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# Livestock Vaccines

UK agriculture is constantly faced with the threats and economic consequences of various diseases of livestock. Vaccination of livestock is one approach to disease prevention and control. This POSTnote examines the use of vaccines and outlines the pros and cons of using vaccination in livestock.

## Overview

- Vaccines are available for managing several livestock diseases in the UK.
- Potential benefits of vaccines include improved animal welfare and public health.
- It can be difficult to differentiate between infected and vaccinated animals. Animals have to be certified as disease-free before they can be exported, so this has led to restrictions on the use of some vaccines.
- Research is underway to develop new vaccines and tests that allow differentiation between infected and vaccinated animals.
- A proposed new EU Animal Health Law that prioritises animal welfare may facilitate vaccine use.

## Background

Livestock diseases impose a considerable economic burden on UK agriculture. For instance, the 2001 Foot and Mouth Disease (FMD) outbreak is estimated to have had direct costs to the public sector of £3 billion.[1] Livestock diseases may fall into one or more of the following categories:

- **endemic** diseases that are commonly found in the UK
- **exotic** diseases that are not usually found in the UK
- **zoonotic** diseases which may be passed to humans from affected animals
- **notifiable** diseases; there is a legal requirement to report such diseases to the Animal Health and Veterinary Laboratories Agency (AHVLA).

Measures for livestock disease prevention and control were outlined in POSTnote 392 and include culling of infected animals, use of antimicrobial medicines such as antibiotics and antifungals, animal movement controls and the use of vaccines. Vaccines are preparations administered to prevent infection and/or reduce disease caused by parasites, microbes such as bacteria and viruses and other organisms. Disease-causing organisms carry molecules known as antigens on their outer surface. If such an organism infects an animal, the animal's immune system recognises the antigens as being 'foreign' and mounts an immune response that may prevent disease. Vaccines are a way of presenting foreign antigens to animals without exposing them to the harmful effects of a disease. This primes the animal so that it can produce a fast and effective immune response should it encounter the infectious agent. A vaccine may contain the whole antigen or just certain parts of it (see Box 1). This briefing looks at the:

- main diseases that affect UK livestock, the availability of vaccines for them and the ways they can be used
- factors that influence decisions on vaccine use
- likely future developments.

## Livestock Diseases and Vaccines

### Main Diseases and Vaccine Availability

Table 1 shows the main diseases that can affect UK livestock. Most of these diseases are endemic, although there have been fourteen outbreaks of exotic diseases such as bluetongue in the last ten years. Vaccination is an available tool for most of the diseases listed in Table 1, except diseases such as liver fluke and bovine tuberculosis

**Box 1. Types of Vaccines**

- **Inactivated (killed) vaccines** contain whole viruses or bacteria which have been inactivated by heat or chemical treatment. They are usually coupled with an 'adjuvant' that acts as a stimulant to enhance the animal's immune response.
- **Live attenuated vaccines** contain whole viruses or bacteria which have been weakened or 'attenuated'. They offer better stimulation of the immune response and require lower doses of the bacteria or viruses. Ideally they should not cause any clinical signs of disease.
- **Subunit vaccines** contain only viral or bacterial antigens which can trigger an immune response. A recent example is a new synthetic vaccine against foot and mouth disease (see Page 4).

**Table 1: Major Livestock Diseases in the UK**

| Disease | Affected animals | Type | Notifiable |
|---|---|---|---|
| Aujeszky's disease | Pigs | Exotic | Yes |
| Bluetongue | Cattle, sheep | Exotic | Yes |
| Bovine tuberculosis | Cattle | Endemic, Zoonotic | Yes |
| Bovine viral diarrhoea | Cattle | Endemic | No |
| Brucellosis | Cattle | Exotic, Zoonotic | Yes |
| Classical swine fever | Pigs | Exotic | Yes |
| Clostridial disease | Cattle, sheep, pigs | Endemic | No |
| Coccidiosis | Poultry | Endemic | No |
| Foot and Mouth Disease | Cattle, sheep, pigs | Exotic | Yes |
| Infectious bovine rhinotracheitis | Cattle | Endemic | No |
| Johne's disease | Cattle, sheep, goats | Endemic | No |
| Leptospirosis | Cattle | Endemic, Zoonotic | No |
| Liver fluke | Cattle | Endemic | No |
| Newcastle disease | Poultry | Exotic | Yes |
| Pasteurellosis | Sheep, poultry | Endemic, Zoonotic | No |
| *Salmonella* | Cattle, pigs, poultry | Endemic, Zoonotic | No |

(bTB). Vaccines may be used in different ways and the various regulatory bodies outlined in Box 2 have placed restrictions on when and how they are used.

### Different Ways of Using Vaccines

Vaccines can be used in several different ways:

- **Routine (prophylactic) vaccination** to prevent disease. For example, routine vaccination of cattle against bovine viral diarrhoea and poultry against Newcastle disease.
- **Emergency vaccination** to control an outbreak, by slowing the spread of a disease. For example, emergency vaccination was used to control the spread of the exotic disease bluetongue in 2007/08 (see Box 3).
- **Wildlife vaccination** can reduce the spread of diseases like rabies from wildlife to livestock. It is hoped that vaccinating badgers against tuberculosis (TB) will reduce bovine TB (bTB, see Box 3).

### Regulation of Livestock Vaccine Use

Various international, European and national regulatory bodies are involved in controlling the manufacture and use of vaccines for controlling livestock disease (Box 2). International bodies such as the World Organisation for Animal Health (OIE) and the European Commission stipulate the time period required to regain disease-free status following an outbreak of an exotic disease such as classical swine fever (CSF) or FMD (Box 3). European legislation restricts the use of vaccines for some diseases. For instance, the prophylactic use of vaccines against bTB and FMD is banned in the EU under Directives 78/52/EEC and 90/423/EEC respectively. Emergency vaccination is allowed in the event of an outbreak of FMD and Directive 2003/85/EC provides guidance for national authorities in deciding whether to carry out emergency vaccination. Factors that inform such decisions on vaccine use are examined below.

**Box 2. Regulatory Bodies for Livestock Vaccines**

- The World Organisation for Animal Health (OIE) is an inter-governmental organisation responsible for improving animal health. It collects and analyses scientific information on animal disease control and makes it available to help member countries to improve the control and eradication of animal diseases. It also publishes standards for veterinary vaccine production and requirements for recognition of disease free status.
- The European Commission (EC) produces legislation to guide livestock vaccination within the EU Member States. The Health and Consumers Department (DG SANCO) monitors the application of EU law and supports national and regional authorities.
- In the UK, preventing and tackling notifiable disease outbreaks is a devolved issue. Defra (the Department for Food and Rural Affairs) funds activities provided on a UK-wide basis such as the National Reference Laboratory for FMD. The UK and each devolved administration have a contingency plan for exotic notifiable diseases and specific disease control strategies for diseases such as FMD, CSF and bluetongue.
- The Veterinary Medicines Directorate (VMD) has UK-wide responsibility for authorising veterinary medicines, including vaccines, and monitoring their quality, safety and efficacy.
- The Food Standards Agency (FSA) assesses and advises on potential food safety risks of residues from veterinary medicines.
- The Animal Health and Veterinary Laboratories Agency (AHVLA) safeguards animal health and welfare as well as public health through research, surveillance and inspection throughout the UK.

## Making Decisions on Vaccine Use

Using vaccines to prevent and control livestock disease as part of an integrated control strategy has several potential benefits. However, economic and practical considerations will shape the role that vaccines play.

### Potential Benefits

Among the main potential benefits of vaccine use are:

- **Improved animal welfare**. Prophylactic and emergency vaccinations can improve animal welfare by reducing the disease burden. Concerted global vaccination campaigns can lead to the eradication of a disease. This was achieved for the first time in 2011 with the eradication of rinderpest, a disease of cattle, domestic buffalo and other ungulates.[2]
- **Improved public health**. Where livestock vaccines are used to control zoonotic diseases, such as brucellosis and *Salmonella*, they can improve public health.
- **Reduced antimicrobial use**. Widespread use of antimicrobials among livestock has been implicated in the emergence and spread of antimicrobial-resistant strains of disease-causing microbes. This could be a serious threat to disease treatment in humans and animals. Use of vaccines to prevent livestock disease can reduce the need for antimicrobial treatment, and thus constrain the spread of antimicrobial resistance.[3]

**Box 3. Case Studies**

**Bluetongue**
Bluetongue is a viral disease which affects ruminants such as cattle, sheep, goats and deer. There are at least 24 varieties or serotypes of the bluetongue virus (BTV). It is transmitted by the bite of infected midges. The first occurrence of bluetongue serotype BTV-8 in the UK was in 2007. In 2008, vaccination was used to control the spread of the disease. An inactivated vaccine for BTV-8 was developed and animals in whole regions where the disease was first identified were vaccinated. The UK was declared bluetongue-free in 2011.

**Bovine Tuberculosis**
Bovine tuberculosis (bTB) is a bacterial respiratory disease of cattle, caused by *Mycobacterium bovis*. The spread of the disease has been on the rise in England and Wales since the late 1980s. Vaccines against TB have been developed based on the attenuated human *M. bovis* Bacille Calmette-Guerin (BCG) vaccines, but none are licensed for use in cattle. Field trials conducted in Ethiopia and in Mexico have shown that the BCG vaccines confer protection of up to 68%.[4,5] However, vaccination of cattle against bTB is banned under EU Directive 78/52/EEC, owing to the inability to differentiate between infected and vaccinated cattle.

Badgers are a wildlife reservoir for bTB in parts of the UK. An injectable badger BCG-based vaccine was licensed in 2010 and is being used by Defra in the Badger Vaccine Deployment Project in an area near Stroud, and by the Welsh government in the Intensive Action Area in Pembrokeshire.[6] Research into an oral badger vaccine, which may facilitate badger vaccination, is ongoing.

**Foot and Mouth Disease**
Foot and Mouth Disease (FMD) is a highly contagious viral disease affecting cloven-hoofed animals. There are 7 serotypes of the FMD virus. The 2001 outbreak in the UK caused by FMD virus serotype O resulted in significant economic losses. Culling was the main method used to control the disease; over 4 million animals were slaughtered. An FMD vaccine is commercially available, but its use is tightly regulated by legislation such as the Foot and Mouth Disease (Control of Vaccination) (England) Order 2006. Vaccination was used in the Netherlands in 2001, but only as a means of slowing down the spread of disease while culling continued (vaccinated animals were slaughtered too). The UK was declared free of FMD without vaccination in 2002.

## Other Factors to Take into Account

*Interference with Diagnostic Tests*
Many diagnostic tests are designed to detect immune responses to infectious agents. Failure to detect these immune responses would usually indicate disease-free status. Vaccination induces these immune responses, and therefore can interfere with certain diagnostic tests. This means that it can be difficult to differentiate between infected and vaccinated (disease free) animals. DIVA (Differentiating Infected from Vaccinated Animals) tests and vaccines are being developed for some diseases (see Box 4), including bTB, but none are available for routine use. Examples of interference with diagnostic tests include:

- the BCG vaccine, which interferes with the two main diagnostic tests for bTB in cattle (the tuberculin skin and gamma interferon tests)
- the vaccine for Johne's disease, which is caused by *Mycobacterium avium paratuberculosis* (MAP), can interfere with bTB diagnosis, possibly because of the genetic similarity between MAP and the bacteria that cause bTB (*M. bovis*).

**Box 4. Differentiating Infected from Vaccinated Animals (DIVA)**
DIVA tests work by testing for specific antigens which are present in the disease agent but not present in the vaccine. For instance, DIVA tests for FMD are being developed that detect proteins produced only in infected animals and not by vaccinated animals. A proposed DIVA test for bTB is based on detecting specific antigens such as ESAT-6 and CFP-10 which are only expressed in *M. bovis* and are absent from BCG. However, DIVA tests add to the cost of vaccination.

DIVA vaccines have also been developed that contain a 'marker' which is not present in the disease agent. In the DIVA vaccines for IBR and Aujeszky's disease, a gene segment has been deleted in the vaccine virus. During testing, detection of this segment implies the animal was infected and not vaccinated.

*Impact on Trade*
Animals have to be certified as disease-free before they can be sold internationally. For instance, the EU has a ban on trading cattle which are not officially TB-free (Directive 64/432/EEC). Interference of the BCG vaccine with the bTB diagnostic tests led to the ban on bTB vaccination of cattle. The development of a DIVA test for bTB (Box 4) could pave the way to allowing trade in cattle vaccinated against bTB under the proposed European Animal Health Law (Box 5).

Vaccination can also extend the time required to regain disease-free status before international trade can resume. While these time periods are stipulated within the EU, UK trade agreements with non-EU states may extend them by up to three (for CSF) to six (for FMD) months.[7] During the 2001 FMD outbreak, the UK regained disease-free status quicker through using culling than it would have through vaccination. The potential loss of trade associated with vaccine use is a key consideration in calculating the likely cost-effectiveness of using vaccines.

*Vaccinating to Cull*
Emergency vaccination is often seen as an animal welfare-friendly alternative to culling in the event of an exotic disease outbreak. However there are several reasons why it might be necessary or desirable to cull vaccinated animals:

- where it is not possible to confirm that a vaccinated animal is disease free (if there is no DIVA test available)
- where the presence of vaccinated animals delays the resumption of trade under international agreements
- where legislation restricts products from vaccinated animals entering the food chain (CSF and FMD)
- in a major outbreak where vaccination has been used to 'buy time' to allow culling and carcase disposal facilities keep up with demand.

*Multiple Serotypes*
Vaccines can be specific to a particular strain or serotype of a disease agent. There are also multivalent vaccines which offer protection against several serotypes. Diseases where multiple serotypes exist can be problematic if an outbreak involves serotypes for which no vaccine is available. In the UK, vaccines for BTV-8 were developed in the bluetongue outbreak (Box 2). But other serotypes such as BTV-1, -6 and -11 circulate around parts of Europe. Vaccines are

**Box 5. The New European Animal Health Law**
The EU Animal Health Law is a new single regulatory framework for animal health, being developed under the EU Animal Health Strategy (2007-2013). The underlying principle of the Animal Health Strategy is that prevention is better than cure. The new law is aimed at setting the general principles for animal health, animal health requirements for trade of live animals and their products and to set principles and measures for disease control. It may see a prioritisation of animal health over trade, and this may lead to changes in some of the current restrictions on vaccination.

available for BTV-1, but not for BTV-6 and BTV-11. Similarly, there are seven serotypes of FMD virus; each requires a vaccine specific to it. An outbreak of a novel disease serotype necessitates the rapid development of a new vaccine. This can be facilitated by international surveillance and by keeping stocks of antigens or vaccines in banks (see below).

*Practicalities*
Any decision to use vaccines to control an outbreak of disease must consider whether sufficient quantities of vaccine can be procured, distributed and administered in the relevant time frame. One way of guaranteeing access to vaccines in an emergency is by maintaining banks of vaccines or antigens. Antigen banks have the advantage of having a longer shelf-life and can be used to produce vaccines rapidly. The EU maintains a vaccine bank for CSF and an antigen bank for high priority serotypes of FMD that can be accessed by Member States.[7]

*Cost*
Costs of vaccination may be covered by Government, or by farmers. The decision on who pays often depends on whether the vaccination programme is voluntary or compulsory. Voluntary programmes such as UK vaccination against bluetongue are usually paid by the farmer, whereas compulsory programmes are usually covered by the State. Funding may also be sought from the EU.[7]

*Consumer Attitudes*
The use of vaccination in food-producing animals is widely accepted. The 2012 survey by the National Office of Animal Health (NOAH) found that most consumers (74%) were aware of vaccination of animals to prevent disease, and many agreed that the use of vaccination is beneficial. Consumers are also more concerned about animal welfare than the use of animal vaccination and see vaccination as a humane alternative to culling.[8]

In light of scares such as bovine spongiform encephalopathy (BSE) and horsemeat contamination, food safety is a concern for consumers. Effective risk communication is important in helping the public make informed opinions and choices. For instance in 2001, the FSA stated that vaccinated animals posed no food safety implications in response to consumer concern during the FMD crisis.[9] The NOAH survey also showed that the Food Standards Agency (FSA) is the most trusted body (52%) to provide information regarding food safety.

## Likely Future Developments

### Research

Defra funds research projects to develop new vaccines against notifiable diseases and evaluate the effectiveness of current vaccines. Such research providers include the AHVLA and the Pirbright Institute. There is also research in the devolved administrations such as the Roslin Institute and the Moredun Research Institute (Scotland) and the Agri-Food and Biosciences Institute (Northern Ireland).

A recent development is a new FMD virus vaccine which addresses some of the drawbacks of the current vaccines. The subunit vaccine is produced without the requirement for infectious virus. This means the vaccine is safer and also assists development of an accompanying DIVA test. A particular improvement in the new vaccine is that it is more stable at ambient temperature and can tolerate fluctuations in refrigeration temperature, which means that the vaccine is less likely to lose its efficacy during deployment.

### New Disease Threats

*Schmallenberg Virus*
Schmallenberg virus (SBV) is a new threat which causes disease in cattle, sheep, goats and deer. It has been detected throughout Europe.[10] It is transmitted by insect vectors such as biting midges, and was first detected in the UK in early 2012. SBV mainly affects pregnant animals, leading to abnormalities in lambs and calves and abortions or still birth. The illness is transient in non-pregnant adult animals, lasting about 6 days, and causes debilitating effects such as diarrhoea and low milk yield. Prior exposure to the virus may lead to immunity against subsequent infection, although it is uncertain how long this natural immunity lasts for. There is currently no licensed vaccine available, although a candidate vaccine is being considered by the VMD for authorisation.

*African Swine Fever*
African swine fever (ASF) is a highly contagious notifiable viral disease of pigs. It has never occurred in the UK, but is endemic in sub-Saharan Africa. ASF can be transmitted by direct and indirect contact, as well as by soft tick vectors, but these vectors are not present in the UK. There is currently no vaccine available against the disease. Regular reports of the disease in Russia and neighbouring countries could mean that the disease is moving closer to Europe, so ASF is under surveillance by the AHVLA.

**Endnotes**

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