The Bovine Tuberculosis Eradication Programme in Northern Ireland

Proposals from the Tuberculosis Strategic Partnership Group (TBSPG)

Scientific peer review

Final report

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31 August 2016

Minor revisions
13 September 2016

Increasing the likelihood that infected animals will be detected

Severe interpretation of the skin test [proposed measure 1]

Increased usage of interferon ɣ [proposed measure 2]

48. Each of these measures *[proposed measures 1 and 2]* will increase the likelihood that infected animals will be detected.

49. There are now a number of studies highlighting the future infection risk posed by animals in known infected herds that are positive under severe interpretation (referred to in the Review) or inconclusive under standard interpretation (including Clegg et al., 2011a,b). Animals positive to the interferon ɣ test are also at increased future infection risk, in circumstances where the positive predictive value of this test is likely to be high (Gormley et al., 2013; Lahuerta-Marin et al., 2015) (see below).

50. As test sensitivity is increased, it is inevitable that some non-infected animals will be incorrectly identified (false positive reactions).

51. As acknowledged in the Review, there are two very different contexts in which interferon ɣ testing is conducted, including:

    a. To increase the likelihood that infected animals will be detected. As outlined in the Review, it is critical that interferon ɣ testing is limited to high-risk groups in known infected herds. Due to the imperfect specificity of the interferon ɣ test (including Álvarez et al., 2012), the positive predictive value of this test will be low unless the test is used in situations where the prevalence of infection is likely to be high.

    b. To provide assurance that bTB skin reactors are indeed infected (this is discussed later).

Increasing the probability that infected animals will be eliminated

Full and partial depopulations [proposed measure 6]

52. There is limited published information about the long-term infection risk following full/part herd depopulation. This strategy was shown to be effective in Irish herds depopulated with bTB during 2003-05 (Good et al., 2011). However, as also suggested in the Review, associated measures to prevent reintroduction were

critical. In the UK after the FMD epidemic, future TB risk on restocked farms was associated with both the restocked cattle (from high risk areas) and bTB persistence on the restocked farm (Carrique-Mas et al., 2008).

53. Research will be needed to consider key elements relating to this measure, including:

    a. The future infection risk in herds following full/partial depopulation.

    b. The practicality and effectiveness of measures to prevent reintroduction of bTB, following full/partial depopulation, both through restocked cattle or as a result of bTB persistence in the locality.

<u>Reducing the infection risk posed to other herds</u>

54. Some of the proposed measures *[proposed measures 7, 8, 9 and 14]* are more effective than others in reducing the infection risk to other herds.

Introducing an additional 6 month test for derestricted herds [proposed measure 14]

55. There is compelling evidence of continuing infection risk, both in herds and individual animals, for an extended period after derestriction, as a consequence of both newly introduced and residual infection. Multiple studies from a range of countries have highlighted the contribution of residual infection to bTB persistence in a herd or locality (including Karolemeas et al., 2011; Dawson et al., 2014; More and Good, 2015; More et al., 2015), and a recent study has noted that higher-than-baseline risk persists for many years subsequent to high-risk breakdowns (Clegg et al., 2015).

56. Under Council Directive 64/432, restricted herds are free to trade (and considered at no greater risk than non-infected herds) once two consecutive clear full-herd SICTT tests are achieved. In contrast, in the Australian programme, all animals present during a breakdown were considered at risk for the rest of their life, and infected herds took a minimum of 8 years to attain the lowest herd risk status (More et al., 2015). The EU legislation is at odds with current scientific thinking.

57. In each of the bTB-affected countries in Europe, there are difficulties with respect to feasible options that can be applied to manage herd risk during the post-derestriction period. In particular, compromises have been sought to limit

disruptions to the normal business of farming whilst also managing the heightened herd risk that can persist for an extended period following infection.

58. The Review proposes an additional 6 month test for derestricted herds (in other words, full-herd tests at 6 and 12 months following derestriction). This proposal is beneficial, as it will provide an additional opportunity, as acknowledged in the Review, to evaluate the infection status of herds known to be at higher-than-baseline risk. However, it will not impact on the free movement of animals once herd derestriction has occurred, with the potential for ongoing spread of infection through animal movement.

59. The Review proposes a range of options, including an additional 6 month test for derestricted herds following all or higher risk breakdowns[10], pre-movement testing, herd testing delayed according to date of reactor removal, restrictions to the movement of inconclusive reactors[11], and contiguous testing. Each of these options has epidemiological merit in reducing the infection risk posed to other herds, and, as acknowledged in the Review, many are currently applied in other countries. Further research would be beneficial to further evaluate these options.

Reducing the number of NVL reactor animals required for a herd to be considered OTW [proposed measure 9]

60. As outlined in the Review, the management of herds with OTW (Officially TB free status Withdrawn) and OTS (Officially TB free status Suspended) breakdowns is fundamentally different. Specifically, disease control is much more rigorous and continues for a longer period following OTW compared to OTS breakdowns.

61. The distinction between OTW and OTS breakdowns varies by country, as described by Abernethy et al. (2013):

    a. In Great Britain, OTF status is suspended if infection is not confirmed, and only one further negative herd test is required.

    b. The policy in Northern Ireland is similar to GB, except that outbreaks with six or more unconfirmed reactors are treated as OTW.

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[10] Noting that breakdown size is an important predictor of future risk (Olea-Popelka et al., 2004; Karolemeas et al., 2011)

[11] As currently occurs in Ireland based on the work of Clegg et al. (2011a,b)

c. In Ireland, almost all outbreaks are considered OTW, except a small proportion (those classified under the so-called 'singleton policy') released early following an epidemiological risk assessment and laboratory analysis (Good and Duignan 2011; Murray et al., 2012).

62. The OTW/OTS threshold has very important implications for national disease control. In particular, there is a need to maximise control efforts in infected herds, and to minimise the problems of residual infection (the persistence of infection in a herd and locality) and infection risk associated with animal movement (More and Good, 2015). As highlighted previously, bTB risk persists in many infected herds despite current legislative requirements for OTW herds (two consecutive clear tests prior to derestriction) (Clegg et al., 2015). Therefore, it is particularly important that requirements are not inadvertently weakened by incorrectly classifying an infected herd as OTS.

63. The appropriate threshold between OTW and OTS is best determined through epidemiological research. There are many relevant insights from existing research including:

a. Future herd bTB risk is not generally associated with either detection of lesions at slaughter (Olea-Popelka et al., 2004) or lesion confirmation (Karolemeas et al., 2011; Doyle et al., 2014).

b. Future bTB herd risk is associated with the size of the breakdown (the number of skin reactors identified) (Olea-Popelka et al., 2004; Karolemeas et al., 2011; Doyle et al., 2014).

64. Research was recently completed in Ireland specifically to address questions relating to the classification of H-herds[12] for the purposes of future bTB risk (Clegg et al., 2016). This study confirmed the key role of past bTB history in determining the future risk of Irish herds, with the odds related to both the severity of and time since the previous restriction. It also illustrates the difficulty in clearly defining H-herds, noting that risk persists for extended periods following a bTB restriction,

[12] In Ireland, herds are considered at higher risk (so-called H-herds) if they experience a bTB episode with at least 2 standard reactors or at least 1 standard reactor and an animal with a TB lesion found at slaughter, and where infection was acquired within the herd. H-herds are deemed OTW, but additional control measures are applied, including badger removal if the infection source was attributed to badgers and three SICTTs (single intradermal comparative bTB tests) at 6 month intervals following de-restriction before returning to annual testing.

regardless of breakdown severity. The study concluded that there is a need for robust controls on H-herds for an extended period post de-restriction.

65. In the Review, the proposed designation of OTW breakdowns is generally consistent with the policy in Ireland, as recently confirmed by the work of Clegg et al. (2015). It would be valuable, in time, to review the proposed policy for Northern Ireland, as further relevant data become available.

Chronic herds [proposed measure 7]

66. As highlighted in the Review, there is currently imperfect knowledge about chronic herds, including measures to resolve or minimise their impact. Given this, the proposal for critical review and further research is entirely reasonable, to address knowledge gaps.

67. Many of the individual measures as proposed in this Review should contribute to reducing the number and impact of these herds. The recent publication by Doyle et al. (2016) is particularly welcome, highlighting risk factors associated with duration and recurrence of chronic herd breakdowns in Northern Ireland.

Requiring a herd test prior to restocking after a bTB breakdown [proposed measure 8]

68. As highlighted in the Review, this requirement provides some disease control benefit, at least in Ireland (Clegg et al., 2013), but is also driven by EU legislation.

69. Legislative requirements are certain to influence future policy decision-making. Therefore, this is a need for clarity post-Brexit concerning the ongoing relevant of EU legislation to Northern Ireland. In addition, it would valuable to conduct research, similar to that completed in Ireland (Clegg et al., 2013):

    a. To provide an overview of movement events associated with each bTB episode.

    b. To determine whether introduction of animals during a bTB episode is associated with increased future bTB risk.

    c. To identify practices relating to the introduction of animals that are the most risky.

Removing restrictions where not epidemiologically justified

Fattening herds operating under alternative conditions [proposed measure 11]

70. Similar measures for fattening herds are also applied in other jurisdictions.

71. Based on the measures as described, there is no infection risk directly associated with the movement of cattle.

72. The risk posed by fattening herds, compliant with each of the suggested conditions, would only be negligible (ie acceptable in the context of national bTB eradication) if there were no contribution from fattening herds to bTB persistence in the locality. The robustness of this measure needs to be formally tested, in time, by determining whether fattening herds pose an increased risk of local bTB persistence in comparison with non-infected herds.

Additional control strategies

Genetic susceptibility of bovines [proposed measure 13]

73. It is now clear that genetics can make a significant contribution to animal health, including resistance to bTB and other infectious diseases. Further, tools for simultaneous selection on these traits and other performance traits are available (Berry et al., 2011). Advances in this area are likely relevant to animal breeding in Northern Ireland.

Programme integrity

DNA tagging [proposed measure 3]

TB reactor – quality assurance checks [proposed measure 15]

74. The Review proposes several measures relating to programme integrity *[proposed measures 3 and 15]*, including DNA tagging and quality assurance checks on bTB reactors. Any steps to limit errors, fraudulent or otherwise, should be supported.

75. There is evidence from several countries, primarily anecdotal, of substantial improvements following the introduction of measures to limit fraud. Ongoing discussions will be helpful, to share experiences with international colleagues.

76. Further, supporting research should be conducted to determine the impact of different measures to limit fraud in the national programme. Field trials are

suggested in the Review, however, observational studies should also be considered.

77. Additional comments with respect to the quality control of field surveillance are included previously, concerning the new contract for the provision of bTB testing services *[proposed measure 5].*

Additional resources to support decision-making and scientific support

78. In the Review, additional measures *[proposed measures 4 and 12]* are proposed to support decision-making and scientific support, including improvements to existing geographic information systems (GIS) and an expansion of genotyping of *M. bovis.* These proposals are very strongly supported.

Geographic information systems

Geographic information system (GIS) [proposed measure 12]

79. GIS is a fundamental tool for many relevant aspects of science, including epidemiology and ecology. It is critical that GIS is able to seamlessly link with other relevant national databases. The data requirements for epidemiological and ecological research are considered in greater detail previously.

M. bovis genotyping

Genotyping of Mycobacterium bovis *[proposed measure 4]*

80. Molecular epidemiology is a well-established discipline, providing insights into the dynamics of infection in animal and human populations. Until recently, however, the use of molecular epidemiology in bTB science has been relatively limited, in large part due to the absence of suitable molecular tools. As outlined in the Review, such tools are now emerging (spoligotyping and VNTR for some years, whole genome sequencing currently), offering an extraordinary opportunity to address a broad range of questions, many with direct implications for the national bTB eradication programme. Of particular interest are questions relating to the maintenance and transmission of bTB, at a range of different scales, both spatial (on a farm, in a locality [potentially between different animal species], nationally) and temporal.

81. Northern Ireland is a world leader in the development and application of these technologies.

82. The genotyping work is a critical national resource, and should be supported, both from Northern Ireland and elsewhere (eg UK competitive funding). It is important that genotyping-related research is conducted in close collaboration with national policy-makers and field veterinarians, to ensure that priority is given to those questions, once answered, that are most likely to contribute to bTB eradication. There is also a need to move rapidly from concept to practical application.

Wildlife and vaccination (Annex C)

Northern Ireland's badger road traffic accident (RTA)/found dead survey

Relevant epidemiological concepts

83. Several important epidemiological concepts are relevant to the badger RTA/found dead survey, relating to the validity and precision of survey results. These issues are considered in detail in the STROBE statement (von Elm et al., 2007; Vandenbroucke et al., 2007).

Study validity

84. Internal validity characterizes the quality of conclusions relative to the population under study (Toma et al., 1999).

    a. Minimising confounding, namely those variables that could lead to a distortion in the effect estimate between another variable and an outcome (Toma et al., 1999). In related work from Wales, a range of potential confounders were considered during multivariable analyses, including age, sex and season (Goodchild et al., 2012). Carcass weight and stage of decomposition are further potential confounders.

    b. Minimising information (measurement) bias[13]. The Review outlines research conducted in support of an agreed uniform protocol for sample collection and laboratory procedures (organs to be collected, diagnostic methodology to be used etc). The protocol used for culled badgers in Ireland is described elsewhere (Byrne et al., 2015).

85. External validity relates to the possibility of extrapolating the study conclusions (assuming that the interval validity has been confirmed) to other populations (other times and places) (Toma et al., 1999).

    a. A number of inherent weaknesses with badger RTA/found dead surveys have previously been identified, in Northern Ireland and elsewhere, each relating to the representativeness of the study population (Abernethy et al., 2003, 2011; Nusser et al., 2008).

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[13] Bias is defined as systematic error that leads to incorrect quantitative findings (Toma et al., 1999)

i. A non-random sub-population of badgers, collected through a convenience sample. Badgers found dead are a non-random sample, and are unlikely to be typical of all badgers with respect to age, sex or severity of bTB infection.

ii. Geographical bias. The sample population is limited to areas surrounding roads. Therefore, regions with a lower road density or with roads with fewer cars may be under-represented.

iii. Temporal bias. Temporal trends may be missed, if RTAs are not collected over a sufficiently short period of time.

iv. Reporting bias is a particularly concern given the passive nature of the surveillance effort. Motivation to report among farmers, for example, may be linked to the bTB status of their herds.

v. Collection bias. There may be fewer RTAs collected from highways, both because carcasses may be too damaged to retrieve and also because retrieval from these roads is particularly dangerous.

b. A number of strategies have previously been implemented in Northern Ireland to at least partly address these concerns, including strict controls on reporting (solely by defined public officials), the setting of regional quotas, and proactive searching for badger carcasses (Abernethy et al., 2011).

Study precision

86. Study precision corresponds to a reduction in random error (Rothman et al., 2008).

Comments relevant to the Review

In general

87. The Review highlights some of the key questions to be addressed, including temporal and spatial trends in infection prevalence in the badger, and the interrelationship, in terms of *M. bovis* infection, between cattle and badger populations. Similar objectives have been in place since 1999 (Abernethy et al., 2003, 2011). As argued in the Review, the survey will provide valuable insights into the impact on badger populations of the national bTB eradication programme.

Relating to study validity and precision

88. As clearly acknowledged in the Review, it is critically important that the badger RTA/found dead survey is designed and conducted so as to maximise both the validity and precision of the study.

a. With respect to study validity:

i. As reflected above, a range of strategies have previously been used in Northern Ireland to maximise study validity, both internal and external. Concerns with study validity are clearly acknowledged in the Review and in supporting documentation[14], and a range of strategies to maximise study validity are outlined. A critical evaluation of these results with those using different methods (the TVR results, the interventions areas), as outlined below, is recommended.

b. With respect to study precision:

i. The sample size calculations are presented in the Review and in supporting documentation[14]. This work highlights both:

- The current study limitations, with respect to study precision: *'the current sampling strategy provides weak [statistical] power to detect significant inter-annual changes in prevalence at a national Northern Ireland level, with the exception of very large changes in prevalence …'*[14]
- The study precision required: sufficient to allow *'moderate variations in infection prevalence across time (inter-annually) and space (between counties)'*[14] to be detected.

ii. The Review presents a robust case for an increase in sample size.

iii. The sample calculations should be considered a guide to the numbers required. As a point of caution, these calculations are based on the assumptions of probability sampling and random distribution of infection/disease, which do not strictly apply to this survey

[14] Byrne, A.W., 2016, unpublished. Power study guidelines for RTA badger surveillance: the power to detect true inter-annual change

methodology. No alternative methodology is immediately available, although a suggestion for further research is outlined below.

89. Given the challenges faced with respect to study validity and precision, it is important that the study results are published in the international scientific literature, as an important means of ongoing scientific quality control. This is acknowledged in the Review.

Related work

90. The TVR study and the work proposed in intervention area (as outlined later) will each provide insights into both the prevalence and incidence of *M. bovis* in badgers, but in quite localised areas of Northern Ireland. As acknowledged in the Review, a comparison of results from these studies and from the badger RTA/found dead survey in equivalent areas will provide valuable insights into potential biases affecting the badger RTA/found dead survey.

91. Nusser et al. (2008) have outlined some of the challenges of disease surveillance in wildlife populations using convenience sampling. These are further elaborated by several authors, including Rees et al. (2011) and Leslie et al. (2014), primarily in the context of early detection and case finding. Consideration should be given to the use of modelling to investigate biases associated with the RTA/badger found dead survey in Northern Ireland, and potential practical sampling alternatives. This approach would also allow sample size calculations to be refined.

Wildlife vaccination

<u>Wildlife and the epidemiology of bTB in cattle</u>

The role of badgers

92. The Review correctly summarises current scientific knowledge with respect to the role played by badgers in the epidemiology of bTB cattle (Corner et al., 2011; Ní Bhuachalla et al., 2015). Badgers are an important maintenance host[1] for *M. bovis*, acting as a reservoir of infection[2] with spillover of infection to cattle, on the island of Ireland (More, 2009), in Great Britain (Godfray et al., 2015), and likely in parts of mainland Europe (Payne et al., 2013, Hardstaff et al., 2014).

93. The Review is also correct in suggesting that eradication will only be possible if all infection sources, including badgers, are addressed. There are several supporting evidence sources:

a. As suggested in the Review, several large-scale culling projects have demonstrated substantial and sustained reduction in the bTB risk of associated cattle herds. The measured impact was greater in Ireland (Griffin et al., 2005; Kelly et al., 2008) than in England and Wales (Donnelly et al., 2007; Jenkins et al., 2008).

b. As stated previously, in complex systems such as *M. bovis* infection in animal populations, it is extremely unlikely that eradication is achievable unless all factors contributing to persistence and spread are addressed. This has been a key lesson from the successful Australian bTB eradication programme (More et al., 2015), and from experiences in several other countries, including New Zealand (Livingstone et al., 2015) and the USA (O'Brien et al., 2011).

c. The presence of an infected wildlife reservoir is recognised as a key constraint to bTB control or eradication in many countries, both in Europe (Godfray et al., 2013; Gortázar et al., 2014, 2015) and elsewhere (O'Brien et al., 2011; Miller and Sweeney, 2013; Gortázar et al., 2015; Warburton and Livingstone, 2015).

A role for other wildlife species?

94. Currently, there is limited knowledge of the role of other wildlife species in the epidemiology of bTB on the island of Ireland. In this context, concern has been raised about the considerable expansion in several deer species in Ireland, including red, sika and fallow deer (Carden et al., 2011). As outlined in the Review, research is needed to assess the role of deer in the epidemiology of bTB in cattle in Northern Ireland, and whether intervention is warranted.

Key epidemiological concepts

95. The following concepts from basic epidemic theory are relevant (see Halloran, 1998; Viana et al., 2014):

a. The basic reproductive number, R_0, is the expected number of secondary cases caused by a single infectious individual in a fully susceptible population.

i. R_0 is a composite of the number of contacts per unit time, the duration of infectiousness and the transmission potential per potentially infective contact (collectively known as *'the adequacy of contact'*).

b. *R*, the effective reproductive number, is the expected number of secondary cases caused by each infectious individual in a partially immune population.

i. $R = R_0x$, where x is the proportion of contacts that are susceptible.

c. In a single host system, infection would be eradicated if *R* could sustainably be reduced to <1. In a multi-host system, the *R* of the system is influenced by both within- and between-species transmission (Dobson et al., 2004).

d. It is not necessary to immunise every individual in order to stop transmission of an infectious agent through a population. Herd immunity refers to the reduction of infection or disease in the unimmunised segment as a result of immunising a proportion of the population (John and Samuel, 2000).

96. Consistent with basic epidemic theory, options to limit transmission from badgers to cattle are reliant on either a reduction in either the adequacy of contact or the proportion of the population susceptible.

a. Options to limit adequacy of contact have been restricted to efforts to reduce the number of contacts per unit time, noting that practical options are currently not available to limit the duration of infectiousness in badgers or the transmission potential from infectious badger to cattle given contact. Strategies to reduce the number of contacts per unit time between badgers and cattle has been undertaken either through:

i. Badger culling. This strategy is currently being used extensively throughout Ireland, in areas with cattle bTB breakdowns that cannot be attributed to cattle movement (for further detail, see Byrne et al., 2015).

ii. Improved biosecurity (relevant to badger-to-cattle transmission), to limit contact between badgers and cattle. As discussed later in this document, a number of risk mitigation strategies are proposed, and strategies to successfully exclude badgers from housing have been demonstrated (Judge et al., 2011). As yet, however, there is as yet no empirical evidence linking improved biosecurity with reduced wildlife-related risks (More, 2009; O'Hagan et al., 2016).

b. Options to reduce the proportion of the population susceptible. Two strategies are being considered, including:

i. Badger vaccination. As outlined in the Review and by Robinson et al. (2012), considerable progress has been made towards a bTB vaccine for badgers, primarily as a collaborative effort between Ireland and the UK. In pen-based trials, in vaccinated compared to control badgers, there was a significant decrease in the number and severity of gross lesions, lower bacterial load in the lungs, and fewer sites of infection (Corner et al., 2010; Chambers et al., 2011; Murphy et al., 2014). Several field trials have been conducted, in the UK (Carter et al., 2012) and Ireland (Aznar et al., 2011, 2013, 2014), and final results from the Irish trials will become available shortly. A further trial is underway in six counties of Ireland, scheduled to end in December 2017, to determine whether vaccination is not inferior to area-wide targeted badger culling in maintaining a herd-level risk of bTB in cattle (O'Keeffe et al., 2016).

ii. Cattle vaccination. Under current EU legislation, bTB vaccination in cattle is prohibited, because it may interfere with current bTB diagnostic methods. Detailed consideration of the research required in support the use of cattle vaccination in the UK is outlined by the European Food Safety Authority (EFSA Panel on Animal Health and Welfare (AHAW), 2013), focusing on evaluation of both vaccine efficacy and the performance of a test to *'Detect Infected among Vaccinated Animals'* (DIVA). Chambers et al. (2014) provide further detail.

97. Of these four options, only two are considered in detail in the section immediately following, namely badger culling and badger vaccination. The other two options (improved biosecurity (relevant to badger-to-cattle transmission), cattle vaccination) may prove useful into the future. At this point, however, there is insufficient scientific knowledge to support the inclusion of either improved biosecurity (relevant to badger-to-cattle transmission) or cattle vaccination in a national bTB eradication programme.

a. Improved biosecurity (relevant to badger-to-cattle transmission). This issue is considered in further detail under 'Farm practice and biosecurity'. *At this point in time,* there is no empirical evidence linking improved biosecurity with reduced wildlife-related risks.

b. Cattle vaccination. A substantial number of technical and non-technical issues will need to be resolved before cattle vaccination could be considered for use in Northern Ireland. A summary of current knowledge is presented elsewhere (EFSA Panel on Animal Health and Welfare (AHAW), 2013; Chambers et al., 2014).

A critique of the proposed approach

The Review proposal

98. The TBSPG recommends a long-term strategy of widespread badger vaccination throughout Northern Ireland, using the only available licensed bTB vaccine bacille Calmette–Guérin (BCG), specifically to limit badger to cattle transmission, as an integral part of a national disease control strategy. The TBSPG indicate that injectable vaccine will be used initially, moving to oral vaccination once available. Oral vaccine will be deployed via an effective bait.

99. In areas of increased bTB risk, the TBSPG recommends that badger removal precede vaccination, using an intervention area design. This includes a control (removal) area surrounded by a ring vaccination area. This is considered in detail later.

Is badger intervention necessary?

100. As highlighted elsewhere, there is now conclusive evidence, both from Ireland and the UK, that badgers are an important contributor to bTB epidemiology in cattle.

101. International experience has shown that bTB eradication will only be achieved through an integrated approach, by simultaneously addressing all factors that meaningfully contribute to the persistence and spread of *M. bovis* in all infected animal populations.

102. The rationale for badger intervention is consistent with current knowledge.

What options are available, to limit badger-to-cattle transmission?

103. Based on the material presented under 'Key epidemiological concepts', only two options are current feasible for further consideration, including:

a. Limiting the adequacy of contact

i. Badger culling. As outlined by Abdou et al. (2016), culling strategies can be either selective (based on the infection status of the animal, as determined by an animal-side test) or not.

b. Reducing the proportion of the population susceptible

i. Badger vaccination. As outlined by Abdou et al. (2016), options for vaccination include either oral (dependent on bait uptake rates) or parenteral (dependent on trapping efficacy) administration.

Will widespread badger vaccination work?

104. This question has been the focus of intensive research for some years, both in Ireland and the UK. The results of pen trials have been very encouraging (Corner et al., 2010; Chambers et al., 2011), with the main protective effect being a reduction in the severity and progression of disease following *M. bovis* challenge. Field trials have been completed in both the UK and Ireland, and again early results from the UK have been encouraging (Carter et al., 2012). It is reasonable to expect vaccination to reduce *M. bovis* prevalence in badgers, and in cattle in high bTB prevalence areas, over time. However, no data are yet publicly available to assess the magnitude and timing of these effects (Godfray et al., 2013). The final

results from the Irish field trial (the Kilkenny vaccine trial; Aznar et al., 2011, 2013, 2014) will be available shortly.

105. A number of modelling studies have been undertaken (including Smith et al., 2001; Hardstaff et al., 2013; Abdou et al., 2016), generally highlighting the value of long-term vaccination in reducing bTB incidence in badger populations. Further detail is given below.

106. The proposal is scientifically sound, but will need to be reviewed as further information becomes available, in particular the results of the Kilkenny badger vaccine trial. It is important to note that widespread vaccine deployment, in areas previously subject to badger culling, is currently being conducted in six Irish counties. This study is seeking to determine whether vaccination is not inferior to area-wide targeted badger culling in maintaining a herd-level risk of bTB in cattle (O'Keeffe et al., 2016). The results of this work, to be completed at the end of 2017, will also be of relevance to the proposed national strategy in Northern Ireland.

Is it reasonable to move to oral vaccination, once available?

107. Only two practical vaccination routes are available: parenteral (subcutaneous, intramuscular) and oral (Robinson et al., 2012). Both routes have been used extensively, but only in pen and field trials. Parenteral vaccine is currently licensed for use in badgers in the UK, whereas oral vaccine is not.

108. The concept of oral vaccination is attractive, particularly in terms of ease (and potentially, cost) of delivery. However, a number of issues need to be addressed, relating to both vaccine safety and efficacy. Several authors highlight some of the issues under consideration, including the potential for BCG exposure by non-target species, including cattle (Robinson et al., 2012, 2015).

109. The proposal is scientifically sound, but will need to be reviewed as further information becomes available. This is clearly acknowledged in the Review. In the proposed trial of an oral vaccine in Northern Ireland, key questions to be considered would need to include the cost, effectiveness and safety of this method of vaccine deployment (Chambers et al., 2014)

Is badger removal necessary before implementing a widespread vaccination policy?

The scientific rationale

110. In humans, the BCG vaccine is included as part of the childhood vaccination programme in many countries. However, the efficacy[15] of BCG in preventing pulmonary tuberculosis (TB; caused by infection with *M. tuberculosis*) is known to vary greatly in different circumstances. In a recent meta-analysis of randomized clinical trials[16], it was demonstrated that BCG confers protection against pulmonary TB when administered both in infancy and at school age, provided children were not already infected with *M. tuberculosis* or sensitized to other mycobacteria (Mangtani et al., 2014).

111. As with people (Andersen and Doherty, 2005), there is no evidence of either a beneficial or detrimental effect of BCG in infected badgers (Chambers et al., 2014). Because it is ineffective in infected animals (Robertson et al., 2012; Chambers et al., 2014), vaccination has the potential to provide benefit only to those animals that are not infected (or otherwise sensitized to mycobacteria) at the time of vaccination[17].

112. Pseudo-vertical transmission[18] is believed to be an important feature of *M. bovis* infection in badgers, and may be a key factor in maintaining infection within local populations (Ní Bhuachalla et al., 2015). In infected setts, therefore, it is plausible that cubs may become infected with *M. bovis*, or exposed to other (environmental) mycobacteria, whilst young. Logically, the force of infection[19] will be greater in high compared with lower prevalence badger populations.

Field concerns

113. Collectively, these issues have raised concerns as to whether badger vaccination alone will be sufficient to limit transmission, initially between badgers, and subsequently to cattle, given the current force of infection in the badger population. In Ireland, *M. bovis* infection in badgers can be very high (reaching

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[15] The percentage of vaccinated individuals that are protected.
[16] Randomised clinical trials are recognised as the most rigorous way to determine whether a case-effect relationship exists between treatment and outcome (Sibbald and Roland, 1998).
[17] There may be additional benefit subsequently, if herd immunity is established, to non-infected animals.
[18] Via the respiratory route during the rearing phase rather than *in utero.*
[19] Hazard rate of infection from a defined source to susceptible host individuals in a defined population (Viana et al., 2014).

43.2% in hot-spot areas in Ireland; Corner et al., 2012). Further, in undisturbed badger populations, infected animals are long-lived (Ní Bhuachalla et al., 2015), and therefore an ongoing source of infection.

114. Differing results have been observed in Ireland and GB with respect to the impact of culling on the prevalence of *M. bovis* in the emergent badger population.

   a. In Ireland, a significant reduction in the prevalence of *M. bovis* infection over time has been observed in areas of proactive culling, both in the four area trial (among the emergent badger population during 1997-2002; Corner et al., 2008) and throughout the country during 2007-13 as part of the national programme of targeted badger removal (Byrne et al., 2015). In the national programme, repeated culling is conducted once an area has been recruited.

   b. In GB, in contrast, an increase in *M. bovis* infection in badgers was observed with successive proactive culls in the Random Badger Culling Trial (RBCT), especially where landscape features allow badgers from neighbouring land to recolonize culled areas (Woodroffe et al., 2006).

115. Given this background, and based on the evidence presented, the current thinking in Ireland is that culling will be required in areas of high bTB risk prior to mass vaccination, specifically to reduce the prevalence of *M. bovis* infection in the re-emergent badger population. Practical steps have been taken in this direction, as described by O'Keeffe et al. (2016), with the establishment of widespread vaccine deployment, in areas previously subject to badger culling, in six Irish counties. As indicated previously, this study has been designed as a non-inferiority trial, to determine whether vaccination is not inferior to area-wide targeted badger culling in maintaining a herd-level risk of bTB in cattle. By default, the study is also evaluating the transition from focused culling to a national badger vaccination programme.

Evidence from modelling

116. Modelling studies have provided further insights into this question.

   a. Using a spatial simulation model, Abdou et al. (2016) have highlighted the limited impact of vaccination alone on bTB infection in badger populations, and the substantial improvement when vaccination was preceded by 5 years of culling.

b. The results of Smith et al. (2001) and Wilkinson et al. (2004) are broadly similar. Smith et al. (2001) found that cattle herd breakdowns and bTB prevalence were most effectively reduced by first introducing a proactive element (such as proactive culling) followed by vaccination or culling. If this proactive element was avoided, the impact of vaccination alone on bTB prevalence in badgers took many more years to achieve (Wilkinson et al., 2004).

c. Hardstaff et al. (2013) found that vaccination alone could be an effective disease control strategy for bTB in higher-density badger populations, but only with annual deployment of a vaccine with an efficacy of around 80%. The effectiveness of this strategy was reduced by the presence of external sources of infection.

117. The proposal is consistent with current scientific knowledge, apart from the above-mentioned RBCT results. Ongoing research in Northern Ireland will be critical, in particular questions relating to badger ecology and epidemiology during the proposed intervention studies. The modelling studies should be updated as further information becomes available.

<u>Further critique of the proposed badger intervention programme</u>

118. The Review proposes a badger intervention programme, to allow for the strategic removal of badgers from areas of high bTB prevalence in cattle. The proposed programme would be implemented in bTB problem areas, where bTB incidence in cattle is high, recurrent and/or persistent. A 'ring vaccination' area would surround the control (removal) area, with intervention in each area (either culling or vaccination, as relevant) continuing over a four-year period. An appropriate sample strategy will be implemented to establish the prevalence (and where possible, also the incidence) of infection in the target intervention area.

a. <u>The control (removal) area</u>

i. The stated rationale is to reduce the level of bTB in a wildlife reservoir directly associated with bTB breakdowns in associated cattle herds.

ii. Relevant scientific issues are considered in detail in the section above.

iii. The Review presents the expected consequences of removal versus TVR, given a series of simplistic assumptions. If these assumptions are correct, the fall in *M. bovis* prevalence in badgers will be much more rapid following badger removal compared with TVR.

b. The ring vaccination area

i. The stated rationale is linked to events in both the control area (facilitating the immigration of vaccinated badgers from border areas) and bordering areas (mitigating against perturbation).

ii. The ring vaccination area has been introduced directly in response to concerns that the perturbation effect will occur as a consequence of badger removal in the control (removal) area. As outlined in the Review, the perturbation effect (Godfray et al., 2013) is a hypothesized chain of consecutive effects triggered by badger culling, including substantial changes to the spatial and social organisation and territorial behaviour of badger populations (social perturbation), increased contact and transmission of *M. bovis* infection between badgers, increased contact between cattle and the disturbed badger population, and increased infection risk in associated cattle (More et al., 2007).

iii. During the RBCT in the southwest of GB, there was evidence in support of the perturbation effect, including social perturbation and associated increases in *M. bovis* prevalence in both badgers (Woodroffe et al., 2006) and cattle (Donnelly et al., 2007).

iv. In Ireland, social perturbation is well described (O'Corry-Crowe et al., 1996). However, there has been no evidence of associated increases in *M. bovis* prevalence following badger removal, either in badgers (Corner et al., 2008; Byrne et al., 2015) or cattle (Griffin et al., 2005; Kelly et al., 2008; Olea-Popelka et al., 2009). In recent years, there has been a long-term trend of falling herd bTB prevalence in Ireland (Abernethy et al., 2013). This has occurred coincident with a long history of targeted badger removal (for example, 7,284 badgers removed in 2008 (Sheridan, 2011) from an estimated national population of approximately 84,000 (Sleeman et al., 2009)) in response to herd bTB breakdowns where badgers are implicated (Byrne et al., 2015).

v. Reasons for the observed differences between southwest GB and Ireland are uncertain. O'Connor et al. (2012) has suggested a range of possibilities, relating to cattle, badgers and badger controls.

vi. It is also uncertain whether the perturbation effect might occur in Northern Ireland. The Irish experience may be more applicable than the experience from southwest GB as influencing factors, such as bTB epidemiology and badger ecology, are likely more similar across the island of Ireland than between Northern Ireland and southwest England. Byrne et al. (2012) presents a detailed review of badger ecology in Ireland, but with considerable reference to Northern Ireland.

119. The proposed badger intervention programme is seeking to balance two competing objectives, namely the requirement for a low prevalence population in which to introduce a badger vaccination programme, and concerns that a perturbation effect may occur following badger removal. Based on current knowledge, it seems very likely that a mass vaccination programme will be largely ineffective in a high prevalence population. It is much less certain, however, whether badger removal will result in a perturbation effect in Northern Ireland. On balance, and noting the critical need to address badger-to-cattle transmission within an integrated national approach to bTB eradication, the approach as proposed in the Review seems both reasonable and prudent. Using this approach, an area suitable for vaccination will be achieved, whilst also reasonably mitigating against a potential adverse effect. Ring vaccination will also have the effect, as described in the Review, of facilitating the immigration of vaccinated badgers from border areas.

120. Smith et al. (2012) has previously modeled the impact of ring vaccination around areas of badger culling, but using parameter estimates from the RBCT in southwest GB. These authors found that culling plus ring vaccination did mitigate some, but not all, of the adverse effects of the perturbation effect. It would be valuable to rerun this model using parameter estimates from Northern Ireland, once these are available.

121. It is critical that research is conducted in Northern Ireland, as part of the badger intervention programme, to clarify whether the perturbation effect occurs following badger removal.

Additional comments

122. Several authors highlight issues to be considered when designing, implementing and evaluating a badger vaccination programme, including Robinson et al. (2012), Chambers et al. (2014) and Ní Bhuachalla et al. (2015). These include:

   a. Clearly defined objectives and criteria for success

   b. Area of coverage, underpinned by knowledge of bTB prevalence (in time, in space, between social groups)

   c. Strategies to maximise vaccine coverage

   d. Revaccination, taking account of duration of immunity, protection following revaccination, vaccine coverage, population recruitment (births, immigration)

   e. Monitoring strategy, relating to coverage (uptake if oral vaccine), vaccine effectiveness and the epidemiological consequences of vaccination

   f. Length of programme

Farm practice and biosecurity (Annex D)

General comments

123. Biosecurity has been defined as a strategy of management practices to prevent the introduction of diseases and pathogens to an operation and to control spread within the operation (Wells, 2000). In the literature, there are varying uses of terms relating to biosecurity, some different from those used in the Review. For example, in Mee et al. (2012):

a. Bioexclusion relates to preventive measures (risk reduction strategies) designed to avoid the introduction of pathogenic infections (hazards), and

b. Biocontainment relates to measures to limit within-farm transmission of infectious hazards and onward spread to other farms.

124. Biosecurity is a critical aspect of good farming practice, protecting a herd (or industry) from the spread of a broad range of infectious diseases. Further, appropriate risk mitigation measures are well described (including Mee et al., 2012).

125. The implementation of bioexclusion plans on beef and dairy farms (covering both the entry and exit of infectious agents from a farm) is voluntary in most countries (Mee et al., 2012). One exception is larger dairy farms in Denmark, where farmers are required to introduce measures to reduce the risk of introducing animal diseases into the dairy herd and minimize the impact of outbreaks, should they occur (Kristensen and Jakobsen, 2011).

126. There are numerous reports of problems with the widespread adoption of effective biosecurity on farms (for example, Nöremark et al., 2010; Sayers et al., 2013). A number of barriers to adoption have been identified, including:

a. A lack of consensus regarding effective biosecurity protocols

b. The efficacy of such protocols, and

c. Their cost-effectiveness.

127. The Review highlights problems of biosecurity on farms in Northern Ireland (also O'Hagan et al., 2016). Farm biosecurity is relatively poor throughout the island of Ireland, in part due to land fragmentation and animal movement. These were

important considerations leading to the decision for national eradication (as opposed to farm-by-farm control) of BVD from Ireland (Barrett et al., 2011).

Improved biosecurity contributes to disease prevention

<u>Risk mitigation options</u>

128. Risk factors for bTB are increasingly understood, including many that relate to biosecurity risks. In broad terms, there are two key biosecurity-related risks, including:

    a. <u>Contact with infected cattle</u>, either through animal movement or contiguous contact.

    b. <u>Contact with infected wildlife</u> (including an infected environment).

    c. [The role of fomites, visitors, biological material in the spread of *M. bovis* is likely minor]

129. The relative importance of each of these risks is uncertain, and will likely vary in different countries (differing epidemiology, ecology, programme management etc) and over time (Broughan et al., 2016). Therefore, generalization is difficult. In Ireland, White et al. (2013) focused on the relative importance of 'neighbourhood', specifically farm-to-farm spread and spread from wildlife, on bTB persistence. Among the study farms, they attributed 15% of bTB episodes in the study to residual infection, between 0% and 20% to contiguous spread, and between 19% and 39% to wildlife (More and Good, 2015).

130. With respect to the biosecurity risk *'contact with infected cattle'*, risk mitigation measures are robust and generally well understood.

    a. As outlined by Mee et al. (2012), strategies relevant to bTB include:

        i. <u>Concerning animal movement</u> – maintaining a closed herd, minimizing the number of cattle purchased and the number of source herds, purchasing from herds with likely low disease (infection) prevalence, obtaining cattle disease history, testing cattle before movement.

        ii. <u>Concerning contiguous spread</u> – attention to boundary fencing to prevent nose-to-nose contact.

b. Considerable empirical evidence is available highlighting the impact of these measures on infection risk, both for bTB and other directly transmissible diseases of cattle. For many bovine infections, including BVD and Johne's disease, farm-to-farm spread mainly occurs through the movement of infected animals. Therefore, efforts to prevent such movement, through the methods listed above, are critical to success in national control programmes (Lindberg and Alenius, 1999; Geraghty et al., 2014). The infection benefit of closed herds, with no introductions or contact with cattle in neighbouring herds, is well recognised (van Schaik et al., 2002). With bTB, many studies have highlighted the disease risk associated with cattle movement (including Gilbert et al., 2005; Doyle et al., 2016). Further, movement controls are central to relevant EU bTB control legislation8, and to progress in successful national bTB eradication programmes (More et al., 2015).

131. With respect to the biosecurity risk *'contact with infected wildlife or an infected environment'*, the issues are more problematic. To illustrate:

a. There are important gaps in knowledge about aspects of *M. bovis* epidemiology in badgers (see reviews by Corner et al., 2011; Ní Bhuachalla et al., 2015; Broughan et al., 2016).

b. There is uncertainty about how *M. bovis* is transmitted between badgers and cattle (Godfray et al., 2013). Available evidence would suggest that transmission between badgers, and by extrapolation from badgers to cattle, is primarily via aerosol during direct contact. The high prevalence of pulmonary infection strongly supports the lungs as the principal site of primary infection in badgers, with inhalation of infectious aerosol particles ('droplet nuclei', with an aerodynamic diameter of 0.7-7 μm) the principal mode of transmission. Droplet nuclei are formed during normal respiratory air movements, as well as during coughing and sneezing. The conditions required for aerosol transmission and establishment of infection are exacting and principally involve the aerodynamic diameter of the aerosol particle. The most vulnerable sites for primary infection of *M. bovis* are the alveoli, alveolar sacs or alveolar ducts, which are not reached by particles in the respiratory tract of >5μm (Corner et al., 2011).

c. The relative importance of different locations (housing, pasture) with respect to badger-to-cattle transmission remains uncertain. Contacts between badgers and cattle have been reported both in housing (including Ward et al., 2010) and at pasture (including Payne et al., 2015). A recent study has found that direct contact between badgers and cattle is very infrequent, irrespective of whether cattle were housed or at pasture (Woodroffe et al., 2016).

d. A number of risk mitigation strategies have been proposed, including cattle grazing regimes, habitat manipulation, management of latrines, and protection of farm buildings (Ward et al., 2010), addressing risks at pasture and in housing. Further, strategies to successfully exclude badgers from housing have been demonstrated (Judge et al., 2011).

e. The costs of these strategies are likely to vary by farm, but could be substantial. Given the nature of some of these strategies, their effectiveness may be greatly affected by farmer diligence (Judge et al., 2011).

f. To this point, relevant research has primarily focused on the effectiveness with which these strategies might reduce or prevent contact. No work has yet been undertaken (for example, using controlled field trials) to critically evaluate the impact of one or more of these strategies on herd bTB risk.

g. In conclusion, there is as yet no empirical evidence linking improved biosecurity with reduced wildlife-related bTB risks (More, 2009; O'Hagan et al., 2016). Further, the relative effectiveness of different risk mitigation strategies in terms of bTB risk from infected wildlife is also unknown.

<u>Risk mitigation responsibilities</u>

132. It may be useful to view biosecurity from the perspectives of *'who can meaningfully control/who's responsible'?* This has some similarities to the exacerbator-pays approach to cost allocation in the New Zealand bTB eradication programme[9]. Using this approach:

a. <u>Farmers have responsibility for cattle-related biosecurity measures on their farms</u>, noting that farmers can meaningfully control each of the above-mentioned risk mitigation measures to limit contact with infected cattle.

b. The government has responsibility for wildlife-related measures. Protected wildlife can be considered a public good[20], and are therefore the responsibility of government rather than individual farmers. Further, as argued above, there is currently no empirical evidence demonstrating that individual farmers can reduce wildlife-related bTB risks by implementing biosecurity measures on their farms.

Policy considerations

133. The Review highlights several strategies to increase awareness of biosecurity on farms in Northern Ireland, including the development of a checklist to guide biosecurity assessment and the provision of farm-specific biosecurity advice.

a. The proposed strategies are supported, but with caution.

i. At this point in time, proven options are available to effectively limit cattle-, but not wildlife, -related bTB risks. It is important that resources and advice for farmers reflect the best-available science, to ensure that farmers focus their efforts on those biosecurity strategies with proven effectiveness in reducing future farm-level bTB risk. In this context, greater emphasis should be placed on conclusions from prospective (cohort [observational], field trials [experimental]) studies in comparison to cross-sectional or retrospective (case-control [observational]) studies, given the need to distinguish association and causation.

ii. Contact with infected cattle is one of a range of factors that influence future farm-level bTB risk. Further, the effectiveness of cattle-related biosecurity is greatly influenced by ongoing farmer diligence. For these reasons, improved on-farm biosecurity will not always lead to reduced bTB risk. As a consequence, the impact of the proposed measures will be variable, and on many farms may be minimal.

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[20] Public goods and services (for example, national institutions for law and order, public roads, education, hospitals etc.) are generally funded through compulsory taxation and are, therefore, available to all. In economic terms, public and private goods are distinguished using the principles of excludability and rivalry. Purely public goods are those goods from which it is not possible to exclude one consumer without excluding all (non-excludability) and of which the consumption by one person does not reduce its availability for consumption by others (non-rivalry) (Ahuja, 2004).

134. It may also be possible to consider improved farm biosecurity within a broader context, in particular efforts currently being made by Animal Health and Welfare Northern Ireland (AHWNI) with respect to BVD eradication and, shortly, JD control. Of note:

a. Concerns with respect to biosecurity adoption have also been noted on Irish farms (Sayers et al., 2013), despite many years of biosecurity messages as part of the national bTB control programme. Over the last 3 or so years, however, there appears to have been a substantial increase in farmer understanding and awareness of farm biosecurity. This has been attributed to the national BVD eradication programme, which has been compulsory since 2013. Under this programme, all farmers are required to consider farm-level biosecurity decisions to prevent or control BVD on their farms. The national discussion on the issue of PI (animals persistently infected with BVD virus) retention has been particularly useful in this regard, including research quantifying the future risk posed by PI retention to both the index herd (Graham et al., 2015) and its neighbours (Graham et al., 2016).

b. AHI have produced a series of information leaflets for Irish farmers, being practical evidence-based biosecurity measures suited to Irish farms[21]. A scientific paper was also produced, to provide a robust foundation for recommendations (Mee et al., 2012). The leaflets address the following topics:

   i. Understanding infectious diseases

   ii. Bioexclusion: keeping infectious diseases out of your herd

   iii. Purchasing stock: reducing disease risks

   iv. Preventing disease spread within your farm - biocontainment

[21] See http://animalhealthireland.ie/?page_id=395

135. It would be valuable to complement the proposed strategies with supporting research:

a. There is a need for a clearer understanding of the relative importance of the two key biosecurity-related bTB risks in Northern Ireland, including contact with infected cattle and contact with infected wildlife.

b. In time, there is a need for a critical evaluation of the impact of improved farm biosecurity on future bTB risk, including the relative contribution of different biosecurity practices.

c. There is a building body of international literature on motivators for, and constraints to, improved on-farm biosecurity (including Kristensen and Jakobsen, 2011; Frössling and Nöremark, 2016; Shortall et al., 2016). It would be valuable to consider similar studies from Northern Ireland, to identify strategies to encourage livestock farmers to best achieve improved biosecurity.

Improvement notices

136. As highlighted in the Review, improved on-farm biosecurity has the potential to substantially improve animal health on individual farms. However, as highlighted above, improved on-farm biosecurity will not always lead to reduced bTB risk. Given this context, there is a need to review progress and available evidence concerning the impact of improved farm-level biosecurity on future bTB risk in Northern Ireland. This is foreshadowed in the Review.

Informed purchasing

137. As outlined previously, a number of strategies are available to limit the infection risk posed through animal movement, as outlined previously. Each is underpinned by the same principle – seeking to limit the probability that an introduced animal is infected with *M. bovis*. These strategies (and strategy combinations) vary with respect to their failure rate (the % infected among all animals traded). Maintaining a closed herd has a zero failure rate whereas the failure rate for pre-movement testing may be relatively high (given the imperfect operating characteristics of the tests used).

138. In the context of bTB eradication, there are substantial differences between countries with respect to the implementation of these strategies. Using two examples:

a. During the bTB eradication programme in Australia, the movement of cattle between herds was determined on the basis of herd and area risk, to limit the potential for spread of infection to lower risk herds and areas (More et al., 2015).

b. In England and Wales, there has been considerable discussion about a potential role for a risk-based trading scheme, based on the probability of bTB in a herd (Adkin et al., 2016a,b).

139. 'Informed purchasing', as outlined in this Review, is consistent with the above-mentioned principle, seeking to limit the probability that an introduced animal is infected with *M. bovis.* Using this strategy, purchasing decisions are informed by knowledge of past testing history, of the animal and herd. As highlighted in the Review, it is critical that an informed purchasing scheme is practical, transparent and based on accurate and available data.

140. Substantial progress has been made in the identification of animal- and herd-level risk factors for bTB (so-called explanatory models; see reviews by Skuce et al., 2012; Broughan et al., 2016) As yet, however, there has been limited success in translating this knowledge into tools that allow accurate prediction of future bTB risk (so-called predictive models; Karolemeas et al., 2010; Wolfe et al., 2010). For this reason, while past testing history will be useful, future prediction of bTB risk is certain to be imperfect. For this reason, the failure rate from informed purchasing will be non-negligible, and may be relatively high.

141. There is a need for ongoing research to critically evaluate the value of informed purchasing, with respect to infection control benefit to the national bTB eradication programme.

142. From an epidemiological perspective, care will be needed in identifying the data that will most accurately assist an interested buyer. Animal-level test results may be of limited value, or worse, without a clear understanding of the current and past bTB risk of the herd(s).

Farm fragmentation

143. Farm fragmentation is a feature of farming in several bTB-affected countries, including Northern Ireland. As yet, however, this issue has never been comprehensively addressed, in terms of the risk posed to national bTB control and eradication. Therefore, the proposed review is welcomed. As part of this review, epidemiological research will be needed to quantify the impact of farm fragmentation on future infection risk following a bTB breakdown.

144. The proposed interim measure (a notice to limit the risk of spread associated with fragmentation) is epidemiologically sound, but should be revisited once the above-mentioned review has been completed.

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