Inquiry examining the vaccination of badgers and cattle in relation to Bovine TB

A response from the Society of Biology to the
Environment, Food and Rural Affairs Committee
7 January 2013

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Summary of Recommendations

1. The UK must learn from past and current outbreaks in cattle (such as foot and mouth disease and bluetongue) and prioritise the development of allowable vaccination as part of the tool box of control measures for bovine tuberculosis, without contravening EU regulations. Badger vaccination will be useful for isolating infected areas and cattle vaccination will be important in safeguarding future herds. Government must establish a realistic sense of when appropriate cattle vaccinations and DIVA tests could be made available, in order to direct research efforts and funding, and establish a long term bTB eradication plan.
2. We recommend that badger and cattle vaccinations are ultimately employed to combat bTB, given the following:
    a. Research is needed to ascertain a full understanding of the strength of transmission at the inter- and intra-specific level, for both cattle and badgers.
    b. Researchers must determine the effectiveness of BadgerBCG vaccination. The development of a good oral vaccine and appropriate administration will be required.
    c. A cattle vaccine with greater efficacy is needed, and a test to distinguish between the protective and pathogenic immune responses during bovine TB is an absolute requirement. Existing research in these areas must be supported and extended.
3. Field trials are essential and should be coordinated across the UK and Ireland. To aid current research, we recommend that badger vaccination trials (supported by Government and NGO initiatives) are coordinated so that best use is made of the results, training and experimental design. This will decrease costs and generate data indicating which models are most suitable. Trial areas should be large enough and accompanied by control areas to robustly model the effects of the vaccine.
4. Efforts towards improving the UK's reputation and influence regarding cattle health at the EU level must be supported. The UK should continue to aim for 'disease-free status' for bovine TB and other infectious diseases, and commit to playing a leading EU-wide role in a vaccination programme that would not only benefit the UK, but could be made globally available.

Bovine TB in Cattle and Badgers

1. Bovine tuberculosis (bTB) is a chronic bacterial disease resulting from infection by *Mycobacterium bovis*, a Gram positive, slow growing bacterium. It has a long incubation period and symptoms can take months to develop in cattle, sometimes remaining dormant for years until it becomes reactive due to a stressor (e.g. illness, pregnancy, or old age). bTB can affect nearly all organ systems, but most commonly develops into a respiratory disease. It most often causes lesions to occur in the in the lymph nodes of the head and thorax, and in the lung, spleen, liver and surfaces of body cavities. These lesions are areas of localised *M. bovis* bacteria, which are then spread through respiratory secretions, faeces and milk. *M. bovis* is transmitted between cattle through aerosols when confined or in close contact, and can be ingested.

2. Badgers are one of several mammals that can become infected by *M. bovis.* Infected badgers rarely show signs of bTB, with a high proportion of infections resulting in a lengthy period of latency with few obvious lesions at post mortem examination. As such infected and infectious badgers often live with the disease asymptomatically throughout their natural lives, and shed *M. bovis* through their urine, faeces, sputum and discharge from bite-wounds. Duration of infection on pasture is fairly brief, with a 99% decay rate of *M bovis* varying from 1 – 4 weeks according to excretion in urine, faeces or bronchial pus[1].

3. Transmission of *M. bovis* between cattle and badgers is thought to be through ingestion of the bacterium at badger latrines. Badgers often inhabit woodland close to pastureland (which typically holds a larger number of earthworms), and while cattle generally avoid areas of grass soiled with badger faces and urine, some cattle will graze contaminated herbage, particularly when over-grazing occurs. Furthermore, bTB infected badgers tend to range further than non-infected individuals, have larger home ranges and forage father away from the main sett, increasing the likelihood of encountering cattle[2]. The strength of transmission between cattle and badgers is largely unknown; more information on this transmission pathway is needed to establish where best to invest in vaccination efforts.

4. bTB has been recorded in 'closed herds' (i.e. in this scenario, herds in which no individuals are introduced from external sources), omitting the opportunity of cattle-to-cattle transmission through imported infected animals. The epidemiology of bTB in badgers and proximity to herds identifies them a major reservoir of bTB for onward transmission to cattle in the UK.

5. bTB diagnostic tools for badgers are limited. Post-mortem detection of lesions can be difficult to locate (in certain studies, more than 60% of infected badgers did not have visible lesions[3,4]) and

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[1] Gallgher J. & Clifton – Hadley R. S (2000)

[2] Garnett B.T. et al. (2005) Ranging behaviour of European badgers in relation to bovine tuberculosis infection. *Applied Animal Behaviour Science* 94: 3-4: 331-340

[3] Jenkins H. E. et al. (2008) The prevalence, distribution and severity of detectable pathological lesions in badgers naturally infected with *Mycobacterium bovis. Epidemiology and Infection* 136: 1350–1361.

[4] Murphy D. et. al. (2010) The prevalence and distribution of *Mycobacterium bovis* infection in European badgers (*Meles meles*) as determined by enhanced post mortem examination and bacteriological culture. *Research in Veterinary Science* 88: 1–5.

may be confused with lesions from other diseases[5]. Ante-mortem serological tests tend to have a low sensitivity (but are likely to identify heavily infected individuals), and tests based on cell-mediated immunity responses to infection are more sensitive but are more difficult (and expensive) to develop. In cattle, serological testing is improving through use of a wider antigen range and more sensitive detection methods[6]. A combination of several tests has achieved a higher level of diagnostic accuracy [7], but again, this may prove expensive and difficult to apply in the field.

Vaccination

6. The TB vaccine *Bacillus Calmette-Guerin* (BCG) is an attenuated strain of *M. bovis*, used to vaccinate cattle and badgers. BCG has historically been thought to hinder the progression of TB, but not preclude the disease (this has been contested by research in a number of mammals including humans and cattle[8,9,10]). However it is generally agreed that in infected badgers, the vaccination will have little effect.

Injectable BadgerBCG

7. Defra have invested over £16m on research into TB vaccinations for badgers since 1994[11]. The injectable vaccine (known as BadgerBCG) was successfully licenced by the AHVLA in 2010[12], after it was shown to decrease disease burden in badgers. BadgerBCG did not appear to prevent infection, but reduced the severity and progression of TB in infected animals, which may reduce the risk of onward transmission from badgers to cattle[13]. The Food and Environment Research Agency (FERA) has undertaken modelling work on BadgerBCG and its potential to reduce the incidence of confirmed herd breakdowns[14]. Most of the current vaccination areas are relatively small and therefore have little statistical power to test these models. Suitable unvaccinated control areas are also needed for comparison to allow researchers to be confident in the effects they attribute to vaccination.

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[5] Gallagher, J. (1998). The natural history of spontaneous TB in wild badgers. Doctor of Veterinary Medicine Thesis, University of London.

[6] Vordermeier M. et al (2011) Mycobacterium bovis antigens for the differential diagnosis of vaccinated and infected Cattle. *Vet Microbiol*. 151(1-2):8-13

[7] Drewe JA, Tomlinson AJ, Walker NJ, Delahay RJ (2010) Diagnostic Accuracy and Optimal Use of Three Tests for Tuberculosis in Live Badgers. *PLoS ONE* 5(6): e11196.

[8] *Oysal A. et al. (2005)* Effect of BCG vaccination on risk of *Mycobacterium tuberculosis* infection in children with household tuberculosis contact: a prospective community-based study. *Lancet* 366, 1443–1451.

[9] Ameni G. et al. (2010) Field evaluation of the efficacy of Bacille Calmette Guerin (BCG) against bovine tuberculosis in neonatal calves in Ethiopia. *Clin. Vaccine Immunol.* 17, 1533–1538.

[10] *Corner L. A. et al. (2009)* Oral vaccination reduces the incidence of tuberculosis in free-living brushtail possums. *Proc. R. Soc. B* 276, 2987–2995.

[11] Defra; Research into bovine TB

[12] VLA; First tuberculosis vaccine for badgers is authorised

[13] Chambers et al (2010), Bacillus Calmette-Guérin vaccination reduces the severity and progression of tuberculosis in badgers Proc Biol Sci. 2011 June 22; 278(1713): 1913–1920. Published online 2010 December 1.

[14] Smith et al. (2012) Comparing Badger (*Meles meles*) Management Strategies for Reducing Tuberculosis Incidence in Cattle. PLoS ONE 2012 1 June 27: 7(6): e39250.

8. Defra introduced the BadgerBCG vaccine in summer 2010 as part of the Badger Vaccine Deployment Project (BVDP), which originally planned to vaccinate badgers in the six areas in England most affected by TB in cattle. The incoming government reduced the number of areas covered by BVDP from six to one, which is near Stroud, Gloucestershire[15], being run mainly to maintain Fera's capability to vaccinate badgers, and to train others who wish to apply for a licence[16]. By the end of the season in 2012, 137 lay vaccinators were trained, and a total of 2,167 badgers have been vaccinated since the BVDP began. Defra will continue to fund training courses into 2013.

9. NGOs are also undertaking badger vaccination programmes. The National Trust began a £320, 000 trial vaccination programme in Killerton, Devon in 2011 which is set to end in 2015. The work is to be carried out by Fera's wildlife management specialists. The Wildlife Trusts have initiated their own local vaccination programmes on their reserves. Gloucestershire Wildlife Trust's (GWT) five year vaccination programme is the most established. It covers seven sites and is currently ending its second year, with a comprehensive report already available[17]. Shropshire Wildlife Trust commenced a vaccination programme in autumn 2012, working in partnership with Cheshire Wildlife Trust, and more Wildlife Trusts are developing future vaccination trials[18].

10. The Welsh Government bTB strategy includes vaccination of badgers in the 'intensive action area' (a bTB endemic area of approximately 288km^2) as part of its four year Strategic Framework for Bovine TB Eradication announced in March 2012[19], replacing the proposed culling[20]. Over 1,400 badgers have now been vaccinated in the intensive action area[21].

11. The Department of Agriculture and Rural Development in Northern Ireland began modelling a vaccination programme that involves testing live badgers, vaccinating and releasing the test-negative animals and removing the test-positive, known as a TVR approach. The results of this modelling will inform a study to test the TVR approach in field conditions, which is likely to use a serological test which will identify the most highly infected badgers[22].

12. GWT have costed their BCGBadger vaccination programme at an average of £51 ha $^{-1}$ for the first year of vaccination, including capital and consumables, training and staff time (excluding stakeholder liaisons and Public Relations). As this work was largely unprecedented, considerable staff time was spent on planning and design of the vaccination programme.

13. Vaccinator training for the Wildlife Trusts is purchased from FERA. Defra are providing funding for Voluntary and Community Sector (VCS) organisations covering 50% of the cost of becoming an accredited and certified lay vaccinator in 2013. Defra also provides start up grants for licenced schemes.

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[15] Defra; Changes to badger vaccine deployment project
[16] Fera; Badger vaccine deployment project
[17] McGlone G. (2011) Gloucestershire Wildlife Trust Nature Reserves Badger Vaccine Deployment Programme 2011
[18] The Wildlife Trusts Briefing (2012) Bovine TB: A vaccination strategy for badgers and cattle
[19] Welsh Government Bovine TB Eradication Programme
[20] Ares E. (2012) Badger Culling. House of Commons Library Standard Note SNSC-5873
[21] Welsh Government Badger vaccination total tops 1400
[22] Northern Ireland Assembly Committee for Agriculture and Rural Development. Bovine TB Review: DARD Briefing. 11 September 2012. Official Report (Hansard)

14. GWT recommend that costs are cut through;
    a. A free advisory service at the planning and deployment stages of a vaccination programme.
    b. A faster and cheaper licensing service for the FERA Certificate of Competence.
    c. A more coordinated approach to badger vaccination at the national level. This would enable information to be shared more effectively, reduce costs to landowners and sharing of equipment to lower capital costs.

Oral BadgerBCG

15. Defra have spent £6m on research into oral badger vaccines since 2005-06[23], and are planning to invest a further £15.5m in vaccine development over the next four years to continue this work, according to Defra's chief scientific adviser and chief veterinary officer[24].

16. Oral vaccination is likely to be more cost effective than the injectable vaccine, requiring less staff time and equipment, and may offer the best long-term prospect for delivering BadgerBCG over a wide area[25], given steps are taken to minimise or prevent dominant animals from consuming large quantities of vaccine baits[26], and ensuring non-target animals are not adversely affected[27] (including cattle) . However it is likely to be several years before these vaccinations are available; Defra predicts it will be available in 2015[28].

17. Research areas include formulation and bait development, efficacy and safety studies, field deployment studies and preparing and submitting a licensing dossier for assessment by the Veterinary Medicines Directorate. Corner *et al.* (2010)[29] found 'a significant protective effect of BCG vaccination' in their study of oral vaccinations. Aznar *et al.* (2011) [30] used oral application of the BadgerBCG in their report on field trials to assess different control and eradication options for bTB in cattle in the Republic of Ireland, and trials using badger bait completed in 2011 and 2012 revealed that once developed an oral vaccine would be taken up by the population with ease.

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[23] Mr Paice, Written Answers (Hansard) 504-505W Bovine Tuberculosis: Disease Control 14 July 2011
[24] Boyd I. & Gibbens N. Badger cull furore is distracting attention from the real problem. Guardian.co.uk 11 October 2012.
[25] Delahay, R J.*et al*. (2003). Vaccinating badgers (*Meles meles*) against *Mycobacterium bovis*: The ecological considerations. *Vet. J.* 166, 43-51.
[26] Buddle B. M. et al. (2011) Update on vaccination of cattle and wildlife populations against tuberculosis. *Vet Microbiol*. 2011 Jul 5;151(1-2):14-22
[27] Robinson P.A. et al (2012) BCG vaccination against tuberculosis in European badgers (Meles meles): a review. *Comp Immunol Microbiol Infect Dis*. 35(4):277-87
[28] Defra, Annex C: Badger TB Vaccines, September 2010
[29] Corner LA. *et al* (2010) Oral vaccination of badgers (Meles meles) with BCG and protective immunity against endobronchial challenge with Mycobacterium bovis.
Vaccine. 2010 Aug 31;28(38):6265-72. Published Online 2010 July 15.
[30] Aznar I. *et al.* (2010) Trial Design to Estimate the Effect of Vaccination on Tuberculosis Incidence in Badgers, *Veterinary Microbiology* 151, 104-111

Cattle TB vaccine

18. By the end of March 2010, Defra had invested over £23m on the development of cattle vaccines and associated diagnostic tools[31]. Defra has budgeted £15.5m for research into developing effective cattle TB vaccines over the next four years.

19. Defra models predict vaccinating cattle that are tested annually will cost around £170m to £180m over the period from introduction in 2012 to the end of the modelled period in 2026. The expected fewer breakdowns and less routine testing potentially saving up to one fifth of the costs of the current policy measures[32].

20. BCG is currently the vaccine used in cattle, and provides a certain degree of herd protection. It may fully protect or decrease disease severity in some cattle, but is unlikely to have any effect on cattle with existing infections. It is important to note that field trials of efficacy have not been possible in the UK due to EU regulations (see below); however testing in overseas cattle shows a protective efficacy of BCG between 56% and 68%[33].

21. Defra state that development of an alternative vaccine is a 'longer-term goal'[34]. The most promising vaccination strategy to date involves using BCG to prime the immune system, then introducing subunit vaccines with protective antigens present in BCG to boost the immune system[35].

EU Legislation & DIVA testing

22. The UK farming industry relies heavily on trade within the EU, and would be severely impacted if cattle trade was restricted. It is also important to note that the UK is believed to have a poor reputation at the EU level regarding cattle disease. We must be seen to be making a serious commitment to cattle health through research and farm-based measures, and learn from past outbreaks (such as with foot and mouth disease[36]) in order to have influence within the EU.

23. There are legal and practical barriers to vaccinating cattle against Bovine TB. bTB vaccination of any kind is currently prohibited under EU Directive 78/52/EEC and associated directives; this legal framework needs to be addressed before cattle vaccinations can be made available.

24. bTB vaccinations are prohibited because there is not a suitable diagnostic test that differentiates between infected and vaccinated animals (i.e. a DIVA test) . Cattle are routinely tested for TB using

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[31] Defra; Research into bovine TB
[32] Defra; Options for vaccinating cattle against bovine tuberculosis
[33] Ameni G. (2010) Field Evaluation of the Efficacy of *Mycobacterium bovis* Bacillus Calmette-Guérin against Bovine Tuberculosis in Neonatal Calves in Ethiopia. *Clin Vaccine Immunol*. 17(10): 1533–1538.
[34] Defra; Cattle Vaccination
[35] The Jenner Institute; Bovine Tuberculosis Vaccine Programme
[36] The Royal Society; Infectious Diseases in Livestock. Policy Document 19/02 July 2002

a skin test called the Single Intradermal Comparative Tuberculin Test (SICTT), which relies on the use of tuberculin as a diagnostic antigen. As BCG is a sensitising vaccine it can interfere with the skin test producing a false positive in some uninfected, vaccinated cattle. 'Reactors', whether they are vaccinated or infectious animals will be culled and trade restricted.

25. Diagnostic tests with suitable sensitivity and specificity are needed so that all and only infectious cattle with bTB are identified and removed. It is also worth noting that cattle can carry bTB and not be infectious (i.e. the lesions are contained), and some cattle can be infectious without showing symptoms of infection (known as 'anergy'). False-negative responses to testing can also be seen in animals that are immunocompromised; for example those animals with a poor immune response, which have recently calved or are at the late stages of the disease. False-negative responses can also occur in tests soon after infection.

26. DIVA antigens have been defined using comparative genome and transcriptome approaches. These include ESAT-6 and CFP-10; antigens whose genes are expressed in *M. bovis*, but absent from BCG or environmental mycobacteria [37].

27. ESAT-6 and CFP-10 have been used in the Bovigam test (a blood-based gamma interferon release assay which is used in support of the SICTT) to improve the specificity of the test[38], and in skin test reagents; this resulted in a response rate of 78% of naturally infected tuberculin-positive cattle, and induced no skin responses in BCG-vaccinated cattle despite their being sensitized for strong tuberculin responses. Inclusion of antigen Rv3615c enhanced skin test sensitivity in naturally infected cattle without compromising specificity[39]. Research on further biomarkers is being done, to both enhance diagnostic performance and sensitivity directly, or to alleviate negative effects by supressing these biomarker responses.

28. If a suitable DIVA test was developed, it would have to be approved at the EU and international levels before legislation is changed. This would be led by the Health Commissioner, and is thought that once agreement is reached, these changes could be made relatively quickly[40].

[37] Vordermeier M. et al. (2001) Use of Synthetic Peptides Derived from the Antigens ESAT-6 and CFP-10 for Differential Diagnosis of Bovine Tuberculosis in Cattle. *Clin Diagn Lab Immunol*. 2001 May; 8(3): 571–578.
[38] Vordermeier M. et al (2011) Mycobacterium bovis antigens for the differential diagnosis of vaccinated and infected Cattle. *Vet Microbiol*. 151(1-2):8-13
[39] Whelan A. O. et al (2010) Development of a skin test for bovine tuberculosis for differentiating infected from vaccinated animals. *J Clin Microbiol.* 48(9):3176-81.
[40] European Commission Press Release Statement from the European Commission regarding an article in the Mail on Sunday 21 October

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