



Options for vaccinating cattle against bovine tuberculosis

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1 Executive summary

- E1. This document seeks to establish whether in principle, vaccination of cattle against bovine TB (bTB) is a viable policy for controlling disease in GB.
- E2. This summary sets out the main constraints around efficacy, legality, acceptability and practicality of cattle vaccination. These have been used to define a set of options which represent the most likely scenarios for how a cattle vaccine may be deployed. The detailed arguments leading to these conclusions are set out in **Section 2** and are referenced throughout this summary. Detailed options scenarios on how vaccines might be used are set out in **Section 3**. These scenarios will be used to help steer the research programme by defining research priorities and the necessary vaccine properties required to deliver vaccination in these ways. A high level economic assessment is summarised in **Section 4**
- E3. Cattle vaccination has potential benefits to reduce prevalence, incidence and spread of bTB in the cattle population. Vaccination could help prevent breakdowns by preventing herds becoming infected by any source - wildlife or cattle and could also reduce the severity of a herd breakdown. Vaccination that is less than 100% effective will not guarantee all cattle are fully protected from infection and therefore vaccination alone cannot be used to define disease free status (section 2.2)
- E4. Lead vaccine candidate in the short to medium term is BCG. The disease control benefit relies on the efficacy of the vaccine, appropriate coverage and level of uptake. Uptake will be affected by the balance of efficacy and cost to the individual. Benefits will be realised over a number of years although will plateau out if constant pressure from wildlife remains. A prime-boost approach may enhance protection (section 2.3)
- E5. EU legislation will need to be amended to allow *any* cattle vaccination.
- E6. The use of the tuberculin skin test to define OTF status in trade legislation creates difficulties when using 'sensitising vaccines' such as BCG which give skin test false positives. EU legislation will need to be amended to allow use of a vaccine which sensitises cattle to the tuberculin skin test without trade restrictions being imposed on live animals i.e. through the recognition of a new test which is capable of distinguishing between infected and vaccinated animals, with consequential amendments to domestic legislation.
- E7. Milk from animals sensitised to the skin test could not be consumed under current legislation. Changes to EU trade legislation will need to be appropriately worded to ensure that the prohibition in the EU hygiene legislation does not apply to vaccinated but not infected animals.

- E8. Currently there are not adequate powers in domestic legislation to make vaccination for bTB compulsory and this will need to be addressed through section 2(2) regulations/amendments to primary legislation.
- E9. Making changes to EU legislation is likely to be challenging as the majority of Member States have, or are on track to get, full OTF status and therefore it may be difficult to muster the necessary support for making changes. (section 2.4)
- E10. Not all vaccinated animals would be protected from TB and therefore vaccination alone will not be sufficient to demonstrate disease free status without testing and allow trade in those animals. A differential diagnostic test to Differentiate Infected from Vaccinated Animals (known as a 'DIVA' test) could be used alongside the skin test, where necessary, to confirm whether the animal is indeed infected.
- E11. Acceptable efficacy of the DIVA test and vaccination must 'coincide' to allow use without trade restrictions this may require use in a sub-optimal age range. EU acceptance of a DIVA test will depend upon it being accredited by the OIE. If appropriate amendments to EU legislation were achieved such a test could be used in herds with sensitised skin test positive animals in order to prevent OTF status being suspended and to continue to facilitate trade in accordance with the trade directive requirements
- E12. In the absence of an EU accepted DIVA test BCG based cattle vaccines are not considered viable.
- E13. Non-sensitising next generation vaccines could be used without a DIVA test or trade restrictions, but amendments to Directive 78/52 on eradication plans will still be necessary. (section 2.5)
- E14. Identification of vaccinated animals may need to be a key component of any vaccination programme. Certification would provide a number of benefits to farmers, government and the veterinary profession including:
- demonstrating the requirement for a DIVA
 - monitoring compliance and evaluating efficacy of vaccination programmes
 - supporting the use of booster vaccines
 - buyer and seller confidence
- E15. Not identifying or certifying may potentially reduce the cost of administering vaccination as certification in particular would limit who could administer the vaccine to vets. However, not certifying would equally increase the costs of DIVA testing. A number of different potential methods of identification and certification exist but will all have some additional costs and the regulatory burden associated with them (section 2.6)

- E16. Cattle vaccination policy could be voluntary or compulsory each with associated issues and benefits. Voluntary approach has minimal regulatory burdens but would be very sensitive to costs and any potential trade issues. It may be possible to use incentives to improve uptake. Compulsory vaccination allows control over targeting, uptake, certification and monitoring (section 2.7)
- E17. Who pays will potentially have a significant impact on the level of uptake particularly in relation to the costs of DIVA testing for both routine and pre-movement testing. Government is unlikely to be able to provide “new” money to fully fund cattle vaccination. It will most likely be a business decision for individual farmers whether to vaccinate. Farmers have indicated they would be less willing to contribute to the cost of a compulsory system. (section 2.8)
- E18. There are potential roles for government, industry, vets and other organisations in a cattle vaccination programme. Involvement of the veterinary profession will be important to prescribe and potentially administer the vaccine and to provide advice and guidance to farmers. While administration of vaccines are not generally restricted and can be carried out by the vet or the farmer in practice certification requirements may limit this. Government and industry’s roles in monitoring will be important. In the long term government’s role may be limited to providing guidance, monitoring and enforcement (section 2.9)
- E19. The vaccine will be administered subcutaneously or intramuscularly for practical ease. Ideally vaccination will be targeted to calves within the first 6 weeks of birth but timing will also need to consider the requirements of DIVA testing and practicality. Older animals may also be vaccinated as part of the initial rollout to give more rapid herd immunity (section 2.10)
- E20. Blanket vaccination of all cattle may deliver the greatest benefits but would also involve significant costs a targeted approach may be more sustainable. Taking into account veterinary advice and the delivery requirement to easily identify target herds, vaccination should be targeted to all herds (including those with organic status) that are subject to annual or more frequent TB testing. Under a compulsory system discretion should exist to impose, following a veterinary risk assessment, vaccination on any other herd e.g. because of its size or purchasing practices (section 2.11)
- E21. If all cattle subject to 1 yearly surveillance bTB testing are subject to vaccination at birth with BCG the number of vaccines required per year could be a maximum of 1-2 million doses (section 2.12)

1.1 Scenarios for use

E22. The majority of the difficulties surrounding cattle vaccination outlined previously particularly around legality and trade will apply equally to all options. These therefore represent potential barriers to cattle vaccination as a whole rather than factors to determine between different scenarios to use.

E23. In the event a vaccine is developed for cattle that: i) confers protection; ii) reduces the transmission rate; iii) is accompanied by the development of a satisfactory DIVA test and iv) is permissible under EU and domestic legislation, scenarios 1-4 below may be feasible.

E24. As a result of the constraints around trade issues options which would result in significant restrictions on trade are not being considered.

1.1.1 Scenario 1: Compulsory vaccination of all cattle

E25. All cattle are vaccinated against bovine TB. By vaccinating the maximum number of animals the greatest disease control may be realised. This option is likely to yield the greatest gross benefits, but it would also have the greatest costs. It is not at all targeted nor risk based.

1.1.2 Scenario 2: Compulsory vaccination of high risk herds

E26. This scenario would be a risk based approach and would aim to reduce the risk of disease transmission within herds in endemic areas. It would also reduce the risk of disease spread into clear herds and into wildlife populations if vaccinated but infected cattle are moved.

E27. By targeting herds on annual and possibly two yearly TB testing, the intention is to focus on herds at most risk of becoming infected or passing on infection as well as those herds with a high level of persistent infection thus minimising the cost of implementing the measure whilst realising maximum disease control benefits.

1.1.3 Scenario 3: Compulsory vaccination of high risk herds accompanied by the option of voluntary vaccination

E28. As for scenario 3 disease in high-risk herds would be managed by compulsory vaccination. However, vaccine used to not be limited to these areas with the option for anyone else wishing to voluntarily vaccinate their herd able to do so based on their own consideration of the costs and benefits.

1.1.4 Scenario 4: Voluntary vaccination

E29. Voluntary vaccination would allow individual farmers in consultation with their vets to determine if vaccination would be worthwhile in the individual situation. Government would produce guidance to encourage those at highest risk to vaccinate their animals. This approach may be particularly suited to the use of non-sensitising vaccines if they become available.

1.2 Economic assessment of lead option

- E30. Two variations of compulsorily vaccinating high risk herds have been assessed. The first defines the vaccination of high risk herds as cattle in annual testing parishes; the second as cattle in both one and two yearly testing parishes. For both variations we have modelled the potential costs and benefits of vaccinating cattle with BCG once in their lifetime as neonates.
- E31. The model predicts vaccinating cattle in yearly tested parishes would cost around £170 million to £180 million over the period from introduction in 2012 to the end of the modelled period in 2026. It predicts benefits from fewer breakdowns and less routine testing of between £150 million and £250 million, potentially saving up to one fifth of the costs of the current policy measures. The benefits from vaccinating cattle in yearly tested parishes are likely to justify its costs over this period.
- E32. The second vaccination policy covers cattle in both one and two yearly testing. The extra benefits of wider vaccination are quite small, however the extra costs are substantial, making this option more costly than the baseline. It will be necessary to carry out further runs of the model to represent other scenarios.
- E33. It is important to note that this economic analysis is based on a model that makes a number of assumptions which may prove to be inaccurate.

1.3 Conclusions

- E34. This paper sets out the most feasible scenarios for the widespread use of cattle vaccines. The analysis demonstrates that if BCG based vaccines will need to be used in conjunction with a DIVA test and that such a programme of vaccination could be cost-effective.
- E35. It is also clear that the most significant barriers to use are legal and the resultant trade implications. Changes to legislation will be required before any cattle vaccines can be used.
- E36. The scenarios identified are the lead options and therefore give a reasonable basis on which to make decisions regarding prioritisation of the vaccine programme. The next step of the process will be to develop a business case for cattle vaccination based on these findings
- E37. However, it is recognised that changes in the disease picture and other factors may alter some of the issues discussed. The use of BCG based vaccines in the absence of a DIVA test has been dismissed and the reasons for this are considered unlikely to change. However, no other options have been completely eliminated.

E38. This paper was discussed with stakeholder groups at a meeting on the 3rd of April 2008 and has been endorsed by them.

E39. The groups who have agreed to endorse this paper and its conclusions are:

- NFU
- BVA
- BCVA
- Badger Trust
- RSPCA
- FUW
- NFU Wales
- LAA
- The National Trust
- The Wildlife Trusts
- Defra TB Advisory group
- NBA - NBA participated in the discussions and supports the evidence in the paper. However, they have concluded based on this evidence, cattle vaccines are not a viable option and should not be a priority for resources

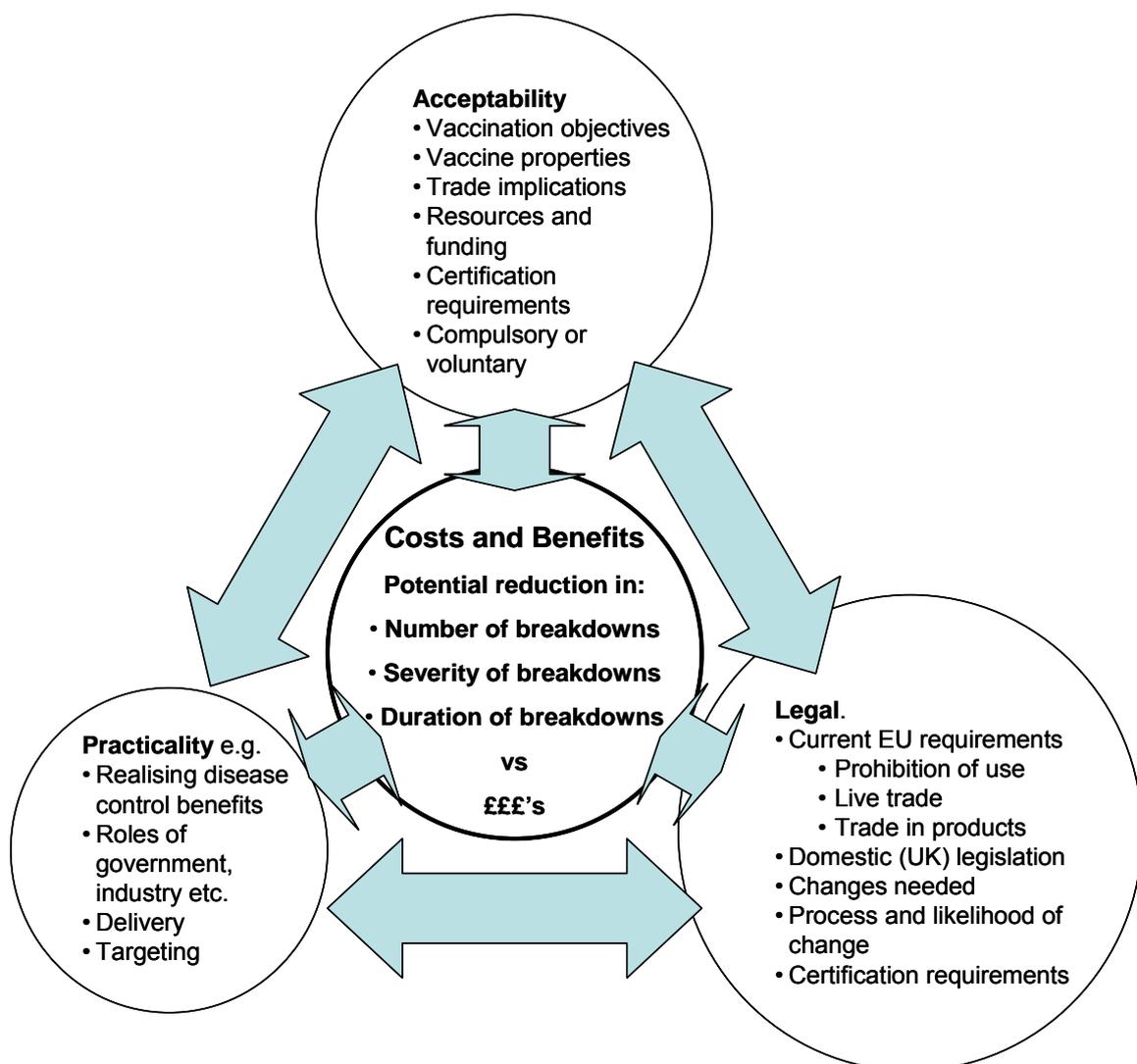
2 Key issues

1. Key issues surrounding vaccination of cattle to control bTB are set out below. At the end of each section key conclusions are identified which will be used to develop the options

2.1 Introduction

2. BTB is a serious infectious and zoonotic disease of cattle. There are four main reasons for Government intervention in controlling the disease:
 - *Protection of public health* - historically this has been the main reason for Government intervention on bTB, based on risks to consumers from milk and meat. There are also minimal occupational health risks,
 - *International trade* – the presence of bTB on a farm is potentially an impediment to EU trade in live cattle and cattle products
 - *Protect/promote animal welfare* – cattle are currently exposed to a level of disease which is resulting in the slaughter of around 22,000 animals each year, and
 - *To protect the interests of wider society/economy* – the existence of a reservoir of infection in wildlife, particularly badgers, is a significant factor in our ability to control the disease in cattle. However, badgers are protected by law and are valued by wider society.
3. Assessed against these reasons, vaccination of cattle against bTB may provide a proportionate intervention to control disease which strikes the right balance on behalf of society.
4. One of the 12 goals of the Government strategic framework for the sustainable control of bovine tuberculosis (bTB) in Great Britain (2005) is to “continue to develop a sound scientific evidence base by supporting research to improve our understanding of the disease and generate new tools, particularly in relation to diagnostics and vaccines...” the framework goes on to state “...it is hoped that these [vaccines] will deliver the prospect of eventual eradication of bTB in cattle. “
5. Whilst vaccines on their own are unlikely to deliver eradication, as part of a wider package of measures they have the potential to be a very effective control mechanism. Work to develop vaccines was begun in 1998 in response to the recommendations of the Krebs report (1997). Krebs recommended that vaccine research be given high priority and that legal and trade implications of vaccinating against bTB be addressed. Defra commissioned research on both cattle and badger vaccines and associated diagnostic tests and now has an extensive research programme in place. To date Defra has invested £17.8M in vaccine research with just under £11million of this focused on cattle vaccines and associated diagnostic tools.

6. This research has now reached the stage where several potential vaccine candidates have been identified that, with further funding, could be taken forward to develop an anti-tuberculosis vaccine. Now that the basic properties of likely vaccines are understood it is now possible to consider the other part of the Krebs recommendation; the legal and trade implications. Before further financial investment by Government into this area of work it is necessary to demonstrate (in principle) that a vaccination policy could indeed lead to either the control or eradication of TB in cattle. This requires preliminary thinking into how a vaccine would be deployed and the costs and benefits involved. This includes consideration of legal, trade, practicality and acceptability issues to determine whether a vaccination policy is feasible.
7. These issues cannot be considered in isolation and will interact and constrain each other. The diagram below summarises these issues and their interactions. For cattle vaccination legal constraints and the acceptability of consequential trade issues are the greatest potential barriers.



8. Clarity on the available policy options will provide a framework for assessing the relative merits of each vaccine candidate. Policy will determine to some degree the characteristics required of a vaccine, including setting the minimum limits of vaccine efficacy required. This will be an important criterion for assessing whether vaccines that are developed are good enough. Exploring potential policy options at this stage serves to both justify further expenditure on vaccine research and influence the direction of future research. Additionally, prior consideration and a clear plan of getting the vaccine from laboratory to field will ensure against a delay in implementing a vaccine policy once a suitable product is available.
9. Cattle TB vaccine research is being actively pursued in a number of countries including USA and NZ, although no other country is actively considering vaccinating cattle against TB. The USA has a cattle TB vaccine research programme to retain the option of cattle vaccination and to support their wildlife vaccine development effort¹. New Zealand also supports a cattle TB vaccine research programme. The EU is currently funding a research proposal that is in part aimed at cattle TB vaccine development under Framework Programme 7 'Development of rational strategies for the eradication of bovine tuberculosis'. The UK is actively collaborating in a number of these initiatives.
10. As none of these countries have yet used TB vaccination in the field there is no direct policy comparison that can be made. However, cattle are routinely vaccinated against a number of other diseases and there are numerous examples of vaccination policies for other animals and diseases that we can refer to and draw from, in developing options for vaccinating cattle (see **Annex 1**).
11. There are a number of different ways in which vaccination could be used to tackle TB in cattle, each with associated issues including cost, legal constraints, practicality, stakeholder acceptability and commercial viability. This document sets out a number of issues that have been identified as critical to successfully implementing a cattle vaccination policy and presents possible options for overcoming the barriers identified. The potential policy options presented have been developed taking into consideration feedback from the industry and advice from scientific, epidemiological, veterinary, economic and legal experts.
12. It is recognised that, while work on cattle vaccination is progressing, a deployable vaccine is still several years away and that a number of factors which would impact on any delivery policy could change significantly in that time. This includes the overall level and distribution of disease, the general farming landscape and Government policy. The aim throughout the paper has been to maximise the choices available rather than to adopt specific policy approaches and the sensitivity of the

¹ R. Waters, personal communication

conclusions to the potential changes identified above has been considered. It is expected that policy development in this area will be an evolving process as more information becomes available. This paper therefore represents a starting point for this process.

2.2 Cattle vaccination objective

13. The main aims of cattle vaccination are to reduce the prevalence, incidence and spread of bovine TB in the cattle population – reducing the number and severity of breakdowns. It is unlikely that a vaccine will be developed that confers sterile immunity to all vaccinates, therefore if used as an isolated measure it is unlikely to achieve sufficient control or eradication of bTB in cattle. However, vaccination as part of a wider control programme comprised of a raft of complementary measures could make a significant contribution to the effective control of bTB.
14. In addition to the disease control objectives there is also the objective of reducing the overall economic impact of the disease both to the farming industry and the taxpayer.

2.2.1 Reducing bTB incidence and spread

15. BTB is a serious problem in cattle in some areas of GB, though it currently affects a small proportion of the national herd. Around 6.5% of cattle herds tested in 2006 sustained a new TB breakdown, although this percentage varies considerably between regions. The majority of breakdowns are confined to discrete regions within GB where bTB is endemic. Ninety five percent of confirmed new breakdowns in GB took place in the South West of England, West Midlands and Wales. The incidence of pathology or culture-confirmed herd breakdowns is highest in Gloucestershire, followed by Hereford and Worcestershire, Devon, Cornwall and Gwent. On average, a total of 6.0 reactors are identified per confirmed breakdown whereas in unconfirmed ones this average is 1.7.
16. Total numbers of new bTB breakdowns were increasing by an average of 14.5% year on year from the mid 1980's until mid-2003 when the TB testing backlog that built up during the Foot and Mouth (FMD) outbreak of 2001 was finally eliminated. Thereafter, the number of total and confirmed bTB breakdowns recorded in GB has been growing at a much lower rate, although the incidence of bTB is still high by comparison to most EU countries. The causes of the long-term increase in bTB in GB are not well understood as there are likely to be many factors involved. Whilst wildlife is implicated in disease transmission, there is uncertainty about the relative contribution of infected cattle and badgers to the incidence of TB. A key advantage of vaccinating cattle is it would protect recipients from infection whatever the source.

17. Movements of infected cattle can result in translocation of infection between herds. Bought-in infected cattle can amplify the infection within the herds resulting in spread of TB within- and between-herds. If this spread is not checked, it may eventually lead to the establishment of new TB “hotspots” in areas previously considered free from TB. Once established, these TB hotspots can be very difficult to eliminate, particularly if the infection spills over into wildlife hosts capable of acting as alternative reservoirs of *Mycobacterium bovis* (*M. bovis*) the bTB bacterium.
18. Likewise, movements of infected cattle also contribute to the overall incidence of TB in the so-called endemic bTB areas. Pre-movement testing is an existing measure that reduces the risk of disease spread through cattle movement although it does not eliminate the risk. By vaccinating cattle, the risk of introducing TB into an uninfected herd or seeding infection into wildlife when cattle are moved to herds in low bTB incidence areas would be further reduced. Therefore a cattle vaccine that is either protective and/or reduces transmission risks would reduce incidence, prevalence and geographical spread of disease when used in conjunction with existing bTB control measures.

2.2.2 Reducing the severity of breakdowns

19. In this context reducing the severity of breakdowns means reducing the numbers of reactor cattle in each breakdown and the duration of the breakdown where a herd is under movement restrictions.
20. In areas of endemic bTB incidence the protection conferred by vaccination could reduce the number of breakdowns by stopping herds becoming infected from wildlife. It could also reduce the severity of breakdown and spread of disease by preventing multiple animals in the herd from acquiring infection from other cattle and other wildlife.
21. Reduced infectivity in cattle might result in a lower rate of inter-herd spread of infection which might lead to fewer reactors per breakdown. It might also reduce intra-herd spread of infection and lower the risk of spreading infection into wildlife reservoirs.
22. Vaccination of cattle is likely to reduce the reproductive rate of bTB within the overall cattle population thereby contributing to a reduction in incidence, prevalence and spread. However, the identification of a single reactor animal is sufficient to constitute a herd breakdown and result in movement restrictions being imposed on a herd.
23. Therefore, from an individual farmer’s perspective, a vaccine that cannot guarantee all animals within a herd are 100% protected from acquiring TB will mean they still run the risk, albeit much reduced (probably at least by 50%), of experiencing a herd breakdown. The industry have indicated that for the individual farmer it is the consequential movement restrictions that have the greatest impact and therefore a single animal breakdown

can have as significant an impact and one with multiple reactors. Even the reduced risk may therefore still be sufficiently great to make the time and financial costs involved in vaccinating a herd sufficiently burdensome to be unattractive to individual herd owners, despite the overall benefits to disease control. This also has important implications for vaccine efficacy discussed in the next section.

24. The fact that vaccinated animals are not 100% protected also means that being vaccinated is not sufficient to define an animal as disease free.

Summary

- Cattle vaccination has potential benefits to reduce: prevalence, incidence and spread of bTB in the cattle population
- Vaccination could prevent breakdowns by preventing herds becoming infected by wildlife and cattle and reduce the severity of a herd breakdown
- Vaccination that is less than 100% effective will not guarantee all cattle are fully protected from infection and is not sufficient to define an animal as disease free

2.3 Realising disease control benefits

2.3.1 Vaccine efficacy

25. Lead vaccine candidates emerging from current ongoing research (see **Annex 2**) are likely to:
 - be prophylactic and not therapeutic (i.e. prevent rather than cure existing infection),
 - be based on the human TB vaccine Bacille Calmette Guerin (BCG) , and
 - not exacerbate existing disease if administered to an already infected animal.
26. Experimental evidence indicates that cattle are most responsive to BCG when the vaccine is administered to neonates (calves less than 6 weeks old). Vaccination early in life also reduces the chance of prior sensitisation to environmental mycobacteria which could affect responsiveness to vaccination. Likewise vaccination is not expected to have any beneficial effect in already infected cattle so earlier vaccination reduces the likelihood of the animal already being infected.
27. It is unlikely that a cattle vaccine will be developed in the short to medium term (i.e. within the next 5 years) that confers over 80% protection against bTB in the vast majority of cattle although this is currently a long-term research aim.
28. In the short to medium term what is more probable, is that a BCG vaccine is available that confers full protection against *M. bovis* infection

to 50% of vaccinated animals². Of the 50% that remain susceptible to infection, over half will be partially protected and have a much reduced capability of transmitting *M. bovis* should they become infected. The benefits of vaccination are likely to last for at least 12 months. Detailed definitions of full protection and partial protection can be found in **Annex 3**.

29. The protection elicited by BCG could potentially be enhanced by a 'prime-boost' regime. This involves 'priming' cattle by vaccinating them initially with BCG and then subsequently 'boosting' with a recombinant vaccine. It is hoped that this will result in increasing protection up to 80%. The development of a booster vaccine is a medium term (5-10 year) goal. A timetable for development and widespread use of a BCG and recombinant booster vaccine can be found at **Annex 4**.
30. The development of non-BCG vaccines is being funded by Defra but the availability of such a product is a longer term (over 10 years) goal. This line of research, as with similar endeavours in the field of human TB vaccines, is at the early stages and the characteristics and benefits of such vaccines cannot be predicted at this stage. This research is conducted in close collaboration with human medicine i.e. uses same potential candidates but with additional work on suitable adjuvants for use in cattle.

2.3.2 Vaccine uptake

31. The full potential benefits of vaccination will only be realised if the appropriate coverage and level of uptake are achieved. Maximum disease control benefits could be realised without vaccinating the entire cattle population. This is dependent on appropriately targeting a subset of the population which will be dictated by the characteristics of the epidemic as well as the properties and efficacy of the vaccine. That is whether vaccination confers protection and/or reduced transmission and by how much.
32. For the individual herd the situation mirrors the bigger picture, not all animals in a herd would need to be vaccinated (or indeed fully protected by the vaccine) for a beneficial effect to be realised. This is due to the concept of 'herd immunity' where the individuals which are protected by the vaccination reduce the disease pressure on unprotected individuals to the extent where they are unlikely to be exposed. For an individual herd owner it might make sense to vaccinate their animals as they may see a benefit, even if on a national scale uptake is too low to significantly impact on disease.
33. However, as noted above, a single reactor causes the breakdown with the consequential restrictions and the individual farmer will need to weigh the potential costs against the residual risk. The balance of efficacy

² Zuckerman, Lord., 1980. – Badgers, Cattle and Tuberculosis, HMSO. 107pp.

versus cost to the individual will therefore have a significant impact on uptake in the absence of a compulsory requirement.

34. How best to target a cattle vaccine is covered in the section 2.10 and is based on veterinary advice that takes into account different levels of risk between different cattle herds. This advice assumes that the appropriate changes to EU legislation will be achievable (see section 2.3).

2.3.3 Timescale of benefit realisation

35. With current control measures in place, modelling predicts vaccination of cattle with BCG could lead to an observed impact on incidence and prevalence of disease in cattle within a few years of vaccine implementation. Ultimately the level of disease incidence in cattle would be kept at bay but bTB would not be eradicated due to constant infection pressure from wildlife on those animals not fully protected.

Summary

- Lead vaccine candidate in the short to medium term is BCG
- The disease control benefit relies on the efficacy of the vaccine, appropriate coverage and level of uptake
- Uptake will be affected by the balance of efficacy and cost to the individual
- Benefits will be realised over a number of years although will plateau out if constant pressure from wildlife remains
- A prime-boost approach may enhance protection

2.4 Current Legal Framework

36. BTB is a highly regulated disease. There are a number of pieces of legislation which have a significant impact on the viability of cattle vaccination both at the international and domestic level. The areas covered by key pieces of legislation are:
 - The requirement that the use of cattle vaccines for bTB be prohibited under national eradication plans (EU Directive 78/52/EEC)
 - requirements for testing to allow trade in *live* cattle (EU Directive 64/432/EEC) and implementing domestic legislation (Tuberculosis (England) Order 2007)
 - Food legislation requirements for trade in cattle *products*
 - The powers available to make vaccination compulsory (Tuberculosis (England) Order 2007/ Animal Health Act 1981)
37. A full discussion of the legal requirements surrounding cattle vaccination can be found in **Annex 5**. The key implications are outlined below.

2.4.1 Prohibition of vaccine use

38. EU Directive 78/52/EEC and associated directives set out the criteria for national plans for the 'accelerated eradication' of bTB, which Member States are required to produce. One of the criteria is a requirement to prohibit "anti-tuberculosis vaccination" under these plans. The adoption of a practice that was contrary to the requirements for such a plan, or a failure to prohibit vaccination would be very likely to be considered contrary to EC law.
39. In order to allow a domestic bTB vaccination policy it will therefore be necessary to suitably amend this legislation or risk infraction proceedings.

2.4.2 Legislation affecting live trade

40. EU Directive 64/432/EEC aims to facilitate intra-community trade by ensuring that only animals with proven disease-free status can be exported to other Member States. Cattle must come from a herd with Officially Tuberculosis Free (OTF) status, i.e. no 'reactor' or 'inconclusive reactor' animals, in order to be traded. OTF status is determined through use of the Single Intradermal Comparative Tuberculin Test (SICTT commonly referred to as the tuberculin skin test) on each animal in the herd – if animals are deemed to have given a positive reaction to this test, OTF status must be suspended. This directive also forms the basis of the current test and slaughter policy, the powers for which are set out in domestic legislation.
41. Some bTB vaccines candidates will interfere (at least for a number of months following vaccination) with the tuberculin skin test by sensitising the animal, producing a positive reaction in an uninfected, vaccinated animal. BCG is one such sensitising vaccine as it is based on a variant of *Mycobacterium bovis* (*M. bovis*), the bTB bacterium. Under current rules herds containing sensitised animals would be unable to maintain OTF status and therefore could not be traded.
42. In order for such animals to be eligible for trade it will be necessary to achieve amendment to the directive so that OTF status can be determined by the use of an alternative or ancillary test to the skin test, which could be used on animals that have been subjected to a sensitising vaccine.
43. How the issues of trade surrounding sensitising vaccines might be addressed is discussed in Section 2.5. Animals vaccinated with non-sensitising vaccines, or indeed those where the sensitisation had waned would not strictly be affected by this legislation and could be traded as normal. However, it needs to be borne in mind that the Directive's trade rules are predicated on the basis that vaccination will not be taking place

and therefore the Commission could have reservations about such an approach.

2.4.3 Legislation affecting trade in products

44. Products from bTB infected herds and particularly reactor animals are tightly controlled.
45. Regulation (EC) No 853/2004 which sets out hygiene rules for food of animal origin stipulates that raw milk must come from cows belonging to a herd which is officially tuberculosis free. Milk from non-OTF herds can still be used but must be pasteurised and milk from cows that give a positive reaction to a bTB test cannot enter the food chain.
46. As noted above, a sensitising vaccine would give false positives to the skin test and therefore prevent milk from these animals being used. This regulation takes its definition of OTF status and the applicable bTB tests from the 64/432/EEC trade directive. In order to overcome this potential restriction therefore the trade directive must be changed so that a positive reaction to the skin test but a negative to an alternative or ancillary test is not considered a “positive reaction” for the purposes of that Directive or, in turn, the EU hygiene legislation.
47. Regulation (EC) No 854/2004 sets out official controls on production of food of animal origin and requires animals that have reacted positively to the tuberculin test to be slaughtered separately to other animals. The tuberculin skin test is specified in the text without reference to other regulations. It is hoped however that an amendment to Regulation (EC) 854/2004 will not be necessary if the trade directive is amended appropriately. If an ancillary/alternative test is recognised, there will no longer be a requirement that all skin test positive animals (to that test alone) be slaughtered. It is highly arguable that Regulation 854/2004 separation requirements only apply when skin test positive animals are required to be slaughtered under the trade directive.
48. In the absence of an amendment to the trade directive recognising an alternative/ancillary test to the skin test (meaning that sensitised but not infected animals do not need to be slaughtered), sensitised animals would need to be slaughtered separately from non-reactors.

2.4.4 Legislation affecting the ability to require vaccination

49. The Tuberculosis (England) Order 2007 currently prohibits vaccination against bTB except under the authorisation of the Secretary of State. Furthermore, the Animal Health Act which confers powers on the Secretary of State to “cause” vaccination only does so for a limited number of prescribed circumstances. These are not considered sufficient to allow widespread compulsory vaccination for bTB.

50. To implement a compulsory vaccination policy which falls outside the scope of such 'prescribed circumstances' we need an amendment to the TB Order 2007/new regulations made under section 2(2) of the European Communities Act 1972 (as has been done for FMD and Avian Influenza vaccination policies) or a Bill amending the Animal Health Act 1981 to provide for wider vaccination powers. In either case, the appropriate amendments to EU legislation must first be achieved.
51. We are assessing the process and likelihood of being able to address and remove the barriers mentioned previously. Negotiation at EU level is likely to be a protracted and difficult process without certainty that we can secure a successful outcome. The majority of EU Member States are already OTF or firmly on track to achieve such accreditation without the use of vaccines, which may make it difficult for the UK to muster the necessary support to amend the legislation.
52. The consensus among stakeholders was that framing the issue of cattle vaccines for bTB as part of a wider discussion on controlling infectious disease in livestock at EU level may provide the most effective route to securing change. Whilst this may impact on the overall timetable there would be a greater prospect of success, especially if approached alongside gaining a consensus of expert scientific opinion for example through EFSA committees.

Summary

- EU legislation will need to be amended to allow *any* cattle vaccination
- The use of the tuberculin skin test to define OTF status in trade legislation creates difficulties when using 'sensitising vaccines' such as BCG which give skin test false positives
- EU legislation will need to be amended to allow use of a vaccine which sensitises cattle to the tuberculin skin test without trade restrictions being imposed on live animals i.e. through the recognition of a new test which is capable of distinguishing between infected and vaccinated animals, with consequential amendments to domestic legislation.
- Milk from animals sensitised to the skin test could not be consumed under current legislation. Changes to EU trade legislation will need to be appropriately worded to ensure that the prohibition in the EU hygiene legislation does not apply to vaccinated but not infected animals.
- Currently there are not adequate powers in domestic legislation to make vaccination for bTB compulsory and this will need to be addressed through section 2(2) regulations/amendments to primary legislation.
- Making changes to EU legislation is likely to be challenging as the majority of Member States have, or are on track to get, full OTF status

2.5 Trade implications

53. As noted in the previous section the current reliance on the tuberculin skin test to designate OTF status presents significant difficulties for the use of vaccination where the vaccine *does* sensitise the animal to the tuberculin skin test. The lead candidate cattle vaccines for bTB are all based on BCG and fall into this category of 'sensitising' vaccine.
54. By only allowing animals with proven disease free status from OTF herds to be traded the risk of spreading the disease is minimised. Not all vaccinated animals would be protected from becoming infected or infectious and therefore vaccination alone will not be sufficient to demonstrate animals are disease free and allow trade.
55. For sensitising vaccines it is not possible to use the skin test to distinguish infected vaccinated animals from non-infected vaccinated animals and therefore demonstrate disease free status. To address this issue we are developing a differential diagnostic test to Differentiate Infected from Vaccinated Animals (known as a 'DIVA' test) to be used alongside the skin test. However, we would need to get this accepted at the EU and international level.

2.5.1 DIVA test

56. The DIVA test will be based on the same biological assay as the current 'gamma interferon (IFN- γ) test' which is currently used alongside the skin test to improve specificity in certain prescribed circumstances.
57. BCG vaccination produces for a certain time post-vaccination a reaction to the skin test because the vaccine is based on a variant of *M. bovis*, the bTB bacterium. This reaction to tuberculin will subside over a certain period post-vaccination and the animals will then be tuberculin test-negative (this time period has to be defined, but current evidence suggests that the majority of animals, >90% will revert to test-negative status within 1 year). However, the vaccine strain does not contain all of the same antigens as the disease causing strains. In simple terms the DIVA test is a blood test which looks for a reaction to those antigens of *M. bovis* which are only present in the disease causing bacteria but not the vaccine. A positive result therefore indicates infection.
58. In order to allow all vaccinated cattle to be traded the DIVA test will need to be effective on cattle from the age of vaccination. Experimental evidence suggests that the vaccine is most effective in neonates (under six weeks) therefore the DIVA test will also need to be effective at this age. However, the current IFN- γ test is only recommended for use from six months of age. The test will function effectively below this age but may result in some drop-off in accuracy (sensitivity or specificity) compared to older animals. It may therefore be necessary to identify a

'compromise' target age range for vaccination where the vaccine and the diagnostic test are both sufficiently effective or to accept some potential trade restrictions on younger animals. The latter as explained in section 2.5.3 is not an advisable course of action.

59. In order to get EU acceptance the test will need to be accredited by the OIE (The World Organisation for Animal Health), this will also facilitate the trade of vaccinated cattle outside the EU.
60. There is a validation process which the test must be subject to before an OIE application can be submitted. Once the application is submitted the approval process takes around 4-5 months. The full validation and approval process is provided in **Annex 6**.

2.5.2 BCG with a DIVA test

61. The DIVA test would be used when a vaccinated animal gives a positive reaction to the skin test (i.e. will be used as an ancillary test to the skin test). In such cases the DIVA test will confirm whether the animal is indeed infected or whether the positive response to the skin test is due to vaccination with BCG.
62. However, the nature of the test makes it impossible to guarantee the disease status of an animal. As with existing antemortem diagnostic tests for TB, there will be a number of false positive and false negative test results since neither the specificity nor the sensitivity respectively is likely to be 100%. The diagnostic accuracy of the new test will have to be assessed in field trials of herds of known TB status, which has already been done for some prototype DIVA reagents. In order to get the test accepted in EU legislation it will need to be at least as good as the current skin test in terms of sensitivity. However, data is available to suggest that the prototype DIVA reagent will satisfy this criteria, although as noted above this will need to coincide with the recommended age of vaccination.
63. If EU legislation could be changed to accept the DIVA test as an ancillary test to determine the disease status of vaccinated cattle, then herds which had positive results to the skin test but all negative results to the DIVA test could maintain their OTF status and both live animals from those herds and their products could be traded freely.
64. Used alongside the skin test the DIVA would require good record keeping and certification. Permanent identification of animals would ensure vaccinated animals were not slaughtered as reactors and equally resources were not used to test unvaccinated animals with the DIVA test. This is discussed in section 2.6.

2.5.3 BCG without a DIVA test

65. A DIVA test may not be available at the same time as BCG vaccine or it may not be possible to get the necessary accreditation or legislative changes in place.
66. In the absence of a DIVA test, it is possible to deploy a BCG vaccine and achieve disease control benefits however, there would be legal restrictions and therefore trade implications.
67. Options for using BCG without a DIVA test include:
 - Restricted zoning on a geographical basis – e.g. vaccinating animals in zones that are determined geographically, within which trade of live cattle is restricted. Cattle in ‘Restricted zones’ would be subject to vaccination. All vaccinated cattle would need to be identified and certified, or
 - Compartmentalisation on a herd basis– e.g. vaccinating herds at most risk of being infected or passing on infection. Trade of live cattle from vaccinated herds would be restricted and only permitted to move between herds with similar vaccination status. All vaccinated cattle would need to be identified and certified.
68. These options would significantly limit domestic trade to certain areas or categories of animal.
69. All international trade of live vaccinated animals would be prohibited. In addition milk from vaccinated animals could not enter the food chain. Without changes to the food legislation this would limit such an approach to beef cattle and severely reduce the disease control benefits. Such a change to the food legislation to accommodate such a policy is considered highly unlikely.
70. Vaccine sensitivity may wane after a period of time and so vaccinated animals may no longer give a reaction to the skin test and therefore be able to be tested and traded as normal. However, initial experiments indicate that this period will be at least a year and the difficulties around trade and milk use would still apply.
71. Industry has indicated that farmers are unlikely to voluntarily use cattle vaccines if it would result in *any* restriction of trade. Equally, a policy compelling them to use the vaccines and accept consequential restrictions would arguably be equivalent to a quantitative restriction on exports and would risk a successful challenge in the domestic courts or possibly infraction by the Commission. Achieving the necessary uptake levels to impact on the disease will therefore be very difficult with any trade restrictions in place.
72. Taking into account all of these constraints cattle vaccination with BCG based vaccines in the absence of a DIVA test is not considered a viable option.

2.5.4 Next generation vaccines

73. The development of second and third generation non-sensitising vaccines against bTB that do not interfere with the tuberculin skin test would enable vaccinated herds to maintain their OTF status under the current EU trade directive. This would enable trade of vaccinated animals and would overcome one of the major obstacles associated with vaccinating cattle using BCG.
74. There is already proof of principle that a vaccine that does not interfere with the tuberculin skin test can be produced. However, the availability of such vaccines is a long term goal and over 10 years away.
75. Providing EU legislation permitted anti-tuberculosis vaccination in cattle, there are no legislative trade implications surrounding vaccines which do not sensitise animals to the skin test. Although clearly we would need buy-in from the EU that the vaccine was not giving rise to anomalous test results and thereby endangering the control of the disease in the Community. It is not clear whether in the absence of other trade barriers vaccinated animals would attract a premium or discount compared to unvaccinated animals. Indications from the farming industry are that it will depend on a number of factors including geographical origin and cannot be predicted at this time.

Summary

- Not all vaccinated animals would be protected from TB and therefore vaccination alone will not be sufficient to demonstrate disease free status without testing and allow trade in those animals
- A differential diagnostic test to Differentiate Infected from Vaccinated Animals (known as a 'DIVA' test) could be used alongside the skin test, where necessary, to confirm whether the animal is indeed infected
- Acceptable efficacy of the DIVA test and vaccination must 'coincide' to allow use without trade restrictions this may require use in a sub-optimal age range
- EU acceptance of a DIVA test will depend upon it being accredited by the OIE
- If appropriate amendments to EU legislation were achieved such a test could be used in herds with sensitised skin test positive animals in order to prevent OTF status being suspended and to continue to facilitate trade in accordance with the trade directive requirements
- In the absence of an EU accepted DIVA test BCG based cattle vaccines are not considered viable
- Non-sensitising next generation vaccines could be used without a DIVA test or trade restrictions, but amendments to Directive 78/52 on eradication plans will still be necessary.

2.6 Requirement for identification of vaccinated animals

76. If vaccination with a sensitising vaccine was being widely used reactor cattle would need to be tested with a DIVA to demonstrate whether or not their positive reaction was due to vaccination or disease. There would be two options for deciding when to use a DIVA test:
- all reactor animals where there was a chance the animal might be vaccinated would undergo a DIVA test
 - vaccinated animals would be identified at vaccination and only identified reactors would undergo a DIVA test

2.6.1 No identification

77. Any reactor where a farmer claimed, or suspected, the animal had been vaccinated would require a DIVA test to prove its disease status.
78. The DIVA test will be substantially more expensive than the standard skin test. The inability to clearly identify animals requiring the DIVA test would result in any animals being unnecessarily tested with the consequential unnecessary cost to the industry/individual farmer.
79. An advantage of this approach would be that vaccination itself could be performed by the farmer, a vet would only be required to prescribe the vaccination. This could present a saving in terms of vet callout fees and would allow animals to be vaccinated at the optimum time for the disease control and the individual business rather than being grouped to make a veterinary visit more cost-effective. Farmers routinely administer other injections and the cost savings involved may help increase uptake. However, as noted above this would have to be offset against the cost of unnecessary DIVA testing.
80. There would be no record of how or when the animal was vaccinated. This would not only make DIVA testing difficult but also make the management and implementation of any boosting regime more complicated and potentially less effective. It would also impact on the ability to monitor the efficacy and safety of the vaccine.

2.6.2 Vaccination with certification

81. Certification would enable identification of cattle that had been vaccinated. There are benefits for Government, the farming industry and the veterinary profession of being able to distinguish vaccinated animals for the purposes of monitoring, trading, buyer assurance and establishing compliance with vaccination protocol.
82. The primary benefit of certification would be to enable farmers to demonstrate that cattle may be responding positively to the tuberculin

skin test because they have been vaccinated, rather than because of disease and therefore request a DIVA test to determine whether they are infected or not. Thus saving money on unnecessary tests.

83. Similarly, from the Government perspective certification would avoid the use of vaccination as grounds for questioning the skin test results and provide a means by which Government could monitor implementation, compliance and impact of a vaccination policy. This would include assessment of the level of uptake and coverage of vaccination within the cattle population. Certification would also facilitate enforcement activity if vaccination was a statutory requirement.
84. A vet will need to know the vaccination status of individual cattle in order to determine if an animal requires vaccinating or boosting. This may be critical if repeated vaccination at short intervals has detrimental consequences on an animal's health. It would also benefit the farmer to know when an animal's vaccination is due to avoid unnecessary expense of vaccinating animals that have already been duly vaccinated.
85. Market operators may wish to provide vaccination status details of cattle being sold through the market. If a mechanism was in place for vaccination status to be recorded, market operators could request a copy of this record so they can be confident of the status of the animals they are selling.
86. Certification would provide buyer assurance to farmers who wish to know whether cattle that are eligible for vaccination have been vaccinated. By introducing cattle into their herd that have not been vaccinated when they should have been would place the existing herd at greater risk.
87. Although self certification by farmers may be possible it would negate a number of the advantages outlined above particularly the degree of faith that could be placed on such a record. The most practical alternative is therefore for vets to certify vaccination. However, vets would only be prepared to certify if they themselves had performed the injection. This adds an additional cost to vaccination from the requirement for a vet to attend.
88. In addition to the veterinary costs there will also be a degree of bureaucracy associated with certification which will also have additional costs. The scale of these costs will depend upon the method of certification chosen.

2.6.3 Methods of identification of vaccinated animals

89. There are several options available for certifying and identifying vaccinated cattle. These vary from marking the animal directly, having some form of certification travel with the animal or recording vaccination information on a central database.

90. Directly marking vaccinated cattle allows immediate identification. However, there are limitations to this approach. It only confirms an animal has been vaccinated in the past but does not provide a complete vaccination history, i.e. whether it has received subsequent booster vaccines and immunisation dates. There may be the need for additional paperwork containing this information to go alongside the direct marking. There would also need to be a method in place to ensure that unvaccinated cattle were not marked incorrectly.
91. Requiring certificates to travel with cattle would enable both identification of vaccinated cattle as well as provide the vaccination history of the animal. These would enable some of the advantages around buyer assurance to be realised. However, this approach would increase the regulatory burden on farmers and vets in producing and retaining individual animal records. The certificates could be standalone documents or incorporated into existing documents such as the cattle passport.
92. A central database (e.g. Cattle Tracing System (CTS) online) would allow the full vaccination history of individual animals to be recorded. This information would be available at all times to the both herd owners and government officials. This would allow the herd owner to use the information as needed e.g. to provide proof of vaccination. Government could also use the information for monitoring purposes (including levels of compliance, side- or adverse effects in the vaccinated cattle population) and enforcement purposes. As with a paper-based system there would be some additional regulatory burden involved in entering the information and systems would have to be in place to allow for those farmers/veterinary practices without suitable computer access.
93. The precedence set by other vaccination policies in terms of certification varies depending on the nature of the disease and vaccine and the objectives of the vaccination programme. For example, cattle vaccinated against Foot and Mouth Disease must be identified with an ear tag, have their passport stamped and a written on-farm record maintained. Whereas for Bluetongue Disease, a record must be maintained at herd level unless the cattle are going for intra-community trade.

Summary

- No certification or identification may potentially reduce the cost of administering vaccination but would equally increase the costs of DIVA testing
- Certification or identification will provide a number of benefits to farmers, government and the veterinary profession including:
 - demonstrating the requirement for a DIVA
 - monitoring compliance and evaluating efficacy of vaccination programmes
 - supporting the use of booster vaccines
 - buyer and seller confidence
- Certification or identification would limit who could administer the vaccine
- a number of different potential methods of certification and identification exist but will all have some additional costs and the regulatory burden associated with them

2.7 Compulsory or voluntary vaccination

94. A number of different vaccination protocols are outlined in **Annex 1**. Some of these use voluntary vaccination while others are compulsory. The system adopted depends very much on the nature of the disease, the scale of use required to achieve the disease control benefits and the costs and incentives surrounding vaccination.

2.7.1 Voluntary vaccination

95. A voluntary approach, as taken with Bluetongue vaccination would minimise the regulatory burden and therefore might seem ideal. However, in terms of disease control there is likely to be a minimum level of uptake required in order to establish herd immunity and maximise the benefits of vaccination.

96. If levels of voluntary uptake are insufficient or the coverage inappropriate, then vaccination might not yield the benefit that could otherwise be achieved if use was optimised. Farmers have indicated that a vaccine would have to have been demonstrated as being highly effective for voluntary uptake to be significant. If there are any potential barriers to trade as a result of vaccination, either legal or perceived (e.g. market value of animals) then voluntary use is unlikely to succeed.

97. Incentives to comply with vaccination requirements could help encourage voluntary uptake and could include making vaccination a requirement to qualify for compensation or provide recompense for the cost of vaccination if a vaccinated herd suffers a breakdown. Voluntary vaccination would still need to be subject to sufficient controls around

identification and DIVA testing to ensure there were no additional trade restrictions.

2.7.2 Compulsory vaccination

98. Making vaccination compulsory would help ensure appropriate targeting and uptake of vaccines to realise maximum benefits.
99. Additionally, the implications of vaccination on the trade, of both live cattle and produce, are sufficiently great that stringent controls to confidently differentiate vaccinated from infected cattle may be necessary. In order to ensure appropriate delivery of the vaccine, both in terms of immunisation protocol and population coverage and to maintain an accurate and comprehensive record of vaccinated animals, a compulsory policy may be required.
100. A compulsory regime has some support amongst the cattle industry and veterinary organisations for these reasons. However, there may be a greater reluctance amongst farmers to contribute to the costs of compulsory programme.

Summary

- The policy could be voluntary or compulsory each with associated issues and benefits
- Voluntary approach has minimal regulatory burdens but would be very sensitive to costs and any potential trade issues. It may be possible to use incentives to improve uptake
- Compulsory allows control over targeting, uptake, certification and monitoring

2.8 Resources and funding

101. At this stage it is not necessary or appropriate to agree who should fund a cattle vaccination programme. It is however, necessary to determine that there are some viable funding routes. The discussion below is therefore aimed at identifying (or excluding) possible funding routes rather than identifying definitive positions.
102. There are a combination of options that exist for how a cattle vaccine policy could be paid for. Costs that could be shared between government and farmer are cost of:
 - the vaccine
 - administration of the vaccine
 - DIVA testing

2.8.1 Taxpayers

103. The costs of research and development are being met by taxpayers. To date cattle vaccines and associated diagnostic research has cost just under £11million.
104. Sharing responsibility and costs for management of disease risks is a key part of Defra's Animal Health and Welfare Strategy. Further background on responsibility and cost sharing can be found on the Defra website³. The Strategy states that the livestock farming industry should take a greater ownership of, and financial responsibility for, the animal disease risks posed by bTB. In principle, the taxpayer should only be expected to pay for genuine public good.
105. On the timescales under which vaccines are likely to be available it is possible some form of responsibility and cost sharing may have been introduced. Vaccines policy therefore needs to be considered within potential responsibility and cost sharing (RCS) frameworks.
106. A significant farming industry view is that taxpayers will ultimately benefit from the reduction in disease due to lower testing costs and compensation payments and that government should therefore 'bring forward' the money saved to pump prime funding for the vaccination programme.
107. A similar argument can also be made that as industry currently bears significant costs in relation to bTB it will also accrue the benefits of vaccination and should also be prepared to invest for the future.
108. It is a realistic assumption that government funding for bTB is unlikely to grow to provide sufficient 'new money' to fully support deployment of cattle vaccination. Therefore if consideration is to be given to 'pump prime' funding it will be vital to understand where bTB cattle vaccination might lie in terms of the industry's priorities for funding relative to other areas where taxpayers contribute.
109. It is likely that Government will want to monitor the effects of the vaccination policy. This may require specific investment or be conducted as part of the ongoing process of monitoring the disease.

2.8.2 Individual farmers and the agricultural industry

110. Individual farmers who decide to use cattle vaccination could be expected to purchase and deliver the vaccine themselves. This would become a purely business based decision on whether the potential benefits to the individual justified the expenditure if vaccination is voluntary.

³ <http://www.defra.gov.uk/animalh/ahws/sharing/index.htm>

111. Advice from the industry indicates that for this type of business investment farmers would normally either expect to see returns over a period of less than a year. Farmers would also be more reluctant to pay for vaccination under a compulsory system.
112. Who is responsible for paying for a cattle vaccine policy is likely to have an impact on the uptake by, and acceptability to, farmers. The direct benefits of the policy to the individual farmer will also affect whether they would be willing to share costs.
113. The cost of a cattle vaccine is estimated at £8.25 per dose. The perception of whether this is considered affordable and value for money will influence whether farmers are inclined and prepared to pay.
114. The cost of a DIVA test is estimated at £26 per animal based on the cost of the IFN-g test. All vaccinated animals would be subject to the DIVA test if they showed a positive reaction to the skin test. It is estimated that 50% of the vaccinated cattle population will test positive to the tuberculin test at every routine annual test and so DIVA testing is necessary. Who pays for this additional testing cost is likely to strongly influence take up of vaccination by farmers.
115. This issue is potentially even more acute for pre-movement testing where the need for an additional DIVA test could more than triple the cost of an individual test. Consideration would need to be given to how the costs of DIVA testing could be incorporated into the current pre-movement testing framework to ensure this does not become a significant barrier to uptake.

Summary

- Government is unlikely to be able to provide “new” money to fully fund cattle vaccination
- If voluntary, it will be a business decision for individual farmers whether to vaccinate
- Farmers would be less willing to contribute to the cost of a compulsory system
- Who pays will potentially have a significant impact on the level of uptake particularly with regard to the cost of the DIVA test in relation to both routine and pre-movement testing

2.9 The Roles of Government, industry and others

116. There are a number of different roles in the deployment of a cattle vaccine beyond just providing funding. As with funding there are a number of interested parties who could potentially fulfil these roles.

2.9.1 Manufacture

117. The research and development costs of vaccine are being met by government. However, it is not the role of government to manufacture such products on a commercial basis. A commercial partner is being sought to manufacture the vaccine and to hold the marketing authorisation (MA) required to manufacture and distribute a veterinary medicine. Use of BCG would involve using the same vaccine as used in humans but this would be subject to a separate licence for veterinary use held by the MA holder, who would obtain BCG directly from the human vaccine manufacturer.
118. In addition to allowing the MA holder to sell the product this marketing authorisation also involves full responsibility for maintaining and assuring quality, and checking for, identifying and addressing any adverse effects. In addition to the manufacture and sale of the vaccine the company will therefore also be responsible for pharmacovigilance. The manufacturer may also wish to promote use.

2.9.2 Distribution

119. The distribution chain will be dependent to some extent on how freely available the vaccine product is made. If it is to be openly available under veterinary prescription (it is likely to be classified as a prescription only medicine (POM-V)), it could be sent to veterinary distributors from which the vaccine can be purchased as and when required. There would be an audit trail as the MA holder and distributors are required to keep records of where they supply vaccine to, and the vets will have a record of prescriptions they have written. However, this information will not be readily available for any subsequent assessment should it be required.
120. Alternatively vaccine distribution could be controlled in a similar way to current tuberculin distribution. Animal Health Divisional Offices (AHDOs) would be individually responsible for ordering vaccine directly from the MA holder. Vets, OV's (Official Vets) or farmers would then order vaccines from their respective AHDOs as required. This distribution chain would allow government to maintain accessible records of vaccines provided and herds that have been vaccinated.

2.9.3 Who delivers the vaccine

121. It is assumed that a bTB vaccine (BCG or other) will be a prescription only medicine prescribed by a veterinary surgeon (POM-V). This means that a vet (government and/or private) will need to write a prescription to enable the user to purchase the medicine, however, it does not mean that the vet will necessarily be the distributor. This is in line with other veterinary medicines. Administration of a vaccine classified as POM-V is not restricted and could be carried out by either a vet or the farmer,

depending upon the licensing specifications of the product which will consider such things as safety to the administrator.

122. Since it is likely that any policy would require the vaccination status of the animal to be certified because of the implications it has on OTF status and trade, it is assumed that a vet and possibly an OV, not a farmer, would need to administer the vaccine. This would enable all vaccinated cattle to be recorded and identified which would facilitate monitoring and enforcement of the policy (if compulsory). As noted previously, delivery costs would be reduced if farmers administered the vaccine since there would be no veterinary fees involved, as is permitted, for example, with Bluetongue vaccine. However, there would be no audit trail of which animals had been vaccinated making it hard to determine vaccinated cattle for DIVA testing and to gather data to assess policy impact.

2.9.4 Publicity and guidance

123. Introduction of cattle vaccination whether it is advised as good practice or a statutory requirement would be supported by a comprehensive package of publicity and guidance. The communication would need to be clear about the aim of the policy and manage expectations that vaccination is not a “magic bullet” and that it would form part of a package of measures for controlling bTB alongside the current cattle control measures. Key messages could be promulgated by government and by farming organisations to their membership. Both farming and veterinary organisations have made clear that the advice vets give their clients will be critical to the success of any vaccine policy.

2.9.5 Monitoring

124. Government and farmers alike will want to understand the effects of a cattle vaccination programme to help inform continuing development of the bTB control policy and associated business decisions for farmers. How the policy is monitored will be dependent on the information available for analysis. With a voluntary approach where vaccine is freely available and vaccination is not certified, assessing the impact of vaccination might be more difficult than monitoring a vaccination regime that requires certification or is compulsory.

2.9.6 Enforcement

125. The ability to enforce legislation must be demonstrated if vaccination is made a statutory requirement. It would be possible to use a similar approach to enforce a vaccination policy as used to enforce the existing TB Order. Local authorities could be the statutory enforcement body. This would mean enforcement activity would be delivered by County Councils, Unitary authorities, Metropolitan authorities and London Boroughs, and would be commonly included within the Trading Standards remit of these bodies.

126. Local authorities proactively inspect and enforce a range of legislation while carrying out visits at:
- Farms;
 - Livestock markets;
 - Slaughterhouses;
 - Animal gatherings;
 - Vehicles transporting animals;
127. The focus of local authority enforcement activity is directed through a risk assessment process undertaken in liaison with the relevant Divisional Veterinary Manager. Enforcement is likely to be dependent on permitting Local Authorities access to appropriate central records.

Summary

- There are potential roles for government, farmers, vets and other organisations in a cattle vaccination programme
- Involvement of the veterinary profession will be important and could potentially include: prescribing the vaccine; administering the vaccine; and providing advice and guidance to farmers
- While administration of the vaccine is not restricted and can be carried out by the vet or the farmer in practice certification requirements may limit this
- Government and industry monitoring will be important
- In the long term government's role may be limited to providing guidance, monitoring and enforcement

2.10 Delivery

128. Who might deliver the vaccine has been discussed in the previous section. This section discusses the practicalities of vaccine delivery.

2.10.1 Vaccine format

129. The vaccine will be administered subcutaneously or intramuscularly for practical ease.

130. BCG vaccine will be in a freeze-dried formulation that will need to be reconstituted before use. According to the manufacturer's recommendations, both the BCG and accompanying diluent will need to be stored at 2-8°C in the dark including during transportation. The shelf life of the vaccine in 2 dose vials is 18 months unopened. A larger pack size (BCG Culture) may be used with the number of doses per pack being between 40 and 50 depending on whether a shelf life of 12 or 18 months is applied.

2.10.2 Timing

131. Experimental evidence indicates that cattle are most responsive to BCG when the vaccine is administered to neonates (calves less than 6 weeks old). Vaccination early in life also reduces the chance of prior sensitisation to environmental mycobacteria which could affect responsiveness to vaccination. Ideally the vaccine would be delivered to calves within the first 6 weeks of birth. However, to make a separate visit each time a calf is born may be impractical and on balance it may be preferable to vaccinate batches of calves every 2-3 months as was done with Brucellosis vaccination which was delivered to calves (see **Annex 1**). This decision will need to be based on evidence that increasing the age of vaccination does not affect vaccine efficacy and will also need to take into account the availability of a DIVA test which has been shown sufficiently effective at the age of administration.
132. Whilst BCG is most effective when delivered to neonates, it is likely to have some benefit even when administered to older cattle. Providing BCG does not have a detrimental effect when administered to already infected animals, there would be value in vaccinating all cattle within a herd rather than just neonates in the first year of policy implementation. Such an approach would enable more rapid establishment of immunity at a herd level.

2.10.3 Duration of vaccination programme

133. Unless eradication of bTB can be achieved or a badger vaccine against bTB proves highly effective, it may well be that vaccination remains a significant component of any bTB control programme.

Summary

- The vaccine will be administered subcutaneously or intramuscularly for practical ease
- Vaccination will ideally be targeted to calves within the first 6 weeks of birth but will need to take account of the requirements of the DIVA test and practicality
- Older animals may also be vaccinated as part of the initial rollout to give more rapid herd immunity

2.11 Targeting vaccination

134. Effectively targeting vaccination will help maximise the potential disease control benefits, but also needs to consider the costs involved.

135. To vaccinate all cattle is likely to yield the greatest gross benefits, but it would also carry the greatest costs.
136. To balance risk reduction against practicality and cost, it is proposed that a risk based approach is adopted and vaccination is targeted to cattle or herds most at risk of acquiring infection and transmitting it on. The aim would be to prevent increase of bTB within, and spread of infection from, the vaccinated herds.
137. The veterinary advice (see **Annex 7**) states that a vaccine that is preventative rather than therapeutic should be targeted to OTF herds that are at highest risk of becoming infected.
138. High risk herds could be defined by a number of risk factors including:
- the herd's tuberculin testing history;
 - cattle purchase history
 - the local risk of TB
 - herd size
 - business practices
139. In addition to the afore mentioned groups, there may be some additional benefit of vaccinating non-OTF herds, to reduce the risk of intra-herd spread thereby bringing down the prevalence and severity of infection in a herd and the risk of transmitting it to other herds and to local wildlife.
140. In summary the veterinary recommendation is to subject the following categories of cattle to vaccination:
- all OTF herds situated in annual TB testing areas (or with linked holdings or detached grazing in such areas) that have undergone a tuberculin herd skin test with negative results in the recent past,
 - any OTF herds outside annual testing areas that are considered at high risk of suffering a TB breakdown by virtue of their TB history, size or cattle purchase practices, and
 - additionally, the vaccine could be deployed in infected herds with a high incidence of reactors or persistent infection.
141. One of the most readily available indicators of herds that are at the highest risk of being infected is the routine bTB testing interval to which they are subject i.e. 'the herd testing interval' (HTI). This reflects the disease risk arising from: the geographical location of the herd; past history of TB breakdowns; and certain business activities that present an increased risk of cattle being infected – e.g. importers of Irish cattle, bull hirers, cattle dealers etc. Herds subject to 1 and possibly 2 yearly routine surveillance TB testing would serve as a useful proxy for cattle that would benefit from vaccination.
142. There will be certain groups of cattle that ideally would be vaccinated from a disease control perspective but for reasons of practicality or business needs may have to be exempt e.g. unpasteurised milk

producers. Vaccination of organic herds will not affect their status so it will be possible to vaccinate such herds without affecting their classification.

Summary

- Blanket vaccination of all cattle may deliver the greatest benefits but would also involve significant costs a targeted approach may be more sustainable
- Taking into account veterinary advice and the delivery requirement to easily identify target herds, vaccination should be targeted to all herds (including those with organic status) that are subject to annual or more frequent TB testing.
- Under a compulsory system discretion should exist to impose, following a veterinary risk assessment, vaccination on any other herd e.g. because of its size or purchasing practices

2.12 Vaccine market

143. The size of the market for cattle vaccines will depend upon level of uptake. This will be influenced by a number of factors such as how the vaccine is targeted, the cost and the efficacy and whether or not a vaccination policy is a statutory requirement or voluntary.

144. If all cattle subject to 1 yearly surveillance TB testing are subject to vaccination at birth with BCG, the number of vaccines required per year could be a maximum of 1 – 2 million doses.

Summary

- If all cattle subject to 1 yearly surveillance bTB testing are subject to vaccination at birth with BCG the number of vaccines required per year could be a maximum of 1-2 million doses

3 Lead scenarios

145. Based on the implementation options covered in Section 2, policy scenarios for vaccinating cattle are outlined below. They cover voluntary versus compulsory vaccination and targeted versus blanket vaccination.
146. The majority of the difficulties surrounding cattle vaccination outlined above particularly around legality and trade will apply equally to all options. These therefore represent potential barriers to cattle vaccination as a whole rather than factors to determine between different scenarios to use.
147. The control measures in place at the time of implementation will influence how vaccination is best implemented to maximise benefits. Making this assessment is likely to involve a review of the wider TB programme. The cattle industry is likely to have changed by the time a cattle vaccine is available. Herds are likely to be larger, there are likely to be more niche herds and the disease background could be very different. Any changes of this nature will affect the costs benefit assessment of the potential policy options proposed.
148. In the event a vaccine is developed for cattle that i) confers protection, ii) reduces the transmission rate, and iii) is accompanied by the development of a satisfactory DIVA (differentiating infected from vaccinated animals) test and iv) is permissible under EU and domestic legislation, scenarios 1-4 below may be feasible.
149. As a result of the discussion above on trade issues options which would result in significant restrictions on trade are not being considered.

3.1 Scenario 1: Compulsory vaccination of all cattle

3.1.1 Rationale

150. All cattle are vaccinated against bovine TB. By vaccinating the maximum number of animals the greatest disease control may be realised. This option is likely to yield the greatest gross benefits, but it would also have the greatest costs. It is not at all targeted nor risk based.

3.1.2 Description

151. The policy approach would be:
- To initially vaccinate all cattle with BCG in the first year of policy implementation
 - Thereafter, all calves born are vaccinated as neonate (0-42 days).
 - If a recombinant booster vaccine is developed that enhances the protective effects of BCG, then this will be administered to all eligible cattle annually.

- All vaccinated animals would be duly certified and be subject to DIVA testing if they show a positive reaction to the skin test.

3.2 Scenario 2: Compulsory vaccination of high risk herds

3.2.1 Rationale

152. This scenario would be a risk based approach and would aim to reduce the risk of disease transmission within herds in endemic areas. It would also reduce the risk of disease spread into clear herds and into wildlife populations if vaccinated but infected cattle are moved.

153. By targeting herds on annual and possibly two yearly TB testing, the intention is to focus on herds at most risk of becoming infected or passing on infection as well as those herds with a high level of persistent infection thus minimising the cost of implementing the measure whilst realising maximum disease control benefits.

3.2.2 Description

154. The policy approach would be:

- To initially vaccinate all cattle with a Herd Testing Interval of 1 or 1&2 yearly using BCG in the first year of policy implementation.
- Thereafter, all calves born are vaccinated as neonate (0-42 days).
- If a recombinant booster vaccine is developed that enhances the protective effects of BCG, then this will be administered to all eligible cattle annually.
- All vaccinated animals would be duly certified and be subject to DIVA testing if they show a positive reaction to the skin test.

3.3 Scenario 3: Compulsory vaccination of high risk herds accompanied by the option of voluntary vaccination

3.3.1 Rationale

155. As for scenario 3 disease in high-risk herds would be managed by compulsory vaccination. However, vaccine used to not be limited to these areas with the option for anyone else wishing to voluntarily vaccinate their herd able to do so based on their own consideration of the costs and benefits. This would provide an additional level of disease control providing it did not lead to farmers ignoring other measures.

3.3.2 Description

156. The policy approach would be:

- To initially vaccinate all cattle with a Herd Testing Interval of 1 or 1&2 yearly using BCG in the first year of policy implementation.
- Thereafter, all calves born are vaccinated as neonate (0-42 days).

- Vaccination is advised as good practice by government with guidance issued to vets and farmers
- To make the vaccine available to all cattle farmers subject to their vet and being willing to prescribe the vaccine based on their individual circumstances
- If a recombinant booster vaccine is developed that enhances the protective effects of BCG, then this will be administered to all eligible cattle annually.
- All vaccinated animals would be duly certified and be subject to DIVA testing if they show a positive reaction to the skin test.

3.4 Scenario 4: Voluntary vaccination

3.4.1 Rationale

157. Voluntary vaccination would allow individual farmers in consultation with their vets to determine if vaccination would be worthwhile in the individual situation. Government produce guidance to encourage those at highest risk to vaccinate their animals. This approach may be particularly suited to the use of non-sensitising vaccines if they become available.

3.4.2 Description

158. The policy approach would be:

- To make the vaccine available to all cattle farmers subject to their vet and being willing to prescribe the vaccine based on their individual circumstances
- Vaccination is advised as good practice by government with guidance issued to vets and farmers
- If a recombinant booster vaccine is developed that enhances the protective effects of BCG, then this would be made available to all eligible cattle annually.
- All vaccinated animals would be duly certified and be subject to DIVA testing if they show a positive reaction to the skin test.

4 Economic assessment of cattle vaccination

159. The compulsory vaccination of high risk herds (scenario 2) has been subject to an economic assessment to evaluate the costs and benefits of such a vaccination regime. This option has been selected over the others in the first instance because it is the most likely regime to realise the best cost benefit ratio i.e. represent the best value for money.
160. Two variations of Scenario 2 have been assessed using a model developed by the Veterinary Laboratories Agency (VLA). The first defines the vaccination of high risk herds as cattle in annual testing parishes; the second as cattle in both one and two yearly testing parishes. For both variations we have assessed the costs and benefits of vaccinating cattle with BCG once in their lifetime as neonates.
161. The above scenarios have been assessed against a baseline of current policy measures including pre-movement testing. It is also assumed the protection conferred by vaccination will last the lifetime of the animal. The effect on costs and benefits of both: 1) altering the rate of transmission by cattle movements between different parish testing frequencies; and 2) the contribution of badgers to local transmission in yearly tested parishes has been investigated since the value of these parameters are unknown.
162. The model predicts that vaccinating cattle in yearly tested parishes would cost around £170 million to £180 million over the period from introduction in 2012 to the end of the assessment period in 2026. It would result in benefits from fewer breakdowns and less routine testing of between £150 million and £250 million, saving up to one fifth of the costs of the current policy measures. This amounts to a net reduction in the cost of bTB over the whole period in three of the four VLA model runs of between 1% and 5%, i.e. there is a small net benefit ranging from £14 million to £62 million. In the fourth model run, with parameters representing low transmission, vaccination shows a small negative net benefit (a net cost) of £14 million. Taking the four parameter sets together, the benefits from cattle vaccination are likely to justify its costs over this period.
163. The second vaccination policy covers cattle in both one and two yearly testing parishes. The model predicts that the extra benefits of wider vaccination are quite small in all the VLA model scenarios, between £15 million and £30 million. However the extra costs are substantial, from £85 million to £115 million, making this option more costly than the baseline and particularly so in the low transmission model run. Wider vaccination would increase the total costs of bTB by between 7% and 11% compared to vaccination in yearly testing only.
164. Critical to the result is the assumption that the modelled level of protection can be achieved by a single BCG vaccination in the first year of life. It is not yet known whether BCG can achieve this level of efficacy and so it is important to consider how costs might change if a different

strategy were needed. For example, if repeated annual BCG vaccination were needed to achieve the modelled level of protection, then there would be a substantial net cost in vaccinating cattle in yearly tested parishes of between £310 million and £350 million. This would be an increase in the total cost of bTB over the period of between a quarter and a third.

165. It will be necessary to perform further runs of the VLA model to represent higher levels of protection through the use of BCG in the first year of life plus a recombinant booster. These scenarios could then be costed and are likely to produce an economic result for the period somewhere between the once per lifetime BCG and annual BCG discussed above, together with a lower overall level of bTB in 2026.

5 Conclusions

166. This paper sets out the most feasible scenarios for the widespread use of cattle vaccines. The analysis demonstrates that BCG based vaccines will need to be used in conjunction with a DIVA test and that such a programme of vaccination could be cost-effective.
167. It is also clear that the most significant barriers to use are legal and the resultant trade implications. Changes to legislation will be required before any cattle vaccines can be used.
168. The scenarios identified are the lead options and therefore give a reasonable basis on which to make decisions regarding prioritisation of the vaccine programme. The next step of the process will be to develop a business case for cattle vaccination based on these findings
169. However, it is recognised that changes in the disease picture and other factors may alter some of the issues discussed. The use of BCG based vaccines in the absence of a DIVA test has been dismissed and the reasons for this are considered unlikely to change. However, no other options have been completely eliminated.
170. This paper was discussed with stakeholder groups at a meeting on the 3rd of April 2008 and has been endorsed by them.
171. The groups who have agreed to endorse this paper and its conclusions are:
- NFU
 - BVA
 - BCVA
 - Badger Trust
 - RSPCA
 - FUW
 - NFU Wales
 - LAA
 - The National Trust
 - The Wildlife Trusts
 - Defra TB Advisory Group
 - NBA – NBA participated in the discussions and supports the evidence in the paper. However, they have concluded based on this evidence, cattle vaccines are not a viable option and should not be a priority for resources.

6 Annexes

6.1 Annex 1- Examples of vaccination policies for other diseases

6.1.1 Brucellosis Vaccination

Overview

- Combination of voluntary and compulsory vaccination
- Vaccine administered by LVIs or VOs
- Vaccinated calves had to be identified as such by ear tag
- Incentives provided for becoming an accredited herd
- S19 and R45/20– live attenuated vaccine
- Trade was restricted to other Member States with a similar Brucellosis status

Background

172. Bovine brucellosis is a contagious bacterial disease causing abortion and premature calving in cattle. It can cause a debilitating recurrent 'flu like disease in humans, known as undulant fever. Humans may contract the disease by drinking unpasteurised milk from infected cows or by coming into contact with the afterbirth, aborted foetus or uterine discharges from infected cows.

173. A study of bovine brucellosis in 1934 concluded that as many as 40% of cattle herds were infected with brucellosis; this was similar to the estimated prevalence of bovine tuberculosis in cattle at that time. Bovine brucellosis has been eradicated from Great Britain by using a calf vaccination strategy combined with a programme of serological testing and partial herd slaughter to remove seropositive adult cattle.

Calf Vaccination

174. The free calf vaccination scheme, using the so called Strain 19 or S19 vaccine, was introduced in 1962. All female calves were vaccinated at 3 to 6 months of age, vaccinated calves were identified by a specially designed metal eartag containing the letter V on a central disc. All calf vaccination was carried out by LVIs or VOs.

Accredited Herds Scheme

175. The introduction of free calf vaccination was followed by the introduction of a voluntary accredited herds scheme in 1967 to establish a nucleus of disease free herds on a voluntary basis (to qualify as disease a free accredited herd, a herd had to pass two herd tests at least six months

apart, of all eligible cattle, with no serological reactors). All female cattle over 18 months old and entire male cattle over 6 months of age were blood tested and any serological reactors were removed (the S19 vaccine used in female calves under 6 months of age did not cause cross reaction to the serological tests used, provided the vaccinated animals were over 18 months old before they were blood tested). Steers were not blood tested as they cannot transmit brucellosis to other cattle. Cattle from brucellosis free accredited herds were not allowed to contact cattle from non-accredited herds, they had to travel in separate vehicles and markets had separate sections for brucellosis accredited cattle. All farms with accredited herds had to have double fenced boundaries to give at least two yards separation from neighbouring herds. From 1967 to 1971 slaughter of serological reactors was not compulsory, no compensation was paid if the owner chose to slaughter reactors; but premium was paid for milk from accredited herds and an incentive payment was provided for beef breeding cows in accredited herds.

176. Compulsory area eradication commenced in 1971, beginning with the areas (usually counties) with the lowest prevalence of infected herds. Premium payments were ended and compensation was paid for each animal slaughtered because it is affected with brucellosis, or is a reactor when tested for this disease. By 1981 all herds in Great Britain were attested and the calf vaccination programme was ended. Great Britain gained formal recognition as a region of the European Union with Officially Brucellosis Free (OBF) status in 1985; although the first year with no confirmed cases was not until 1991.

Distribution and Storage of vaccine

177. S19 was provided as a live freeze dried vaccine in single dose vials; the vaccine was prepared for use by mixing with diluent immediately before use, the diluent was also provided in single dose vials. It had a long shelf life and could be stored at ambient temperature. All the S19 vaccine used by MAFF during brucellosis eradication was manufactured at the VLA (CVL as it was at the time) Weybridge.

Continuing Surveillance

178. In 1981 the annual herd blood testing of dairy herds was replaced by monthly bulk milk testing. In 1985 annual blood testing of beef breeding herds was reduced to two yearly blood testing. Following a review of brucellosis surveillance, the two yearly blood test of beef breeding cattle ended in April 2007.
179. The national brucellosis surveillance programme continues; the main features are as follows:-

- i) Monthly bulk milk ELISA test for all dairy herds.

- ii) Statutory requirement to report all abortions and premature calvings; criteria are laid down to assist the DVM in deciding which require collection of samples for laboratory testing to rule out brucellosis. In general, all reported abortions in beef breeding cattle are investigated; abortion investigations in dairy herds which are subject to monthly bulk milk testing, are carried out on the basis of risk assessment.
- iii) Post calving blood test of cattle imported from non-OBF regions, this is facilitated by use of the British Cattle Movement System (BCMS) to notify DVMs each week of imported cattle which have calved for the first time in Great Britain (or might be expected to have calved).

180. The last measure was introduced in the year 2002 following a brucellosis risk assessment prepared by the Veterinary Laboratories Agency, which included advice that the most reliable time to detect antibodies to brucellosis in imported cattle is at least two weeks after their first calving in GB.

Reintroductions of Brucellosis of cattle

181. Brucellosis was reintroduced into Great Britain in 1993 when infection was confirmed in a single herd in Anglesey which was found to have imported infected cattle from France. The disease was reintroduced again in two incidents in February and November 2003 when brucellosis was confirmed in four herds in Scotland following the import of consignments of infected cattle from the Republic of Ireland. The cost of dealing with both 2003 incidents in Scotland was approximately £500,000. The disease was contained in both cases. A single case was confirmed in Cornwall in 2004, the origin of this case was never confirmed; but it is likely to have been indirectly linked to imported cattle.

- Notes Compiled by Chris Kilner VA, Surveillance Zoonoses Epidemiology and Risk, FFG, Defra.

6.1.2 Foot and Mouth Disease (FMD) Vaccination

Overview

- Used in emergency situations only
- Government controlled – must be licensed by Secretary of State
- Paid for by Government
- Compulsory
- Administered by independent contractor
- Vaccinated animals to be eartagged, passport stamped and written record kept
- No export of vaccinated animals
- Meat and products from vaccinated animals to be treated

182. Under the [FMD Order](#) the slaughter of susceptible animals on infected premises remains the principal tool for tackling an FMD outbreak. [Vaccination Regulations](#), which transpose the vaccination provisions of the [EU Directive](#) on community measures for the control of foot and mouth disease, have moved the potential use of emergency vaccination to the forefront of disease control, as an adjunct to the basic slaughter policy.
183. The Regulations ban vaccination except under licence by the Secretary of State and also ban the export of vaccinated animals. The Regulations similarly provide for zones of control, both for where vaccination takes place and where it is expressly prohibited, and introduces treatments for meat and other animal products from vaccinated animals.
184. Where protective vaccination is specified, keepers are required to provide any information regarding the animals they are responsible for, to submit animals for vaccination as required and to provide any assistance as may reasonably be required in securing animals to facilitate vaccination.
185. An independent contractor administers the vaccine and is responsible for the identification of vaccinated animals with an ear tag (ear tag must be a particular colour) and making a written record. The FMD Order requires the cattle passport to be stamped. The ear tag must remain for the whole of the life of the vaccinated animal to prevent it from being exported. However, following FMD freedom, vaccinated animals may be traded freely on the domestic market and meat and other products from vaccinated animals does not need to be marked or treated and can be exported.

Targeting vaccination

186. Where protective vaccination is specified, a Vaccination Zone (VZ) will be established of such size as is necessary. A Vaccination Surveillance Zone (VSZ) will also be established, for at least 10km around the VZ, where no vaccination is permitted. Various movement controls apply to both the VZ and the VSZ and products from vaccinated animals are generally required to be either heat treated or deboned and matured.
187. A vaccination programme comprises of three phases.
188. Phase 1 starts on the declaration of a VZ and involves the administration of vaccination.
189. Phase 2 starts 30 days after all the animal in the VZ have been vaccinated, or longer depending on the Secretary of State's discretion. During this phase, a clinical and serological survey of all the premises within the VZ will take place, the outcome of which will determine whether premises are classified as infected, reactor holdings (where animals have to be slaughtered) or free of disease.

190. Phase 3 will start on completion of the measures to be undertaken in Phase 2 or may be earlier for individual premises which have independently been confirmed as free of disease. It is during Phase 3 that the UK would apply to the European Commission for derogations (as set out in the Directive) from treatments for meat and other products from vaccinated animals.

6.1.3 Bluetongue Vaccination

Overview

- Inactivated Bluetongue BTV-8 vaccine
- Individual farmers will be responsible for the costs of vaccination (taking into account the effect of any potential Commission co-funding)
- Distribution of the vaccine through private veterinary wholesale
- Voluntary approach, however, compulsory vaccination will be considered based on existing legal powers if an insufficient number of premises are willing to vaccinate.
- Vaccination must be recorded at herd level. Vaccinated animals intended for intra-community trade must have individual number recorded and must be vaccinated under veterinary supervision.
- Vaccination is only permitted in Protection Zones
- Vaccinated animals must not move out of a Protection Zone unless direct to slaughter or unless they meet a set of criteria

Objective of the delivery plan

191. The objective of the emergency vaccination plan is to reduce the prevalence of infection through mass vaccination of at least 80% of domestic animals of those species susceptible to Bluetongue. In the longer term, vaccination could lead to the eradication of Bluetongue BTV-8 from the UK by creating a sufficient pool of protective immunity in the susceptible animal populations of affected areas such that the virus no longer circulates.

The vaccine

192. Defra has ordered a supply of 22.5 million doses of inactivated Bluetongue serotype 8 (BTV-8) Bovilis vaccine. This vaccine will be available in 20ml (20 dose) and 50ml (50 dose) bottles.

193. In cattle, it is expected that the primary course of vaccination to consist of two doses given three to four weeks apart. Full efficacy of vaccine protection should be established a certain period after completion of the primary course of vaccination, depending on the results from ongoing trials. Protection is expected to be provided for up to 12 months after the primary course of vaccination. Thereafter, single, annual booster

vaccinations would be required, provided a risk assessment states that the vaccination programme should continue.

Voluntary approach/Take-up

194. The option of a compulsory programme has been fully considered, however, the case for compulsion through Government is weak. Despite control measures, the UK will continue to be at risk of introduction of disease through potential cross-Channel vector spread from Northern Europe and the legitimate trade in animals from other Member States; there is no scientific evidence to suggest an immediate prospect of eradication through vaccination. Moreover, a compulsory programme would involve increased regulatory burdens and a level of enforcement to check compliance. Based on some assumptions on the cost involved with this, coupled with other administration costs, makes it over 50% more expensive overall than voluntary vaccination. These considerations, alongside the absence of a public health interest, do not provide a strong basis for government regulation.

195. Provided that the cost of vaccination does not deter high rates of take-up it is deemed better to view vaccination against Bluetongue as an economic and welfare matter, in respect of which individual farmers are best placed to make decisions based on their own assessment of the economic and welfare benefits of vaccination. As individuals farmers will be responsible for the costs of vaccination, it is important to keep costs as low as possible to encourage maximum participation.

196. The advice of industry stakeholders is that take-up is likely to be high in a voluntary scheme, especially if a pro-active approach is taken to promoting vaccination. Therefore it seems that mass vaccination can best be achieved through a voluntary approach, coupled with sustained, intensive and widespread promotion of the benefits of vaccination by a partnership of government, veterinary organisations and industry peer pressure to ensure a high level of take-up of vaccination.

197. Depending on the priorities according to vaccine availability and the epidemiological situation, the programme will be particularly targeted at or limited to certain areas, delivered over a certain time period in order to follow a clear, structured and phased approach.

Targeted approach

198. Vaccination must be carried out in accordance with Council Directive 2000/75/EC which permits vaccination in a Protection Zone, subject to Commission approval of a vaccination plan. The Directive prohibits vaccination in a Surveillance Zone. If vaccination was carried out in a Surveillance Zone it must be declared a Protection Zone.

Who pays

199. The UK seeks any available funding from the Commission for this programme. The farming industry, which will benefit from vaccination, will be responsible for any costs that are remaining.

200. No compensation will be available for any losses due to vaccination. Compensation is only available for the compulsory slaughter of animals infected with Bluetongue but such slaughter would not normally be carried out.

Identification of vaccinated animals and premises

201. It was thought that requiring individual identification for all vaccinated animals would prove a significant disincentive to livestock keepers to vaccinate and would serve little purpose, except for animals which are being moved out of the Protection Zone for intra-community trade.

202. Vaccination must be recorded at a flock or herd level on each premises (i.e. in medicine books). However, when animals are vaccinated with a view to certification for intra-community trade their individual numbers must be accurately recorded and they must be vaccinated under veterinary supervision for the purposes of certification.

Administering the vaccine

203. The vaccines are expected to be issued with a prescription only medicine (POM-v) licence so private vets will be responsible for prescribing vaccine. Livestock keepers will be allowed to administer the vaccine to their animals, under the authority of private vets. However, if the animals are vaccinated in order to be moved out of the Protection Zone for the purposes of domestic or intra-community trade then a level of certification (and therefore, potentially, supervision) from private or official vets may be required.

Movement restrictions

204. Vaccinated animals will not be able to move out of a Protection Zone unless they are being moved direct to slaughter, or they can be certified as vaccinated and meet the criteria set out in Annex III of the Bluetongue Regulation, which includes:

- They were vaccinated more than 60 days before the date of movements (but no longer than the length of the protective immunity)
- They have been PCR tested with negative results 14 days after the onset of protective immunity
- They were previously vaccinated and have been re-vaccinated with the immunity period
- They were kept during a vector-free period more than 60 days before the date of vaccination and after the onset of protective immunity.

Exit Strategy

205. The Bluetongue vaccination delivery plan is valid until 31 December 2008 by which time the programme will aim to have limited the spread of the disease, and either be able to demonstrate a low prevalence of infection or (potentially) eradication of the disease. Ahead of this date, progress of the vaccination programme will be assessed to inform a decision on whether to submit a further plan to continue the programme.
206. Once a decision is taken to end the vaccination programme it will be necessary to conduct some form of sero-surveillance and vector monitoring for up to two years following the last confirmed case to demonstrate the absence of virus circulation.

6.1.4 Avian Influenza (AI) Vaccination ([draft guidelines only](#))

Overview

- Both voluntary and compulsory use of vaccine
- All flocks must be registered on Poultry Flock Register to be eligible for vaccination
- Government funds vaccine bank
- Where voluntary, owners must apply for a licence for to vaccinate their birds and purchase vaccine
- Vaccine must be administered by Private Veterinary Surgeon
- Domestic and international trade permitted depending on circumstances of outbreak
- When export permitted - Small flocks must individually identify vaccination birds at the owners expense. Larger flocks can be identified at flock level

207. Vaccination would not be used in advance of an AI outbreak, nor would it be used as an immediate disease control response. Early reporting, rapid action, biosecurity, culling and surveillance remain the most effective ways of protecting against and controlling an AI outbreak. This is because currently available vaccines have a number of limitations.

Voluntary use of vaccine

208. In the event of an outbreak of AI there may be a requirement to house or separate poultry and other captive birds from wild birds. Where this is impractical over a long term period for bird owners, they are able to apply for a licence to vaccinate their birds, which may then be allowed to be kept outdoors after a specified period provided they could demonstrate certain criteria is being met.

Compulsory use of the vaccine

209. There may be circumstances where Government compulsorily vaccinate poultry or other captive birds as part of the disease control response.

This would involve either serving notices on certain bird keepers requiring that they vaccinate their birds or alternatively declaring vaccination zones.

Targeting

210. The area in which vaccination is carried out – Avian Influenza Vaccination Zone (AIVZ) - would depend on the circumstances of the outbreak at the time. As would the group of birds that would be vaccinated/permitted to vaccinate.
211. The primary vaccination would consist of two inoculations given six to ten weeks apart. Full efficacy of vaccine protection would be established 14 days after the second inoculation and birds would therefore be required to be housed or otherwise separated from wild birds until this period had passed.
212. Protection is provided for up to 12 months after the second inoculation. Thereafter, boost vaccinations would be allowed if a risk assessment states that the vaccination programme should continue.

Identification of vaccinated birds

213. Premises with vaccinated birds must be able to be readily distinguished from premises with non-vaccinated birds. This requires an adequate registration system, which will allow the monitoring of the location and movement of vaccinated birds at both a local and national level.
214. Premises with more than 50 birds must be registered on the GB Poultry Register so their information would also be recorded on the DPDCS or BRP. Premises with less than 50 birds are not legally required to register but to be eligible for vaccination they must first register. Information on the birds that have been vaccinated and subsequent movements could be recorded on either of these systems, based on a template spreadsheet.
215. Depending on the circumstances of the outbreak, small flocks (less than 50) which are being exported may be required to be individually identified, with larger flocks (more than 50) identified only a flock level but with a high degree of control. Government would not specify the type of identification required. The keeper would be responsible for purchasing, obtaining and applying that form of identification.

Trade

216. The use of vaccination would not present any health risks for humans on consumption of the meat and or other products from vaccinated birds. Nevertheless, depending on the circumstances, vaccinated birds may not be eligible to be exported outside the UK.

Administering the vaccine

217. Once the bird keeper has been issued with a licence/notification to vaccinate their birds, the vaccination delivery procedure would be as follows:
218. The bird keeper must inform their local Animal Health Divisional Office of the name of their private vet who will vaccinate their birds, and the age and number of birds to be vaccinated
219. The private vet will receive written authorisation to permit them to source the necessary quantity of vaccine via their normal wholesaler supply chain
220. The owner and private vet must sign a declaration that the vaccination has taken place. This declaration must be sent to Animal Health and contain the following information: name, address and details of the private vet; name and address of the owner of the poultry; location where the birds were/are housed and vaccinated; number of birds of each species that are vaccinated, along with the number of vaccine doses used against the number ordered, and; confirmation that unused doses have been destroyed by an approved method.

Movement restrictions

221. Circumstances will dictate what movement controls are imposed in the relevant declaration or notice. However, such controls are likely to include a restriction on vaccinated birds could only being moved directly to a designated slaughterhouse, or, exceptionally, to other premises after meeting specified veterinary requirements. Once at the new premises, further pre-movement testing may be required before vaccinated birds can move again.

Use of vaccination outside of a disease emergency

222. Since December 2006, English zoos have been permitted to vaccinate their birds against AI because of their vital role in global conservation. English zoos wishing to vaccinate their birds can now apply for permission, subject to meeting the eligibility criteria.

6.2 Annex 2 - List of current Defra funded research and timetable for development and commercialisation of a cattle vaccine

6.2.1 Defra funded research

223. The Defra [website](#) provides details on all Defra funded research projects. Listed below are all the current and recently completed research projects for cattle vaccines and diagnostic tests.

Cattle Vaccines

SE3208	<p>Generation of vaccine candidates against <i>Mycobacterium bovis</i>.</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=8643&FromSearch=Y&Publisher=1&SearchText=SE3208&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3209	<p>Testing of vaccine candidates for bovine tuberculosis using a low dose aerosol challenge guinea pig model</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=8647&FromSearch=Y&Publisher=1&SearchText=SE3209&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3212	<p>Tests TB vaccines in cattle</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=8648&FromSearch=Y&Publisher=1&SearchText=SE3212&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3218	<p>Bovine TB vaccine advisor</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=12388&FromSearch=Y&Publisher=1&SearchText=SE3218&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3224	<p>Continuation of the development for vaccines against bovine TB in cattle</p> <p>http://www2.defra.gov.uk/research/project_data/More.asp?I=SE3224</p>
SE3227	<p>Evaluation of the protection efficacy of vaccines against bovine TB in a natural transmission setting.</p> <p>http://www2.defra.gov.uk/research/project_data/More.asp?I=SE3227</p>

Cattle Diagnostics

SE3203	<p>Blood tests to distinguish vaccinated from TB-infected cattle; IFN assay to improve diagnosis in reactors</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=7425&FromSearch=Y&Publisher=1&SearchText=SE3203&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3008	<p>Detection and enumeration of <i>Mycobacterium bovis</i> from clinical and environmental samples</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=8623&FromSearch=Y&Publisher=1&SearchText=SE3008&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3005	<p>Improved diagnostics for cattle</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=8626&FromSearch=Y&Publisher=1&SearchText=SE3005&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3018	<p>Cost-effectiveness of using the gamma interferon test in herds with multiple tuberculin reactors</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=9585&FromSearch=Y&Publisher=1&SearchText=SE3018&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3028	<p>The development of improved tests for the diagnosis of <i>Mycobacterium bovis</i> infection in cattle</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=10769&FromSearch=Y&Publisher=1&SearchText=SE3028&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3024	<p>Low doses TB infection in cattle; disease dynamics and diagnostic strategies</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=10765&FromSearch=Y&Publisher=1&SearchText=SE3024&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3217	<p>Kinetics of skin test response in bovine tuberculosis</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=9422&FromSearch=Y&Publisher=1&SearchText=SE3017&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3118	<p>Review and economic analysis of the use of PCR assays for <i>M. tuberculosis</i> complex detection and incorporation into routine bovine TB testing.</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=13621&FromSearch=Y&Publisher=1&SearchText=SE3118&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3222	<p>Development of improved diagnostic tests for the detection of bovine tuberculosis</p> <p>http://www2.defra.gov.uk/research/project_data/More.asp?l=SE3222</p>
SE3221	<p>Volatile organic compound analysis for the rapid diagnosis of disease; TB in</p>

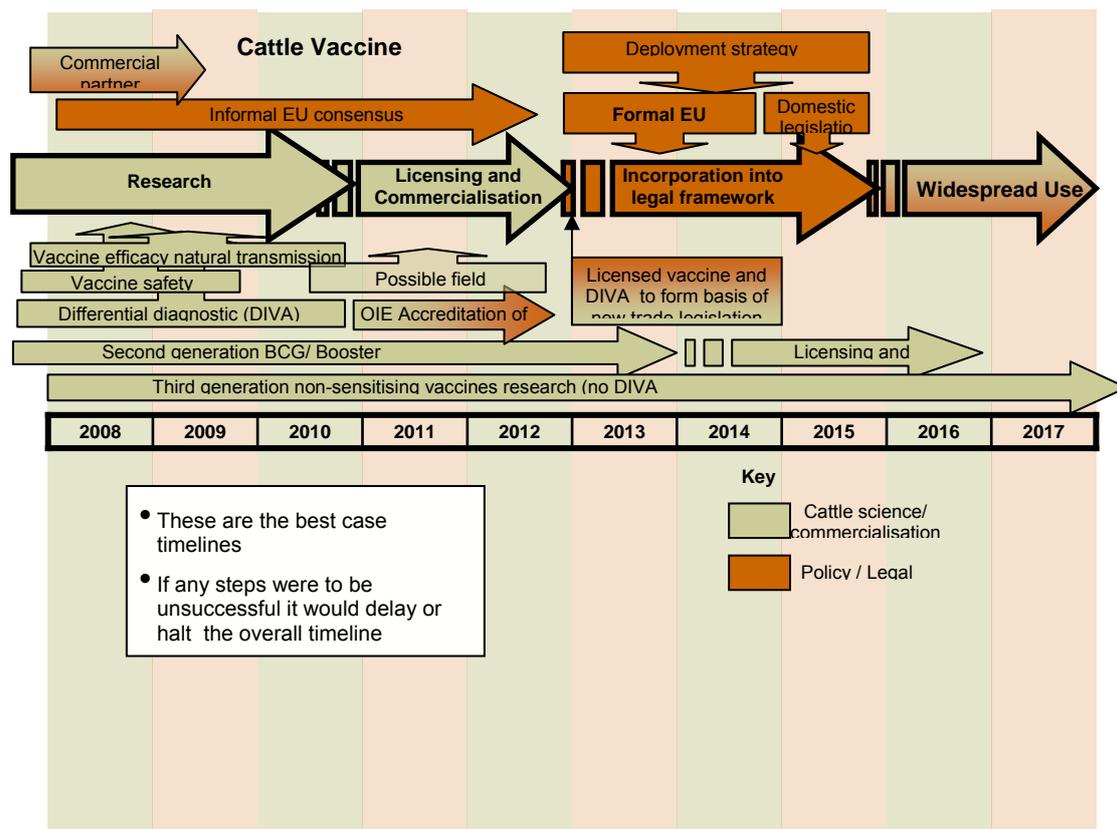
	<p>badgers and cattle as proof of principle</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=13620&FromSearch=Y&Publisher=1&SearchText=SE3221&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>
SE3040	<p>A preliminary analysis of existing data to provide evidence of a genetic basis for resistance of cattle to infection with <i>M. bovis</i> and for reactivity to currently used immunological diagnostic tests.</p> <p>http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=15180&FromSearch=Y&Publisher=1&SearchText=SE3040&SortString=ProjectCode&SortOrder=Asc&Paging=10#Description</p>

6.3 Annex 3 - Efficacy of a BCG cattle vaccine

224. A BCG vaccine is likely to confer full protection against *M. bovis* infection to 50% of vaccinated animals. For both the epidemiological model and economic assessment it is assumed that the protection conferred will last a lifetime. Of the remaining 50% that remain susceptible to infection, it is estimated that over half will be partially protected and have a much reduced capability of transmitting *M. bovis* should they become infected. The benefits of vaccination are likely to last for at least 12 months. The definition of fully protected, partially protected and unprotected are given below.
225. **Fully protected:** Vaccination has induced sterilizing immunity (for up to 12 months) to subsequent exposure to *M. bovis*, i.e. by applying best microbiological practice and post-mortem procedures, the individual animal presents without visible pathology (NVL) and is culture-negative. They may or may not react to the standard SICCT (depending on the infective dose and time between bacillary clearance and test, as well as time between BCG vaccination and infection and test), but will be test-negative when applying DIVA assays.
226. **Partially protected:** Vaccination has induced protective immunity to such a degree that disease progression, after infection, will be delayed or arrested yet disease will be apparent/detectable by the presence of visible pathology (VL) and/or histopathology and/or bacilli detectable by culture. These animals are less likely to transmit disease and therefore contribute to herd immunity and reduce the number of reactors occurring in an outbreak. It is likely that these animals will, over time, test positive to DIVA and standard SICCT test.
227. **Unprotected:** Vaccination has not induced protective immunity after infection with virulent pathogen, individuals will be undistinguishable from unvaccinated controls in respect to visible pathology, histopathology, or bacillary load. They are expected to test positive in DIVA and standard SICCT tests to the same degree as unvaccinated individuals.

6.4 Annex 4 - Timetable for development and commercialisation of a cattle vaccine

228. The diagram below is a high level timeline for the development and commercialisation of a cattle vaccine. The dates provided are the earliest estimate of when a cattle vaccine could be licensed and deployed.



6.5 Annex 5 - Legislative framework influencing vaccination

6.5.1 Introduction

229. Bovine Tuberculosis (bTB) is a highly regulated disease and the introduction of new control methods such as vaccination and the use of novel diagnostic tests will need to be fitted within an existing legal framework.

230. The legal framework comprises both EU and Domestic legislation on disease control and origins of animal products intended for human consumption.

231. This paper sets out the legal framework which we need to work within and possibly amend to introduce cattle vaccination.

6.5.2 Part one – Prohibition of the use of TB vaccine

Council Directive 78/52/EEC of 13 December 1977 establishing the Community criteria for national plans for the accelerated eradication of brucellosis, tuberculosis and enzootic leucosis in cattle.

Requirements of the Directive

232. Council Directive 77/391 as amended by Council Directive 82/400 requires all Member States to have a TB eradication plan which complies with the criteria set out in Council Directive 78/52.

What are the barriers?

233. Article 13 of Directive 78/52 requires member states to ensure “anti-tuberculosis vaccination” is prohibited under their eradication plans. It would seem that the phrase “anti-tuberculosis vaccination” covers both vaccination of cattle and badgers although there is an argument that given the preamble to that Directive talks only of eradication of tuberculosis in cattle, this should be given a more narrow interpretation and treated as a reference to vaccination of cattle only.

234. To introduce vaccination of cattle or badgers as either a statutory requirement or voluntary option, on a large or small scale, it needs to be done in accordance with the requirements of an eradication plan.

What do we need to do?

235. In order to introduce cattle vaccination it is certainly necessary to amend this Directive. It is also advisable to seek amendment in order to pursue badger vaccination as the position in EU law is far from clear. The amendment could be to simply remove the need for prohibition under eradication plans or if pursued in tandem with an amendment to Directive

64/432 could be a more complex amendment covering the promotion of vaccination under national eradication plans. A decision to adopt a simple amendment to allow vaccination would mean this could take place ahead of negotiations on the trade Directive and would give us a broader scope to work with when developing a vaccination policy.

Scope for change

236. There is evidence that would suggest the Commission would be open to persuasion in the use of vaccines particularly for badgers:

- a. The first is in a published European Commission Working Document on Eradication of Bovine Tuberculosis in the EU accepted by the Bovine tuberculosis subgroup of the Task Force on monitoring animal disease eradication (2006). This report makes recommendations, following workshops held during the 4th International Conference, that they suggest should be kept in mind for the design of future strategies. One of these recommendations is “The development of a vaccine for wildlife should be a priority for research”.
- b. The Commission has also recently agreed funding under Framework Agreement 7 for diagnostic and cattle and badger vaccine research.
- c. The recent EU Animal Health Strategy for the European Union (2007-2013) mentions the EU moving to a more flexible approach to vaccination. This is in the context of controlling exotic disease outbreaks but again demonstrates the adapting views on vaccination of the Commission.

Conclusion/Next Steps

237. Amending Directive 78/52 is a priority in moving towards introducing either cattle or badger vaccination. There isn't an in-built review provided within the provisions of the Directive so we need to persuade the Commission to bring forward a proposal. In negotiating with the Commission our position is strengthened if other Member States are also willing to sign up to an amendment to the Directive. We need to identify which Member States might be interested or might benefit from the introduction of a cattle and/or badger vaccination policy. For example, those that have a similar TB problem to ours or that have signed up to the research proposal “Development of rational strategies for the eradication of bovine tuberculosis” looking into diagnostics and cattle and badger vaccine research.

6.5.3 Part two – Restriction on Trade

Live Animals

Council Directive 64/432/EEC on animal health problems affecting intra-community trade in bovine animals and swine.

Requirements of the Directive

238. This Directive aims to facilitate intra-community trade by ensuring that only animals with proven disease-free status can be exported to other Member States. Appendix A of the Directive sets out the criteria for the TB testing frequency that must be met to trade live cattle within Member States. Cattle must come from an officially tuberculosis free (OTF) herd. The Directive treats the skin test as determinative of whether an animal is eligible for intra-community trade and prohibits the export of any animal coming from the same herd as a reactor until that herd is cleared by two consecutive skin tests.

What are the barriers?

239. The current frontrunner for a cattle vaccine is BCG. A vaccine based on BCG may make cattle react to the skin test as if they were infected and in turn the herd would lose its OTF status. Even if there was a test available to distinguish between infected and vaccinated animals (DIVA) which could be used alongside the skin test, the Directive still requires slaughter of any skin reactor animal from traded herds and prohibits the export of any animal coming from the same herd as that reactor until that herd is cleared by two consecutive skin tests.

What do we need to do

240. There are two options that could be considered:

- a. Do not amend the Directive and forgo trade, based on the use of a BCG vaccine. If a herd is not going to be traded it need not have OTF status and therefore in theory need not be tested in accordance with Appendix A of the Directive. However, the purpose of this Directive is to facilitate trade and introducing a policy where OTF status could not be achieved is probably going against the spirit of what the Commission intended. We risk infraction proceedings or a claim in the domestic courts in reliance on article 29 of the EC Treaty (quantitative restrictions on exports).
- b. Amend the Directive to facilitate trade. This would provide for vaccination by Member States and permit the use of a different test to be used alongside the skin test to determine whether a herd has OTF status.

Conclusion/Next steps

241. If this Directive was amended it would a) allow cattle to be vaccinated without forgoing trade and b) if an oral bait badger vaccine was introduced, ensure cattle that consumed the badger vaccine accidentally could retain their OTF status with the use of a DIVA test alongside the skin test.

242. Amendments to this Directive would need to follow Directive 78/52 (Eradication Plan) being amended to permit vaccination. A new diagnostic test would have to be OIE accredited before it could be

included in Directive 62/432 as an adjunct to the skin test to determine OTF status of a herd.

243. As with the above Directive, 64/432 does not have an in-built review provided within the provisions so we need to persuade the Commission to bring forward a proposal.

Animal Health Act 1981 and The Tuberculosis (England) Order 2007
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Requirements

244. The TB Order is made under the Animal Health Act and provides domestic legislation for the control of TB in England. Currently the TB Order only gives power to the SoS to permit vaccination, not require it. Article 13 (1) states that “No person may vaccinate a bovine animal against tuberculosis without the written consent of the Secretary of State.”

What are the barriers

245. The powers under the Animal Health Act 1981 to “cause” vaccination are quite limited. Section 16 provides that “Ministers may cause to be treated with serum or vaccine...any animal or bird a) which has been in contact with a diseased animal or bird, or b) which appears to have been exposed to the infection of disease or c) which is an infected place”.

246. The above creates barriers for a vaccination policy as infected places can only be declared in certain prescribed circumstances as set out in an order and such declarations does not seem to be appropriate for a disease that is endemic in this country. Also, it can't be argued that all the animals that are to be subject to compulsory vaccination have been in contact with or exposed to TB.

247. Therefore, without the relevant requirements relating to vaccination and testing being effected at EU level (it is the trade Directive that provides the appropriate vehicle for doing so), it does not appear that we have the appropriate domestic powers to make TB vaccination compulsory.

What do we need to do

248. Other vaccination regimes, such as foot and mouth and avian influenza, as prescribed in EU legislation, have been implemented using section 2(2) of the European Communities Act 1972, on the basis that neither section 16 nor indeed the wider power in section 1 of the Animal Health Act provides an adequate legal base.

249. Once EU legislation has been amended to allow for vaccination and the trade of vaccinated animals, domestic legislation can be implemented under the European Communities Act 1972. Domestic legislation must be implemented in line with the common commencement dates, either 6 April or 1 October.

Meat related issues

Regulation (EC) No 854/2004 (as amended) of the European Parliament and of the Council laying down specific rules for the organisation of official controls on products of animal origin intended for human consumption

Requirements of the Regulation

250. Requires animals that have reacted positively or inconclusively to tuberculin to be slaughtered separately from other animals and precautions taken to avoid contamination. However, a positive reaction to the skin test does not prevent meat going for human consumption (unless localised TB lesions are revealed in a number of organs) as the Regulation provides that when tuberculosis lesion has been found in the lymph nodes of only one organ or part of the carcass, only the affected organ or part of the carcass and the associated lymph nodes need be declared unfit for human consumption.

What are the possible barriers

251. Vaccinated animals may react positively to tuberculin and therefore be subjected to the above slaughter conditions.

252. If a BCG based vaccine was introduced it wouldn't have an effect on the trade of bovine meat. Although the vaccine would not be 100% effective, it is expected that a majority of the vaccinated reactor animals will show no or little gross TB pathology at post-mortem examination, with their carcasses being judged as suitable for human consumption. The vaccine has to be authorised by the Veterinary Medicine Directorate (VMD).

253. One issue to consider is that there may be a withdrawal period for meat and milk after the vaccination. There may be a period following vaccination of cattle when meat and milk produce can not be consumed. VMD should advise on this point based on whether BCG is excreted and for how long.

254. If the vaccine was to be a live attenuated form then it may persist for a period and be found in meat and milk. This may have implications on public perception and/or safety and impact on the acceptability of meat or milk from recently vaccinated animals entering the food chain. This is despite a number of vaccines being in regular use for other endemic diseases of cattle.

255. A factor to consider when introducing vaccination of cattle is that even if it is introduced within existing food law legislation, the consumer acceptability of food products from vaccinated animals may be a barrier. Although the use of authorised vaccines would pass all authorisation's criteria.

Conclusion/Next steps

256. It is possible to work within this Regulation. The reference to animals testing positive to tuberculin would not need to be amended as if animals

tested positive due to being vaccinated then it wouldn't affect the trade of that animal. At post-mortem stage it would be identified whether there were TB lesions and the meat could still go for human consumption.

Milk

Regulation (EC) No 853/2004 of the European Parliament and of the Council laying down specific hygiene rules for food of animal origin

Requirements of the Directive

257. This Regulation stipulates that raw milk and colostrum must come from cows belonging to a herd which is officially tuberculosis free. It takes its definition of OTF from the trade Directive 64/432. However, in a non-OTF herd, in the case of cows that do not show a positive reaction to the tuberculin test, milk may be used from these animals after having undergone a heat treatment. Milk and colostrum from cows that have reacted positively to the tuberculin test can not be used for human consumption under any circumstances and must be destroyed by the farmer.

What are the barriers

258. If we were to introduce a BCG based vaccine this could result in prevention of milk being used for human consumption due to a reaction to tuberculin because of vaccination rather than the animal being infected.

Conclusion/Next steps

259. A DIVA test would need to be recognised by the Commission and a negative DIVA test alongside the negative skin test would need to define OTF status in the trade Directive 64/432 as outline above.

6.6 Annex 6 - Accreditation of the DIVA test

260. Successful OIE recognition and registration will depend on supplying quality controlled validation data to demonstrate the fitness of the test to fulfil a defined task.
261. [The OIE Standard Operation Procedure for OIE Validation and Certification of Diagnostic Assays](#) defines 'fit for purpose' as "Fit for purpose' means that the test has to be validated to such a level to show that the test's results can be interpreted to have a defined meaning in terms of diagnosis or another biological property being examined. There must be proof for the purpose of the test in a diagnostic/detection setting. Enough information has to be given to show that this is a valid statement. There is a need to define the purpose of the test and demonstrate that sufficient data have been obtained to ascribe some confidence to its use, in statistical terms, to answer a defined question."
262. The validation data is divided in four sections, which can be seen below. This validation must be completed before an application is submitted as the validation data will form the details of the application.

Stage 1 - validation

Calibration

263. Some calibration of a test against standards (in-house at least). Inclusion of some reference standards (in-house at least)

Repeatability data

264. A minimum of three in-house samples representing activity within linear range of assay. Within run tests (quadruplicates preferred). Between run tests (a minimum of 20 runs total, two or more operators, preferably on separate days, where runs are independent). Between serial repeatability, ideally three production batches. Data should include mean, SD, upper and lower control (UCL and LCL) on unprocessed and processed data.

Analytical specificity data

265. Cross-reactivity, near-neighbour data. Document cross-reactivity by comparing samples from animals infected with organisms with similar clinical presentations and organisms that are genetically closely related. Type/group specificity data. Documentation affirming serotype or group specificity.

Analytical sensitivity data

266. Specify standard of comparison (i.e. currently accepted test method). Comparison may include: end-point titrations; earliest time of detection post-exposure, duration of detection post-exposure (if applicable).

Stage 2 - validation

Negative reference animals/samples

267. (Note: Negative refers to lack of exposure to, or infection with, the agent in question).

268. Complete description: age, sex, breed, etc. Immunological status. Relatedness to intended target population. Selection criteria including historical, epidemiological and/or clinical data. Pathognomonic and/or surrogate tests used to define status of animals or prevalence within population. Sampling plan and procedures.

Positive reference animals

269. (Note: Positive refers to known exposure to, or infection with, the agent in question).

270. Complete description: age, sex, breed, etc. Immunological status. Relatedness to intended target population. Selection criteria including historical, epidemiological and/or clinical data. Pathognomonic and/or surrogate tests used to define status of animals or prevalence within population. Sampling plan and procedures.

Experimental animals

271. Complete description: age, sex, breed, etc. Immunological status. Relatedness to intended target population. Exposure. Inoculum, source, dose, etc. Type of exposure – inoculation, aerosol, contact, etc. Sampling plan and procedures.

Threshold determination

272. Complete description of method used: empirical, ROC, mean \pm SD, etc. Descriptive statistics, frequency distribution diagrams, etc.

Performance estimates

273. Irrespective of the method chosen, the standard method(s) of comparison should be run in parallel on all samples, i.e. the test methods in current use.

Diagnostic sensitivity and specificity estimates – with defined reference animals

274. Conventional method using reference animals. Assuming a minimum sensitivity and specificity of 75% with an allowable error of \pm 5% in the estimate at a level of confidence of 95%, the number of reference animals required is 300 for each population. Individual animals must be selected from negative and positive reference populations. Include 2x2

table, calculations for diagnostic sensitivity and specificity including error and confidence. Include same calculations for other tests if being compared with the test in question.

Diagnostic sensitivity and specificity estimates – without defined reference animals

275. Complete description of model used. Bayesian inference, latent class analysis, etc. Describe rationale, priors, supporting data. Population selection criteria, including prevalence estimates. Other test methods evaluated should also include the standard method of comparison. Using best available priors, choose test populations with appropriate prevalence and select animals in sufficient numbers to generate estimates of sensitivity and specificity with an allowable error of $\pm 5\%$ at a level of confidence of 95%.

Agreement between tests

276. Complete description of test methods being compared. Presumptive vs. confirmatory tests. Relatedness of analytes.

277. Potential biases. Complete description of samples tested. Source of samples may include experimental animals sequentially sampled over time. May also include animals or herds defined by reactivity in confirmatory tests or multiple presumptive tests and sampled over a period of time. Describe measures of agreement and explanations for results not in agreement.

Stage 3 - validation

Laboratory identification

278. Selection criteria for candidate laboratories. Location, i.e. country. Status, i.e. regional, national, provincial/state. Level of expertise, familiarity with technology. Accreditation status. Number of laboratories included. Minimum of three laboratories, should also include OIE Reference Laboratory, if possible

Evaluation panel

279. Description of test panel. Selection criteria, number of samples (minimum of 20). Sample volume, allowable number of repeats. Panel composition, i.e. number of replicates, range of analyte concentrations/reactivities. Sample processing requirements, i.e. extractions, spiking, serial dilutions, preservatives, sterilisation. Coding of unknown (blind) samples. Frequency of testing.

Reproducibility

280. Description of type of data/ interpretation. Qualitative (categorical). Quantitative or semi-quantitative data. Single dilution vs. titration. Description of type of analysis. Pre-determined limits, consensus, Youden plots. Descriptive statistics. Include mean, SD, range of results. Should include controls, as well as, blind samples. Number and proportion of accepted/rejected runs should be included.

Stage 4 -validation

Laboratories

281. List laboratories where this test method is in current use. Location, i.e. Country. Status, i.e. Regional, national, provincial/state. Accreditation status.

Test applications

282. For each laboratory. Indicate purpose of test. Integration with other tests. Status test, i.e. official test, supplementary, etc. Throughput, i.e. daily, monthly, annual. Turn-around-times

International reference standards

283. List type and availability of international reference reagents. Source. Negative, weak/strong positive reference reagents. Other key biologicals, e.g. antigens, antibodies, etc.

Inter-laboratory testing programmes

284. Describe programmes involving inter-laboratory comparisons using this test method. National, international. Describe eligibility and number of laboratories participating

International recognition

285. List internationally recognised reference laboratory responsible for this test method and/or biologicals. Listed international standards containing this test method. Listed international programmes employing this test method.

286. Following submission of the application, the form will be checked and processed and once it is considered valid the applicant will be informed of the names of the chairperson and reviewer(s) for the diagnostic test assessment, a procedure number and a timetable for assessment.

287. The total duration of the procedure will be 135 days – with stoppages in time if questions need to be directed to the applicant. An outline of the procedure is below:

- The reviewers provide an initial report to the CRP.
- The CRP prepare a consolidated report and liaise with the other reviewers.
- An assessment report is sent by the CRP to the OIE Secretariat for Validation, Certification and Registry of Diagnostic Assays (OIESVCRDA).
- If any questions arise the OIESVCRDA will send them to the applicant
- The CRP in consultation with the reviewer(s) provide a final assessment report with a clear proposition.
- At the next meeting of the BSC the CRP, if necessary, will present the assessment report and conclusions.

- If successful, the BSC will then propose to the OIE Director General to place the diagnostic test on the register.
- The OIE Director General will take the final decision.
- The OIESVCRDA will notify the applicant within 15 days of a successful application and the information will be published on the OIE web site stating that the test has been approved by the OIE Director General and is proposed for inclusion in the register.
- The final inclusion in the OIE register will be discussed and voted on by the OIE International Committee (comprising the Delegates of the Members Countries) during the General Session through the presentation of a Resolution drafted by the BSC containing a list of recommended validated and certified assays to be registered by the OIE.
- The final inclusion is effective within 7 days of the vote of the OIE International Committee.

288. There is an appeals procedure for cases where the BSC recommended that the test should not be included in the register.

289. Once a diagnostic test is placed on the register, any changes to the test must be declared and justified in advance before approval for implementation.

290. The OIE Central Bureau, through the OIESVCRDA, will require an annual declaration from the applicant stating that the test remains valid and should be retained on the registry. Every 5 years, the OIE will insure that the diagnostic test remains within the current state of the art.

291. A full [timetable](#) is available.

6.7 Annex 7 - Veterinary Advice on the Strategic Vaccination of cattle against infection with Mycobacterium Bovis

6.7.1 Scope

292. This guidance only considers strategies for anti-TB vaccination of cattle.

6.7.2 Question addressed in this document

293. Strategic vaccination of 'high risk' cattle herds (as opposed to mass vaccination of the national cattle herd) has been identified as a possible long-term policy option. This paper attempts to answer the following question:

'In what way could the incidence of TB in cattle be reduced by the strategic use of vaccination targeted to certain cattle herds?'
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6.7.3 Background

294. Vaccination programmes have been successfully used in controlling and eradicating many infectious diseases of farm and companion animals. In farm animals, vaccination is often used in an attempt to reduce the prevalence of endemic diseases to levels such that selective slaughter or depopulation can then be used to eradicate the disease (Martin et al., 1987). This was, for instance, the approach that led to the successful eradication of bovine brucellosis in Great Britain in the late 1980s.

295. The principle behind vaccination is that a minimum density of susceptible animals is required for a contagious disease to propagate within a population. Provided that the basic reproduction ratio (R_0 , the average number of secondary cases caused by one infectious individual during its entire infectious period) can be kept below 1, the epidemic will decline and die off (Thrusfield, 1995). Both vaccination of susceptible animals and culling of infected animals can bring about this reduction in R_0 .

296. Strategic (or targeted) vaccination of at-risk animals or herds is adopted when mass immunisation of the entire population is not considered a practical or cost-effective option. Its aim is to prevent amplification of an infectious disease within (and dissemination from) the vaccinated herds. The identification of the appropriate group(s) of animals to be targeted by such vaccination programme may be difficult when the disease is not confined to clearly defined areas, specific age groups or herd types. This is the situation with bovine TB in GB, where, although transmission rates are considered low (R_0 only marginally greater than 1 [ISG 2007]), several potential transmission routes exist and their relative importance is

not quantified. There is also an incomplete understanding of the range of risk factors for TB and how they contribute to the epidemiological picture.

297. Bovine tuberculosis (TB) is an infectious and contagious, mainly respiratory disease of cattle caused by the bacterium *Mycobacterium bovis* (*M. bovis*). Cattle are the natural host to this bacterium, becoming infected when directly exposed to infectious cattle (and their excretions) or to other infected, infectious animals (and their excretions). In parts of the British Isles the Eurasian badger (*Meles meles*) represents a significant, but as yet unquantifiable, reservoir of *M. bovis* for cattle which is geographically static and not subject to any statutory TB controls. This is in contrast to the commercially traded cattle host, which has been the subject of more or less intensive compulsory test-and-slaughter campaigns since 1950.
298. The infection of a bovine animal with *M. bovis* is usually recognised by the immune response triggered by the host's immune system, which is primarily a cell-mediated one. This suggests that, in theory, it might be possible to develop a vaccine for cattle that could induce some degree of protection against infection with this pathogen, as has happened with *M. bovis* BCG in humans. In reality this goal has proven elusive for decades. Key difficulties relate to the identification of the mycobacterial antigens that elicit long-lasting protective immune responses against infection with *M. bovis*, definition of immunological surrogates of successful vaccination and the fact that immunised animals develop a delayed hypersensitivity response to tuberculin, thus compromising the screening of cattle for TB (reviewed by Newel and Hewinson, 1995; Vordermeier et al., 2006; Vordermeier and Hewinson, 2006).

6.7.4 Working assumptions

299. There are considerable uncertainties surrounding the development of a successful cattle vaccine against infection with *M. bovis* and how it might work in practice. Therefore, in order to provide some veterinary guidance on how to best target vaccination to reduce the incidence of TB in cattle, a number of broad assumptions must be made from the outset:
- a. An efficacious, affordable anti-TB vaccine will, in due course, be developed and licensed for use in cattle in Great Britain;
 - b. Deployment of such vaccine will be acceptable under EU and domestic animal health legislation;
 - c. The vaccine will be unlikely to have 100% efficacy. Even so, deployment of the vaccine will be a potentially worthwhile strategy in that:
 - i. it will be expected to confer a reasonable level of protection against persistent infection with

- Mycobacterium bovis in a majority of naïve (uninfected) cattle;
- ii. and/or
 - iii. lead to a substantial (approx. 50-60%) reduction in the TB pathology scores and mycobacterial loads (and shedding) of cattle challenged with M. bovis after vaccination, compared to unvaccinated cattle (Hewinson and Vordermeier [pers. comm.]; Milián Suazo et al., 2003).
- d. As depicted in the figure below, these two effects could eventually lead to a reduced rate of bTB transmission:
 - i. between cattle herds,
 - ii. within cattle herds,
 - iii. between cattle and naïve wildlife,
 - iv. from infected wildlife to cattle,
 - v. and, importantly, reduce the risk of transmission from cattle to humans.
 - e. The vaccine will have no significant undesirable side effects if administered to infected bovines. In fact, in such situations it may be able to arrest the progression to an infectious stage of cattle with early M. bovis infection.
 - f. A naïve bovine will be able to develop immunity against natural M. bovis challenge from four weeks after vaccination.
 - g. The vaccine will have limited effect on the recirculation of M. bovis infection within the wildlife maintenance host (badger population);
 - h. Vaccination will be used in conjunction with the existing test-and-slaughter bovine TB control regime, although this may be adapted (e.g. testing intervals could be gradually relaxed) if the vaccine turns out to have the desired beneficial effect on TB incidence in cattle;
 - i. A differential in vitro diagnostic assay capable of distinguishing between vaccinated, uninfected cattle and naturally infected animals ('DIVA' test) may or may not be available and may or may not be eventually approved for use in the EU. In any case, it is almost certain that an anti-TB vaccine for cattle will be based on BCG and thus interfere with the intradermal tuberculin test (i.e. the primary screening and pre-export certification test for TB in cattle) at least for some time after immunisation. This makes it highly likely that vaccinated herds will have to be treated differently from non-vaccinated herds for the purposes of OTF certification and trade (zoning, compartmentalisation or some sort of movement restriction);

longer the interval since the last clear tuberculin test, the less meaningful the OTF status attached to a herd is.

6.7.6 Veterinary advice

302. The aim of cattle vaccination would be to create a large pool of cattle herds that are free from *M. bovis* infection and able to withstand future challenge via introductions of infectious cattle or contact with infectious wildlife or their excretions.
303. However, in the absence of a badger cull (or badger vaccine) that could eliminate/reduce the spillover of infection from wildlife in large areas of the country, and the lack of husbandry measures of practical effectiveness in preventing contact between cattle and wildlife, cattle vaccination may have to be maintained for the foreseeable future. I.e. it is at present difficult to envisage an 'exit strategy' for vaccination once it has been deployed.
304. Because a vaccine is not expected to effect a cure in cattle that have already been infected, its use should be concentrated on officially TB-free (OTF) herds that are at the highest risk of contracting the infection.
305. Such herds are likely to be found in areas of historically high TB herd incidence as well as any developing new clusters of TB ('hotspots').
306. Large tracts of the country are only sporadically affected by the disease. However, the epidemiology of bovine TB in GB is not static and the location of new TB hotspots is difficult to predict. The potential for the development of new clusters of endemic infection in currently 'clean' areas remains, despite the implementation of pre-movement tuberculin testing and immediate restrictions on herds with overdue tests. Conversely, not all herds in areas of traditionally high TB incidence have the same risk of suffering a TB breakdown.
307. The identification of the 'highest risk' herds to be targeted for vaccination should be based on variables that are known to increase a herd's risk of acquiring *M. bovis* infection (i.e. herd-level risk factors), namely:
 308. Herd's tuberculin testing history (including number and confirmation status of reactors and slaughterhouse cases);
 309. Cattle purchase history (frequency and numbers of cattle purchased from past reactor herds and herds in areas of high TB incidence);
 310. The area, "local" or "radial" risk of bovine TB, as defined by the incidence in cattle herds in the locality and the infection status of the local wildlife (if known). The frequency of routine tuberculin testing (parish testing interval – PTI), provides a proxy for the likelihood of *M. bovis* infection being present in cattle and wildlife in the area;

311. Herd size (the larger the herd, the more likely to suffer a TB breakdown, due to greater opportunities for exposure to infectious local wildlife, contiguous cattle herds or more cattle purchases).
312. Despite all the above, a cattle vaccine might have a role to play in non-OTF (TB breakdown) herds if suitable routes could be established for marketing their meat and milk. This would not necessarily reduce the herd incidence of TB, but would help manage confirmed, severe TB breakdowns by reducing the risk of intra-herd spread thus bringing down the animal incidence. Within-herd TB prevalence is usually low. So, vaccinating an infected herd would protect the high proportion of cattle that are uninfected. A DIVA test would then be used to detect the truly infected animals within a vaccinated herd. In the absence of such test, the vaccinated infected herds would be kept under some form of restriction until all the animals in the initially vaccinated cohort would have been culled. After this time vaccination would be maintained to ensure that the herd remains free from infection and non-susceptible to future challenge by the organism (reduced recrudescence rate).

In summary, veterinary advice is that, for maximal impact, a hypothetical anti-TB vaccine for cattle should be targeted to all OTF herds situated in annual TB testing areas (or with linked holdings or detached grazing in such areas) as soon as possible after a tuberculin herd test with negative results and no later than 2 months after the test.

Any OTF herds outside annual testing areas that are considered at high risk of suffering a TB breakdown by virtue of their TB history, size or cattle purchase practices, should also receive the vaccination.

Additionally, the vaccine could be deployed in infected herds with a high incidence of reactors or persistent infection (commonly known as the 'problem herds').

6.7.7 References

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6.8 Annex 8 - Glossary of Terms and Abbreviations

AHDO	Animal Health Divisional Office
Antigen	Usually a protein, capable of provoking an immune reaction
Bacterium	A single celled organism; many types are present in the environment and most are essential to support other forms of life; some species can cause disease, in which circumstance these are commonly called “germs”.
BCMS	British Cattle Movement Service: organisation established to manage the Cattle Tracing System in Great Britain.
BCG	Bacille Calmette Guerin, a modified strain of <i>M. bovis</i> used for human vaccination to protect against <i>M. tuberculosis</i>
BCVA	British Cattle Veterinary Association
Biological assay	Type of scientific experiment typically conducted to measure the effects of a substance on a living organism
Bovine tuberculosis (bTB)	A disease caused by the mycobacterium <i>M. bovis</i>
Breakdown (or bTB incident)	When or more reactors are revealed by the tuberculin test, or when disease is suspected in line cattle showing clinical disease or in carcasses with lesions at post-mortem examination
BVA	British Veterinary Association
Cattle herd	A group of cattle that live a collective life together
CFU	Colony forming units i.e. number of bacteria
Cow	A female that has had one or more calves
CTS	Cattle tracing system
Culture	The generation of living tissue cells
Defra	Department for Environment, Food and Rural Affairs
Diagnosis	Identification of an illness or disease by clinical signs or response to a surveillance or laboratory test(s)
DIVA	Differentiate between Infected and Vaccinated Animals
Efficacy	used to describe how good a vaccine is at preventing disease.
ELISA test	A rapid (colour based) biochemical test to detect

	antibodies or antigens
Endemic disease	A disease present in an animal population on a continuous basis
Gamma interferon <i>g-IFN (IFNγ)</i>	A product of white blood cells generated during an immune response
Herd breakdown	When cattle are found to be infected with bovine TB (i.e. when or more “reactors” are found in a herd)
Immunity	Protection against a disease. There are two types of immunity, passive and active. Immunity is indicated by the presence of antibodies in the blood and can usually be determined with a laboratory test.
Incidence	The rate at which new cases of infection arise in a population
Infectivity	The ability of a pathogen to establish an infection
Intramuscularly	The injection of a substance directly into a muscle
Krebs	The Independent Scientific Review Group, chaired by Professor John R. Krebs FRS, that report on bovine tuberculosis in cattle (often referred to as ‘Krebs’, and their report as the ‘Krebs report’), 1997
<i>M. bovis</i>	<i>Mycobacterium bovis</i> – bacteria which causes bovine TB
Mycobacterium	A family of related bacteria
NBA	National Beef Association
NFU	National Farmers Union
OIE	The World Organisation for Animal Health
OTF	Officially tuberculosis free
Prevalence	The proportion of a population infected
Reactor	An animal which gives a positive result (i.e. reacts) to the tuberculin test
Recombinant vaccine	Created by utilising bacteria or yeast to produce large quantities of a single viral or bacterial protein which is then purified
Sensitising vaccine	Vaccine that will give a positive reaction to the TB skin test
Sensitivity (of a diagnostic test)	% of truly infected animals correctly identified
SICTT	Single Intradermal Comparative Tuberculin Test
Specificity	Proportion of uninfected animals correctly identified
Strain	Isolate of a bacterial species which is differentiated from other isolates of the same species by particular

	characteristics
Subcutaneously	Injection into the subcutis
TB	Tuberculosis
Transmission	The passing of disease from animal to animal or to humans
Tuberculin	A protein extract used to diagnose TB in a skin test
Tuberculin skin test	The SICCT test which is used throughout the world to screen cattle, other animals and people for TB, and is the internationally accepted standard for detection of infection with <i>Mycobacterium bovis</i> (<i>M. bovis</i>)
Waning Immunity	The loss of protective antibodies over time
Vaccine	That used to prevent disease by stimulation of an immune response to the causative agent