL
Administered or occurring elsewhere than in the alimentary canal.

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

PCR: POLYMERASE CHAIN REACTION
A DNA amplification process.

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

PREVALENCE
The proportion of a population infected at a particular time.

RBCT: RANDOMISED BADGER CULLING TRIAL

A field trial where areas have been randomly allocated to specific badger culling regimes avoiding allocation of bias. The trial began in 1998 and is expected to end in 2006.

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.

SOP: STANDARD OPERATING PROCEDURE

A set of instructions for field staff carrying out work on the RBCT; 20 SOPs each cover a different task, such as collection/recording of data or carrying out post-mortem examinations.

SPECIFICITY

The proportion of true negatives detected by a diagnostic method.

SUPER EXCRETORS

Badgers, infected with TB, found to repeatedly or consistently excrete *M. bovis*.

TB99 EPIDEMIOLOGICAL SURVEY

A study set up to assess which factors could influence the propagation of TB in cattle.

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 RBCT areas. Each triplet has three trial areas and each trial area is 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 no culling (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.

VETNET

The main Defra Animal Health IT data storage system.