

# Use of vaccines in cattle and sheep production



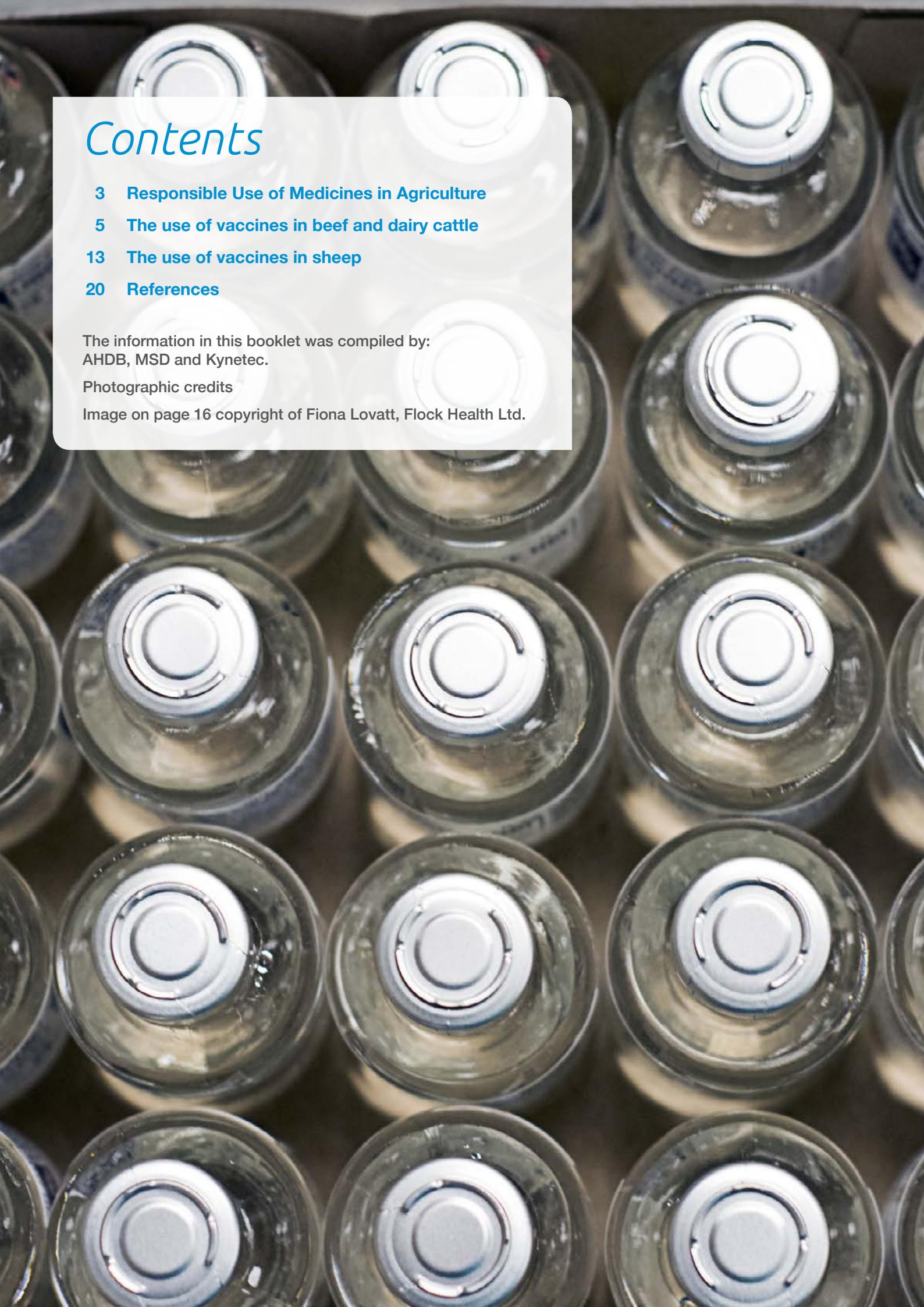
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# Responsible Use of Medicines in Agriculture

Responsible Use of Medicines in Agriculture (RUMA) was established in November 1997 to promote the highest standards of food safety, animal health and welfare in the British livestock industry. It is a unique, independent non-profit group involving organisations that represent all stages of the food chain from ‘farm to fork’. RUMA aims to provide a co-ordinated and integrated approach to best practice in animal medicine use.

In October 2017, targets for further reducing, refining or replacing antibiotic use across the key livestock sectors were announced at a RUMA conference in London. Sector-specific targets were developed by a ‘Targets Task Force’ and facilitated by the RUMA Alliance.

The sheep and beef sectors committed to monitoring the sales of vaccines within their targets. There was a commitment to work with industry stakeholders (e.g., pharmaceutical companies) to monitor the use of vaccinations that target respiratory disease in cattle, aiming for a year-on-year increase between 2017 and 2020. It is difficult to distinguish the use of respiratory vaccinations in dairy and beef cattle from product sales data; therefore, this target and report relates to all bovine animals.

Within its targets, the sheep sector committed to improve the management and control of lameness by increasing uptake of the Five Point Plan.<sup>1</sup> Part of this plan includes vaccination against foot rot where necessary, so it was decided that sales of the foot rot vaccine should be monitored. A further target

concentrated on increasing the responsible control of enzootic abortion by vaccination rather than by treatment with antibiotics, so sales of enzootic abortion vaccination are also monitored.

## Vaccination in farm animal production

The immune system is the body’s natural defence against infection. When an animal picks up an infective agent (e.g. bacteria or a virus), the cells of the immune system respond to try and eliminate the agent and prevent infection and subsequent disease. Sometimes, the immune system cannot respond quickly enough to prevent a disease from seriously harming or even killing animals. One way to give the immune system an edge in the fight against infection is to use a vaccine.

Vaccines prepare animals (or people) to fight infections by pathogenic bacteria, viruses or parasites by imitating an infection and stimulating an individual’s immune system to develop adaptive immunity. A vaccine is a biological preparation and typically contains weakened or killed forms of the microorganism, its toxins, or some of its surface proteins (often referred to as antigens). The vaccine tricks the immune system into recognising the agent as a threat, thus it develops the capacity to destroy it. The immune system stores a ‘memory’ of the pathogen’s antigen. If the animal subsequently picks up that infection (or sometimes even closely related microorganisms) in the future, the immune system will recognise it and respond much more quickly to prevent or reduce the impact of the associated disease.



Vaccination is generally designed to prevent future disease, although it will not necessarily prevent future infection; some vaccines are only licensed to reduce shedding and clinical signs.

The two main classifications of vaccine are live and dead vaccines. Live attenuated vaccines are derived from disease-causing 'wild' bacteria or viruses that have been weakened or 'attenuated' in a laboratory. After being injected, live attenuated vaccines grow and replicate in the animal and produce an immune response. Generally, modified live viral vaccines provoke a satisfactory immune response with a single dose.

Dead or inactivated vaccines consist of killed or inactivated forms of the pathogen or their toxins, inactivated with heat, chemicals such as formalin, or radiation. The immune response to inactivated vaccines is initially not as strong as for live vaccines because the pathogen or toxin does not replicate in the animal. To ensure sufficient memory, a primary course of 2 doses of the vaccine is usually required, with a short interval between these doses.

The full response to a vaccine does not occur immediately; it often takes a couple of weeks after administering the initial course. The immune response after vaccination with inactivated pathogens is not always as strong as the immune response after a 'wild' infection and repeated booster doses are required after a certain period of time to maintain immunity against diseases.

Vaccination is an effective method of preventing infectious diseases and played an important role in the worldwide eradication of smallpox from people and of rinderpest from cattle. Vaccination programmes are an important part of a comprehensive, well-planned herd or flock health control strategy, but are not a substitute for good management practices, such as appropriate attention to biosecurity. Vaccination may not be 100% efficacious and should never be relied upon as a sole measure to prevent disease.

All vaccines used in the European Union (EU) undergo rigorous testing and must demonstrate that they are effective, safe and have a 'positive benefit-risk balance'. Lowering the incidence of disease through vaccination can have a major impact on animal welfare by greatly reducing suffering and distress associated with disease. Vaccination also provides considerable economic benefits because fewer animals become ill or signs are milder. This eliminates or reduces treatment costs and reduces the need to use antibiotics, as well as preventing the reduction in growth, milk production and/or fertility that may otherwise result.

## Vaccination in cattle and sheep

In the UK, more than 40 vaccines are authorised for use to control or prevent disease in cattle and around 20 products are authorised for use in sheep. Appropriate use of vaccines should be part of the herd or flock health plan on all farms, under the supervision of a veterinary surgeon. Farmers are legally required to keep a record of the administration of all vaccines in a medicine book, which must be available for inspection. However, there is currently no national system for collating data on how many animals have been vaccinated.

Data on the number of doses of vaccines authorised for use in cattle and sheep sold in the UK each year between 2011 and 2018 are based on wholesaler data collated by Kynetec.<sup>2</sup> MSD Animal Health has made these data available for this report. Wholesaler sales do not necessarily equate to vaccine usage in that year because, for example, practices may stock up on a vaccine in one year, but use it in the following year, perhaps for commercial reasons or to mitigate potential stock availability concerns. However, the sales data are considered to be the best available approximation.

Data on cattle and sheep populations in the UK have been taken from the Defra report, *Annual statistics on the number of livestock in England and the UK in June and December*. The proportion of cattle or sheep in the 'at risk' population has been estimated using these data and assumptions based on standard industry practices.

The figures do not measure how effectively vaccines were used. The level of protection could be lower because of:

- Poor storage conditions
- Poor timing relative to period of risk
- Poor timing of follow-up booster vaccinations



# The use of vaccines in beef and dairy cattle

## Bovine Viral Diarrhoea (BVD) virus vaccines

Bovine Viral Diarrhoea (BVD) virus is one of the most important viral infections of cattle. The virus infects cattle of all age groups, including the unborn calf. It can cause devastating losses in individual herds.<sup>3</sup>

**The cost:** £40–60m to the national herd in health and productivity loss.<sup>3</sup>

Three vaccines for BVD virus (BVDV) were marketed in the UK between 2011 and 2018:

- **Bovilis BVD** contains inactivated BVDV. The primary vaccination course is 2 doses of vaccine separated by a 4-week interval. A booster dose is recommended 4 weeks before the start of the next gestation for individuals. For herds, the recommendation for boosters is 1 vaccination 6 months after primary vaccination, with revaccinations at an interval no greater than 12 months
- **Bovidec** contains inactivated BVDV. The primary vaccination course is 2 doses of vaccine separated by a 3-week interval. A single annual booster dose is recommended
- **Bovela** (launched March 2015) contains modified live BVDV. The primary vaccination course is 1 dose of vaccine. A single annual booster dose is recommended

Inactivated BVDV is also a component of 3 vaccines that target pneumonia: Bovalto Respi 4, Rispoval 3 and Rispoval 4. These are targeted mainly at stock under 1 year of age. These combination vaccines have not been included in the estimated uptake of BVD vaccines and are instead included in the estimated uptake of vaccines targeted at calf pneumonia.

## Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

The primary vaccination course for vaccines containing inactivated BVDV is 2 doses of vaccine separated by a 3 or 4-week interval. The primary vaccination course for the vaccine containing modified live BVDV is 1 dose of vaccine.

**Denominator:** Common industry practice is to give breeding heifers a primary course of vaccination before first service, at between 1 and 2 years of age, and to give all breeding females over 2 years of age an annual booster vaccination. It was assumed that only female breeding animals should be vaccinated and that the at-risk population was all female cattle over 1 year of age.

## Vaccination uptake

BVD vaccine uptake peaked in 2014. At this time, it was estimated that almost 48% of breeding females over the age of 1 year were vaccinated for BVD – up from 42% in 2011. In 2017, sufficient doses of vaccine were sold to vaccinate 45% of breeding females over the age of 1 year. This dropped to 42% in 2018. The number of BVD vaccine doses sold dropped from 2.7m to 2.4m. The Bovidec BVD vaccine was discontinued in 2018.

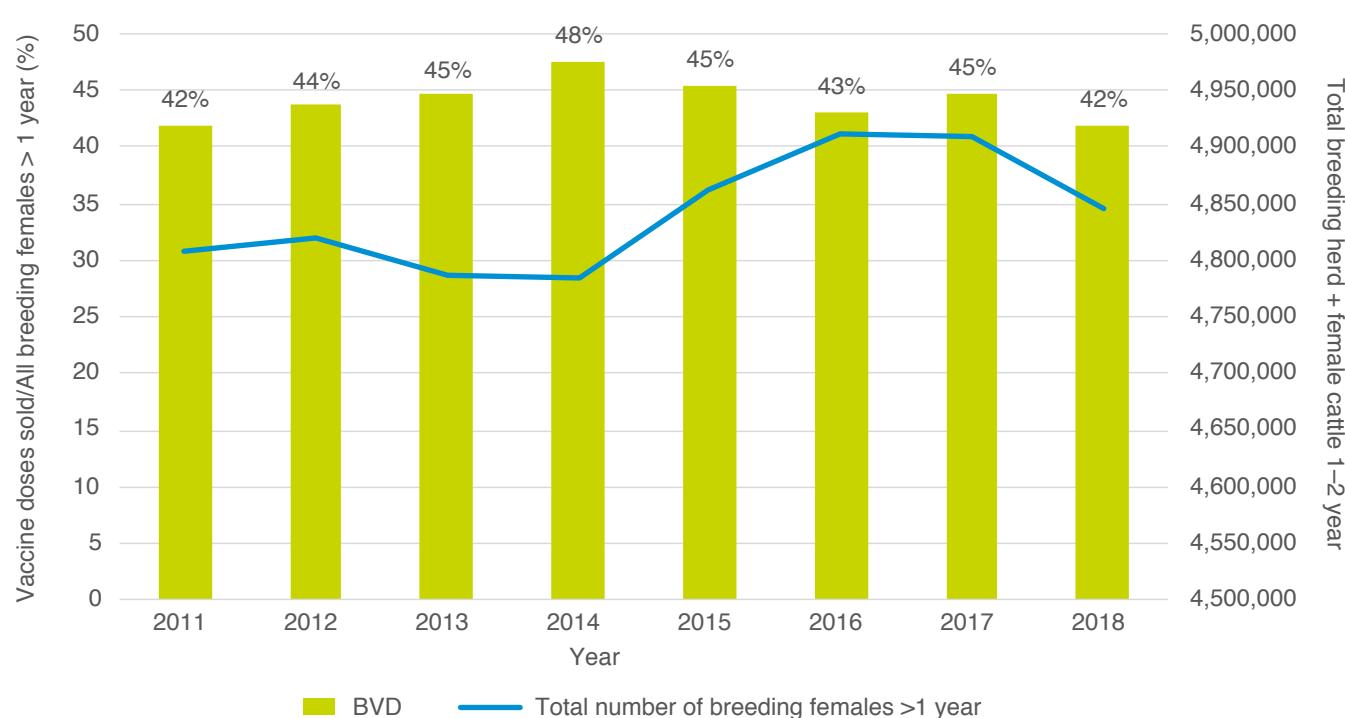


Figure 1. BVD vaccination uptake

More than 1 in 6 adult breeding cows are in herds that are either accredited as being free of BVD, or are working towards being accredited as BVD-free. This status is awarded by cattle health schemes operating to cattle health certification standards (CHeCS), which are not allowed to use BVD vaccines. If the breeding females in these herds were removed from the population of cattle of over 1 year of age that could have been vaccinated, the proportion of those females in the national herd eligible for vaccination that were vaccinated was estimated at 54% in 2017 and 51% in 2018.

## Infectious Bovine Rhinotracheitis (IBR) vaccines

Infectious Bovine Rhinotracheitis (IBR; also known as infectious pustular vulvovaginitis, IPV), is an infectious disease of cattle caused by infection with Bovine herpesvirus type 1. IBR causes severe respiratory disease that can lead to fatal pneumonia. The virus can infect the upper respiratory tract and/or the reproductive tract. Mortality is low, but economic losses can be important. The severity of clinical signs depends on the strain of the virus and the susceptibility of cattle. In adult cows, infection is associated with a severe and prolonged drop in milk yield, reduced fertility and abortions and inflammation of the vulva/prepuce.<sup>4</sup>



**The cost:** £5–7m<sup>3</sup> to the national herd in health and productivity loss.

Seven vaccines for IBR (Bovine herpesvirus type 1 or BHV-1) were marketed in the UK between 2011 and 2018:

- **Bovilis IBR marker live** contains modified live BHV-1. The primary vaccination is a single intranasal or intramuscular dose. The first revaccination should be given 6 months after the primary vaccination. All following revaccinations should be given at an interval of no longer than 12 months
- **Bovilis IBR Marker Inac** contains inactivated BHV-1. The recommended primary vaccination course is 2 vaccinations, with an interval of 4 weeks and a booster vaccination every 6 months
- **Hiprabovis IBR Marker Live** contains live gE-tk- double gene-deleted BHV-1. The recommended initial dose for cattle over 3 months of age is 1 injection of 2 ml given intramuscularly. The animal should be re-vaccinated with the same dose 3 weeks later. Thereafter, a single booster dose of 2 ml should be administered every 6 months
- **Rispoval IBR-Marker Inactivated** An inactivated infectious bovine rhinotracheitis marker (gE-negative) vaccine. The primary vaccination scheme comprises 2 doses, 3–5 weeks apart. Booster vaccinations at 6-monthly intervals
- **Rispoval IBR-Marker Live** A live, freeze-dried, infectious bovine rhinotracheitis marker (gE-negative) vaccine. The primary course for cattle over 3 months of age is 1 intramuscular vaccination. Booster vaccinations should be administered every 6 months. If a live vaccine is given initially, followed by an inactivated vaccine 6 months later, then revaccination with the inactivated vaccine can take place at 12-month intervals
- **Tracherine** contains live attenuated Bovine herpes virus type 1 (BHV-1). The primary course for cattle over 10 weeks of age is a single dose of vaccine. Booster vaccinations should be administered every 6 months

In addition, inactivated BHV-1 virus is also a component of 2 vaccines that target pneumonia: Imuresp RP and Rispoval 4. These are targeted mainly at stock under 1 year of age. These combination vaccines have not been included in the estimate of uptake of IBR vaccines and are instead included in the estimated uptake of vaccines targeted at calf pneumonia.

## Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

All cattle are potentially at risk of IBR. Common industry practice would be for cattle to be vaccinated for the first time before the age of 1 year, with 1 dose of IBR vaccine.

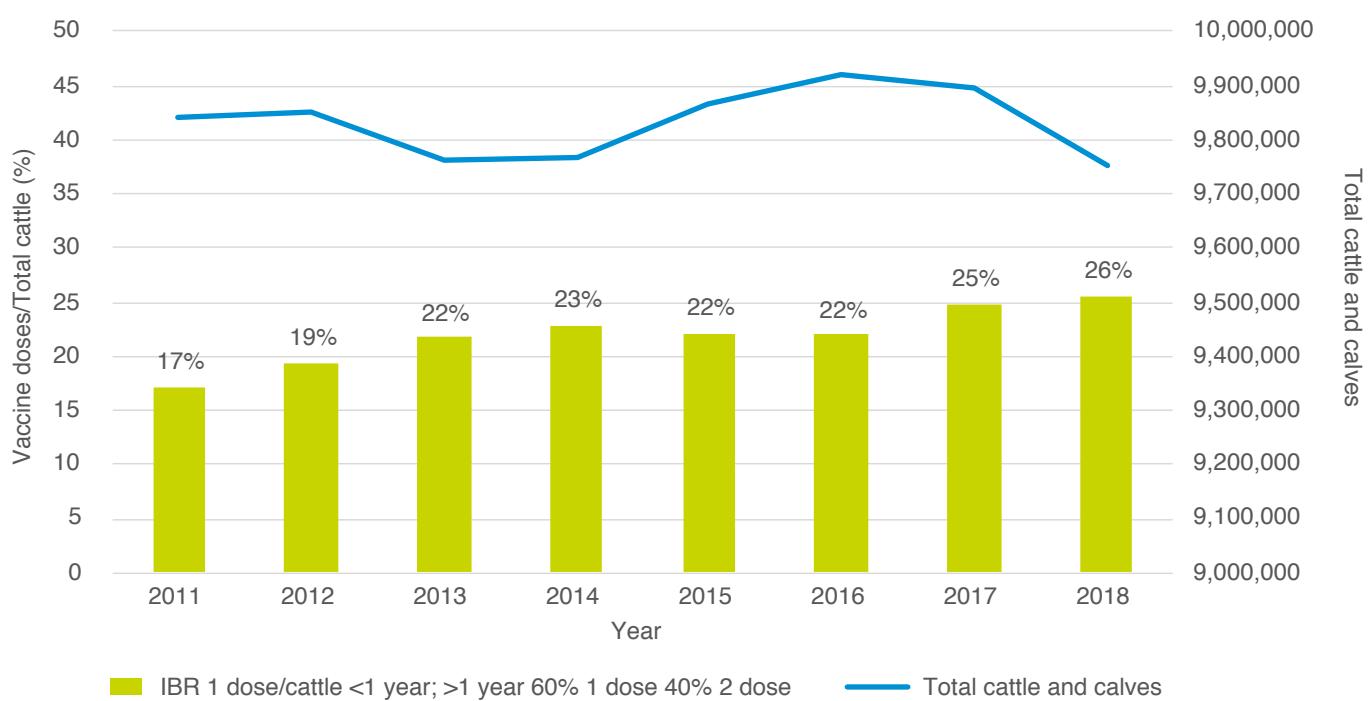


Figure 2. IBR vaccination uptake

Around 40% of farmers who use IBR vaccines in cattle over 1 year of age give 2 boosters annually, but around 60% only give 1 IBR booster vaccine per year.

**Denominator:** It was assumed that cattle of all ages should be vaccinated and that the at-risk population was all cattle and calves in the UK.

### Vaccination uptake

The number of doses of IBR vaccines sold in 2018 was up 1% on 2017. IBR vaccine uptake has increased from 17% in 2011, to a high in 2018, when it was estimated that over 1 in 4 (26%) of all cattle in the UK were vaccinated against IBR. This is an estimate of vaccine uptake and if, for instance, all cattle over the age of 1 year received 1 annual booster vaccination (instead of just 60% of these animals), the vaccination uptake in 2017 would be 1 in 3 (33%) of all cattle.

In 2017, the proportion of adult breeding cows in herds that are in IBR programmes operated by cattle health schemes conforming to CHeCS was just over 2%. Some of these herds will be in the Vaccinated Monitored Free Programmes and using IBR marker vaccines. Excluding the breeding females in these herds from the population of cattle that could have been vaccinated would have made little difference to the figures for vaccine uptake and would have been within the margins of error for the current estimate.

### Leptospirosis vaccines

Leptospirosis is a zoonotic disease caused by bacteria of the *Leptospira* genus. It is a common infection in dairy and beef herds and causes infertility, abortion and poor milk yield. In the UK, the two most important types of Leptospira are *Leptospira borgpetersenii* serovar *Hardjo* and *L. interrogans* serovar *Hardjo*. Infection arises from contact with infected urine or the products of abortion.<sup>3</sup>

**The cost:** £5–25m<sup>3</sup> to the national herd in health and productivity.

Two vaccines for leptospirosis were marketed in the UK between 2011 and 2018:

- **Leptavoid-H** contains inactivated *L. interrogans* serovar *Hardjo* and *L. borgpetersenii* serovar *Hardjo*. The primary course consists of 2 doses with an interval of 4–6 weeks between them. A booster with a single dose should be given annually
- **Spirovac** contains inactivated *L. borgpetersenii* serovar *Hardjo* type *hardjobovis*. The primary course consists of 2 doses with an interval of 4–6 weeks between them. A booster with a single dose should be given annually

### Assumptions

**Numerator:** The number of doses administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

Common industry practice is to give breeding heifers a primary course of vaccination (2 doses) before first service between the ages of 1 and 2 years and to give all breeding females over 2 years of age a single annual booster vaccination.

**Denominator:** It was assumed that only female breeding animals should be vaccinated and that the at-risk population was all female cattle between 1 and 2 years of age and the total female breeding herd over 2 years of age.

## Vaccination uptake

The leptospirosis vaccine was generally taken up by around 1 in 3 of all breeding cattle over the age of 1 year between 2011 and 2017, but uptake was slightly higher in 2012 and 2014 (36% and 37%, respectively). In 2018, the estimated proportion vaccinated was 31%.

In 2017, the proportion of adult breeding cows in herds that are in leptospirosis programmes operated by cattle health schemes conforming to CHeCS was just over 1.7%. Excluding the breeding females in these herds from the population of cattle of over the age of 1 year that could have been vaccinated would have made little difference to the figures for vaccine uptake and would have been within the margins of error for the current estimate.

## Calf enteritis vaccines

Calf enteritis, or calf scour, is a common problem found on most cattle farms in the UK. It can be a major cause of poor growth and calf mortality.<sup>3</sup>

The incidence and severity of disease is highly dependent upon the level of colostral protection that a calf receives within the first 6 hours of life. Several vaccines have been developed to actively immunise cattle against various antigenic components, to induce serological and colostral antibody production. The antibodies in colostrum provide passive immunity to the newborn calf, provided the calf quickly obtains an adequate quantity of high quality colostrum.

**The cost:** £2–12m (*Escherichia coli* infections) and £9–12m (enteric disease)<sup>3</sup> to the national herd. It should be noted that this cost may not include all forms of calf enteritis.

Five vaccines for calf enteritis were marketed in the UK between 2011 and 2017:

- **Bovigen Scour** contains *E. coli* F5 (K99) adhesin antigen and inactivated rotavirus and coronavirus. One dose in the course of each pregnancy, given in the period between 12 and 3 weeks before calving is expected
- **Lactovac** contains *E. coli* K99/F41 and inactivated rotavirus and coronavirus. The primary vaccination course is 2 injections separated by an interval of 4–5 weeks between doses and allowing 2–3 weeks from the time of the second dose until the predicted date of calving. Revaccination is recommended during each subsequent pregnancy
- **Rotavec Corona Emulsion** contains *E. coli* F5 (K99) adhesin and inactivated rotavirus and coronavirus. A single injection should be given during each pregnancy, given in the period between 12 and 3 weeks before calving is expected
- **Trivacton 6** contains *E. coli* K99, Y, 31A and F41 antigens and inactivated rotavirus and coronavirus. The primary vaccination course is 2 injections separated by an interval of 2–4 weeks between doses and allowing 2 weeks from the time of the second dose until the predicted date of calving. Revaccination is recommended during each subsequent pregnancy 2 weeks before calving

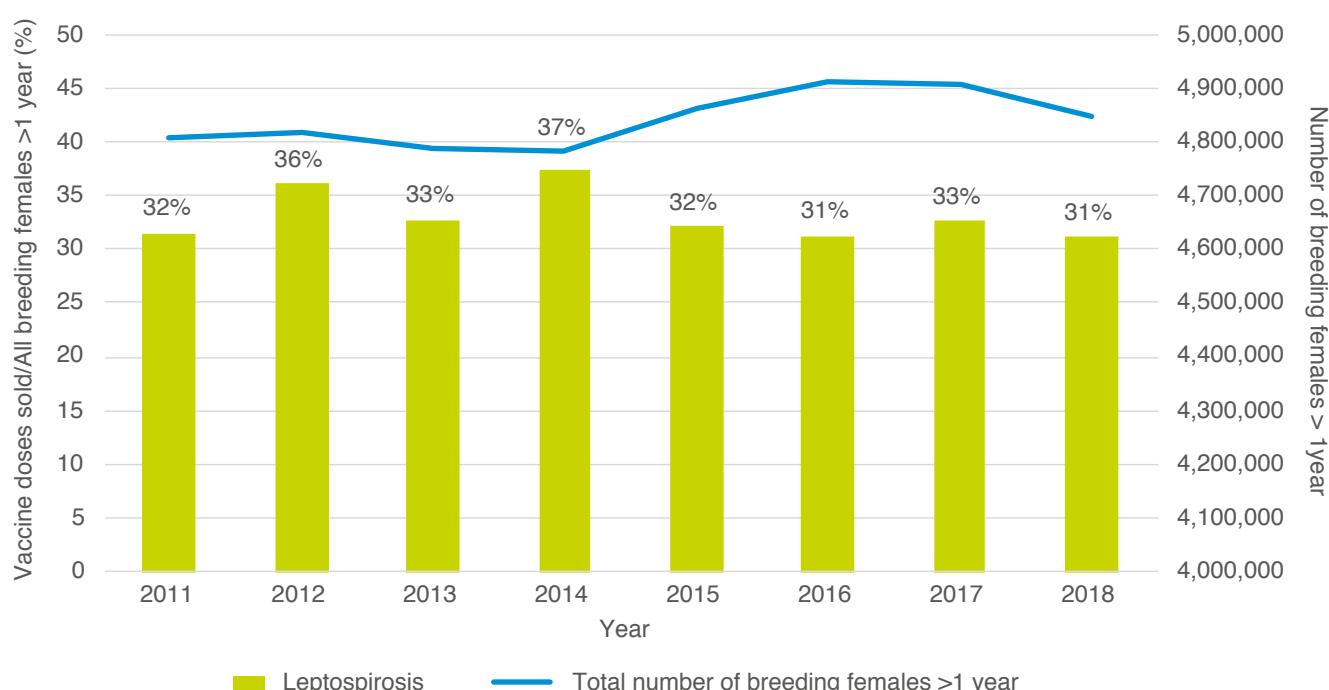


Figure 3. Leptospirosis vaccination uptake

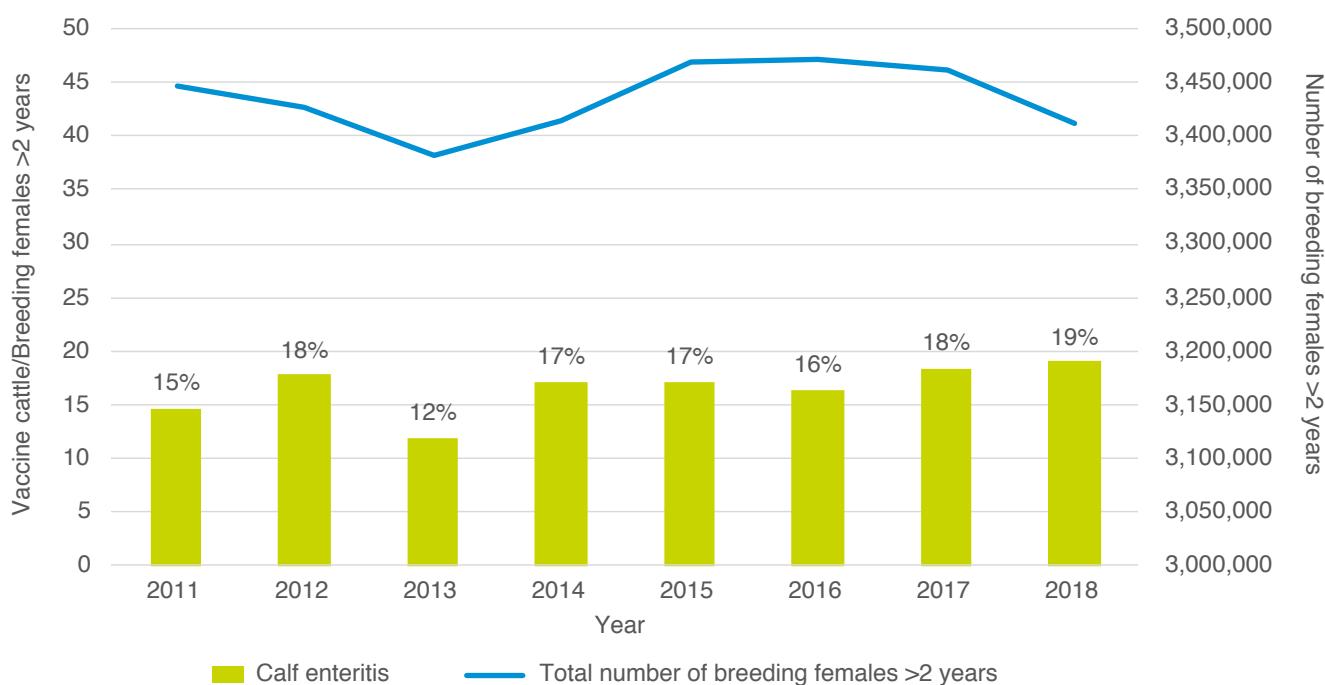


Figure 4. Calf enteritis vaccination uptake

### Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

Only 1 of these vaccines requires 2 doses as a primary vaccination course and, since common industry practice with these vaccines is to give only a single injection as the primary course and 1 injection per pregnancy thereafter, it was assumed that each pregnant animal should receive 1 dose per year.

**Denominator:** It was assumed that only female breeding animals should be vaccinated and that these vaccines would only be given to pregnant female breeding cattle. As most cattle calve down after 24 months and the vaccine is given in late pregnancy, only cattle over 2 years of age were included in the calculation.

The mean age of dairy cattle at first calving is falling<sup>4</sup> and a recent paper reported that almost 1 in 8 dairy heifers calved for the first time at 24 months of age or younger.<sup>5</sup> However, most dairy heifers joining the national herd will be replacing dairy cows being culled, which will not need to be vaccinated; the calving interval for UK-bred pedigree Holstein females was 405 days in 2017.<sup>4</sup> For ease of calculation, it was considered acceptable to use the population of all female cattle over 2 years of age as the target population for this vaccine.

### Vaccination uptake

Uptake of calf enteritis vaccines was the lowest among all the categories of vaccine in this report, with just under 1 in 6 breeding cows vaccinated, on average, between 2011 and 2017. Uptake ranged from a low of 12% in 2013, to over 18% in 2017. The estimated proportion of breeding cows vaccinated increased by 1% to 19% in 2018.

### Pneumonia vaccines

Pneumonia is caused by infections of the respiratory tract by viruses and/or bacteria. Respiratory disease occurs most commonly when either bacterial and/or viral agents are combined with poor air quality and ventilation, poor husbandry and/or stress.<sup>6</sup> Financial losses result from mortality (pneumonia is a major cause of mortality in the first year of life), extra labour and treatment costs, but the greatest loss is from weight loss during illness and recovery.

An effective vaccination strategy for the most common causes of pneumonia on a farm can be an important part of the herd health plan to prevent respiratory disease, in combination with good management and appropriate building design and ventilation.

**The cost:** £80m per year<sup>6</sup> to the national herd (£30 per mild case, £500 when the animal dies).

Twelve vaccines for pneumonia were marketed in the UK between 2011 and 2018:

- **Bovalto Pastobov** contains *Mannheimia haemolytica* type A1 antigen. The primary vaccination course is 2 injections separated by an interval of 3–4 weeks between doses. Revaccination is recommended before each risk period and no more than 12 months after previous vaccination
- **Bovalto Respi 3** contains inactivated *M. haemolytica* A1 and inactivated Bovine respiratory syncytial and Parainfluenza 3 viruses. The primary vaccination course is 2 injections separated by an interval of 3 weeks between doses. Revaccination is recommended 6 months after the primary vaccination course

- **Bovalto Respi 4** contains inactivated *M. haemolytica* A1 and inactivated Bovine respiratory syncytial, Parainfluenza 3 and BVD viruses. The primary vaccination course is 2 injections separated by an interval of 3 weeks between doses. Revaccination is recommended 6 months after the primary vaccination course
- **Bovalto Respi Intranasal** contains modified live Bovine respiratory syncytial virus and Parainfluenza 3 virus. The vaccination course is 1 dose of the vaccine intranasally
- **Bovilis® Bovipast RSP** contains inactivated *M. haemolytica* A1 and inactivated Bovine respiratory syncytial and Parainfluenza 3 viruses. The primary vaccination course is 2 injections separated by an interval of around 4 weeks between doses. If needed, revaccination is recommended 2 weeks before each risk period
- **Hiprabovis SOMNI/Lkt** contains inactivated *M. haemolytica* leukotoxin and inactivated *Histophilus somni*. The primary vaccination course for cattle over 2 months of age is 2 injections separated by an interval of 3 weeks between doses
- **Imuresp RP** contains modified live Parainfluenza 3 virus and Bovine herpesvirus type 1 (BHV-1) virus. The primary course of vaccination for cattle over 10 weeks of age is a single dose. Revaccination every 6 months is recommended
- **Rispoval 3** contains modified live Bovine respiratory syncytial virus and Parainfluenza 3 virus and inactivated BVD virus. The primary course of vaccination for cattle over 12 weeks of age is 2 doses 3–4 weeks apart. If needed, revaccination every 6 months is recommended
- **Rispoval 4** contains modified live Bovine respiratory syncytial virus and Parainfluenza 3 virus and inactivated BVD virus and BVH-1. The primary course of vaccination for cattle over 12 weeks of age is 2 doses 3–4 weeks apart. If needed, the same vaccination scheme is recommended at least 14 days before the period of expected disease challenge
- **Rispoval® Pasteurella** contains inactivated *M. haemolytica*. The primary course of vaccination for cattle over 12 weeks of age is a single dose. If needed more than 17 weeks after previous vaccination, a single vaccination is recommended at least 7 days before the period of expected disease challenge
- **Rispoval RS** contains modified live Bovine respiratory syncytial virus. The primary course of vaccination for cattle over 4 months of age is 2 doses 3–4 weeks apart
- **Rispoval RS+PI3 Intranasal** contains modified live Bovine respiratory syncytial virus and Parainfluenza 3 virus. The vaccination course is 1 dose of the vaccine intranasally

### Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

The recommended primary vaccination course for these vaccines was used to estimate the number of cattle vaccinated in each calendar year.

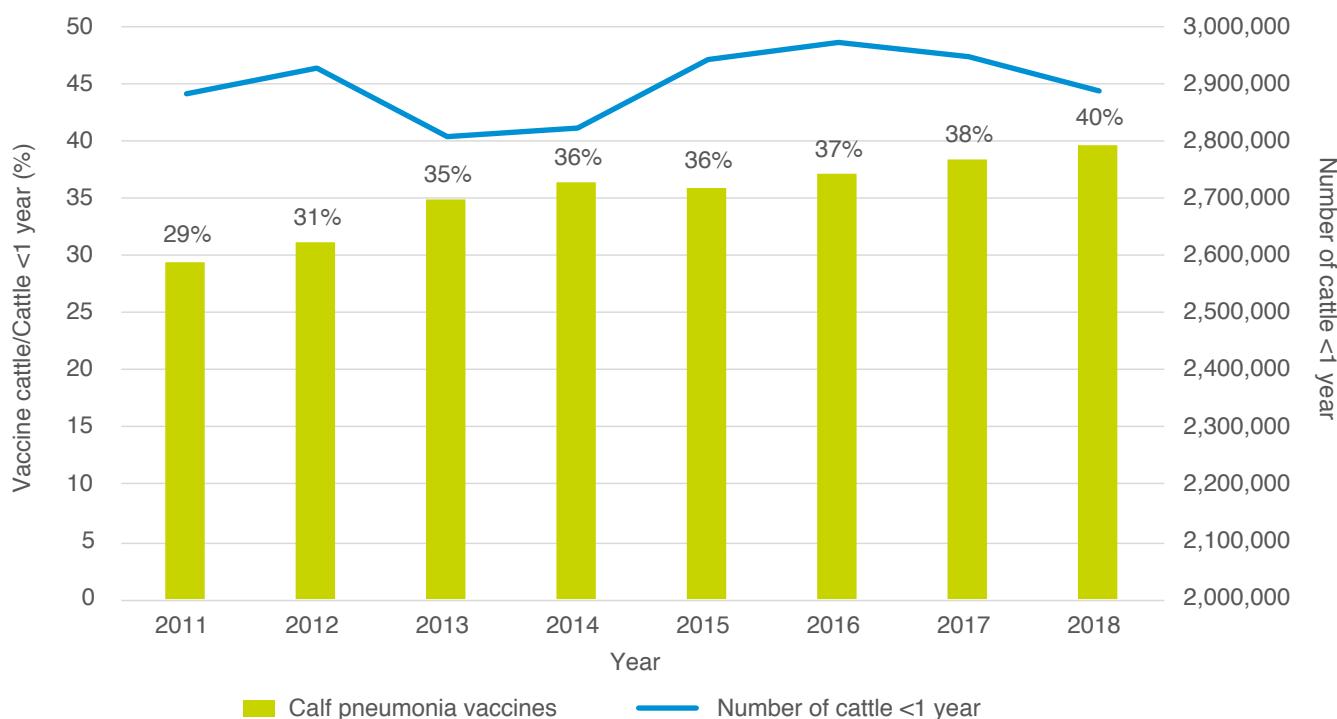


Figure 5. Pneumonia vaccination uptake



**Denominator:** With these vaccines, the common industry practice is to only vaccinate animals in the first year of life. It was assumed that only animals under 1 year of age should be vaccinated; the total population of cattle under 1 year of age was used as the denominator for the target population.

### Vaccination uptake

The uptake of vaccines for pneumonia rose steadily, from 29% in 2011 to 38% in 2017 – an increase of 30%. This was the largest increase in vaccine uptake for the vaccines in this report. The proportion of cattle vaccinated increased further to 40% in 2018 – a 3% increase on 2017.

### Summary

For the cattle vaccines monitored in this report, the total number of doses sold increased by 20% between 2011 and 2017. Sales of vaccines peaked in 2014 and only recovered that level again in 2017. Sales of vaccines dropped by 3% between 2017 and 2018, but were still 16% higher than in 2011.

The drop in uptake in 2015 and 2016 may be related to the collapse in milk prices and in dairy farmer incomes. The fall in the number of vaccine doses sold in 2018 related to reduced sales of BVD and leptospirosis vaccines. There was limited availability of 1 BVD vaccine in 2018. Fluctuations in vaccination rate may relate to issues that affect farmer incomes, such as milk and

meat prices: when incomes fall and overdrafts are under pressure, cost-cutting may lead some farmers to spend less on vaccinations. Other factors may contribute to fluctuations in vaccine sales, but these are outside the scope of this report.

Sales from wholesalers do not necessarily equate to use in that year; estimates of vaccine uptake are necessarily crude because there will have been some use of vaccines in animals outside the denominator population against which vaccine uptake was measured. However, it is still a useful measure of the likely level of protection in the target group.

The analysis includes no estimate of how effectively vaccines were used in cattle. For example, in one survey only 48% of respondents stated that they administered the second dose in the primary course within the recommended timeframe. Fourteen per cent of respondents stated that they vaccinated earlier than the youngest recommended age.<sup>7</sup> Another study found that most fridges used to store vaccines would have failed to keep any stored live vaccines within the recommended storage temperature range.<sup>9</sup>

It is interesting to note that the only vaccine for which there was no drop in uptake in 2015 and 2016 was that for calf pneumonia; there was also little change in the uptake of IBR vaccines. The biggest increase in vaccine uptake between 2011 and 2018 was also for IBR (43%) and calf pneumonia (35%). Overall, there has been an upward trend in the sales of these vaccines since 2011.

In cattle, pneumonia is thought to be responsible for a considerable, but unknown, proportion of antibiotic use. Given the focus on the responsible use of antibiotics, it is promising that farmers may have prioritised spend on these vaccines.

If we exclude the 18% of breeding cattle in herds accredited free of BVD to CHeCS standards that cannot use vaccines, then sufficient vaccine doses were potentially used to cover over 50% of breeding cows. This suggests that around 70% of herds are engaged in either vaccination or accreditation to protect their herds from BVD. In turn, this supports the UK-wide

efforts being made to eliminate BVD. The drop in vaccine uptake, from an estimated 45% of eligible animals in 2017 to 42% in 2018, may have been the result of issues with the supply of 1 BVD vaccine.

Vaccines are important in helping both the beef and dairy cattle sectors to meet industry targets to use antibiotics more responsibly. There was a small fall (2.9%) in vaccine sales in 2018, which was within the margin of error of the analysis performed. The number of doses sold was 16% higher than in 2011 and the third highest recorded in the period.

**Table 1. Vaccine uptake in cattle between 2011 and 2018**

Vaccine uptake in cattle	2011	2012	2013	2014	2015	2016	2017	2018
<b>Cattle &lt; 1 year</b>								
Total number	2,882,124	2,925,381	2,805,692	2,821,564	2,939,446	2,970,831	2,948,192	2,888,432
Calf pneumonia vaccines (%)	29	31	35	36	36	37	38	40
<b>Cattle and calves</b>								
Total number	9,840,128	9,850,583	9,762,925	9,765,127	9,867,061	9,919,436	9,895,124	9,750,599
IBR (%)	17	19	22	23	22	22	25	26
<b>Breeding females &gt;1 year</b>								
Total number	4,809,144	4,819,572	4,786,670	4,784,923	4,861,441	4,911,714	4,908,701	4,846,743
BVD (%)	42	44	45	48	45	43	45	42
Leptospirosis (%)	32	36	33	37	32	31	33	31
<b>Breeding females &gt; 2 years</b>								
Total number	3,447,349	3,425,541	3,381,793	3,414,746	3,470,189	3,471,979	3,461,981	3,411,519
Calf enteritis (%)	15	18	12	17	17	16	18	19
<b>Doses of vaccine sold</b>								
Total	8,462,739	9,348,562	9,325,950	10,135,160	9,694,725	9,557,830	10,133,805	9,839,155

# The use of vaccines in sheep

## Clostridial vaccines

Clostridial disease is the most common cause of sudden death in all ages of sheep in the UK. Examples of clostridial diseases include pulpy kidney disease (*Clostridium perfringens* type D), lamb dysentery (*C. perfringens* type B), struck (*C. perfringens* type C), braxy (*C. septicum*), black disease (*C. novyi*), and botulism (*C. botulinum*). With clostridial diseases, it is not the bacteria that cause disease but the toxins they produce. Cheap and highly effective multivalent vaccines are available; however, deaths caused by clostridial diseases remain high, resulting in considerable losses to the sheep industry.

The following multivalent clostridial vaccines have been marketed in the UK:

- **Bravoxin 10** is a multivalent clostridial vaccine for cattle and sheep. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered at 6–12-month intervals. If the dam has received a full primary vaccination course before pregnancy and receives a booster eight to two weeks before parturition, she can provide the newborn lamb with passive immunity via the colostrum
- **Covexin 8** is a multivalent clostridial vaccine for cattle and sheep. The primary vaccination course for sheep and lambs over 8 weeks of age is a 5 ml initial dose followed by a 2 ml dose 6 weeks later. A booster dose should be administered at 12-month intervals. If the dam has received a full primary vaccination course before pregnancy and receives a booster six to two weeks before parturition, she can provide the newborn lamb with passive immunity via the colostrum
- **Covexin 10** is a multivalent clostridial vaccine for sheep. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered at 6–12-month intervals. If the dam has received a full primary vaccination course before pregnancy, and receives a booster eight to two weeks before parturition, she can provide the newborn lamb with passive immunity via the colostrum
- **Heptavac P Plus** is a multivalent clostridial vaccine for sheep that can also aid in the control of pneumonic and systemic pasteurellosis. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered at intervals of not more than 12 months. If the dam has received a full primary vaccination course before pregnancy and receives a booster six to four weeks before parturition, she can provide the newborn lamb with passive immunity via the colostrum
- **Lambivac®** is a multivalent clostridial vaccine for sheep and pigs. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered within 12-month intervals. If the dam has received a full primary vaccination course before pregnancy and receives a booster six to four weeks before parturition, she can provide the newborn lamb with passive immunity via the colostrum
- **Ovivac P Plus** is a multivalent clostridial vaccine for sheep that can also aid in the control of pneumonic and systemic pasteurellosis. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered within 12-month intervals

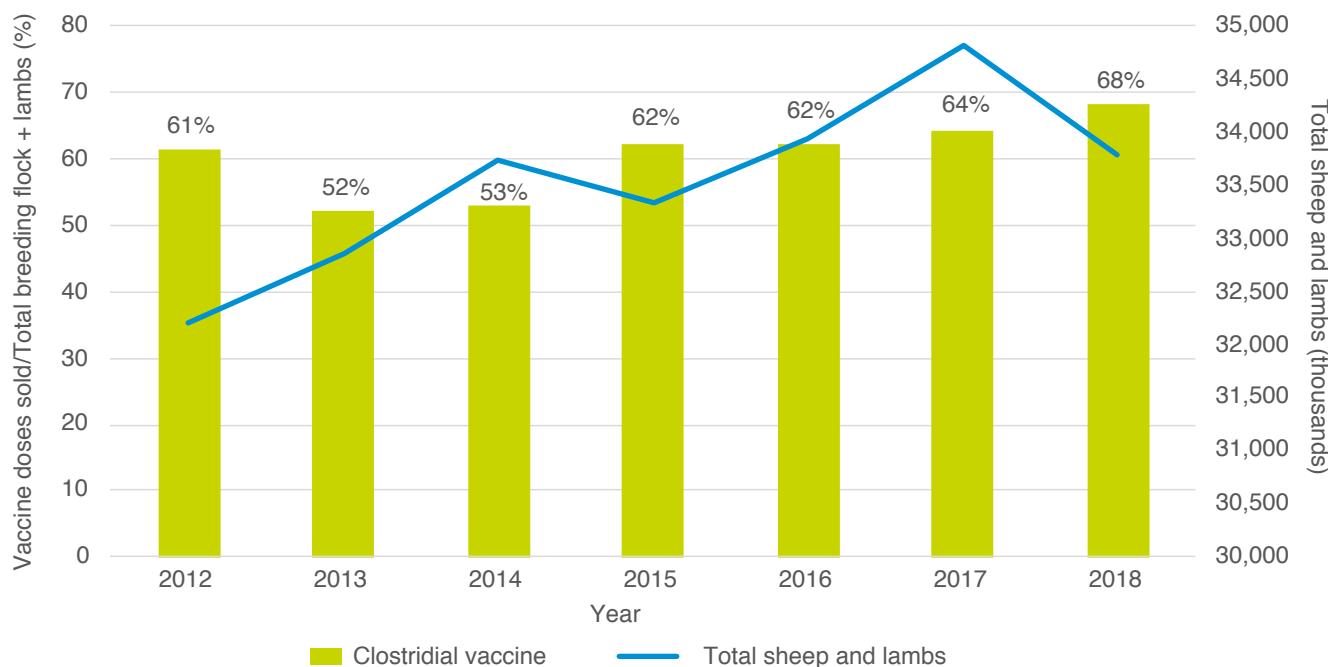


Figure 6. Clostridial vaccine uptake

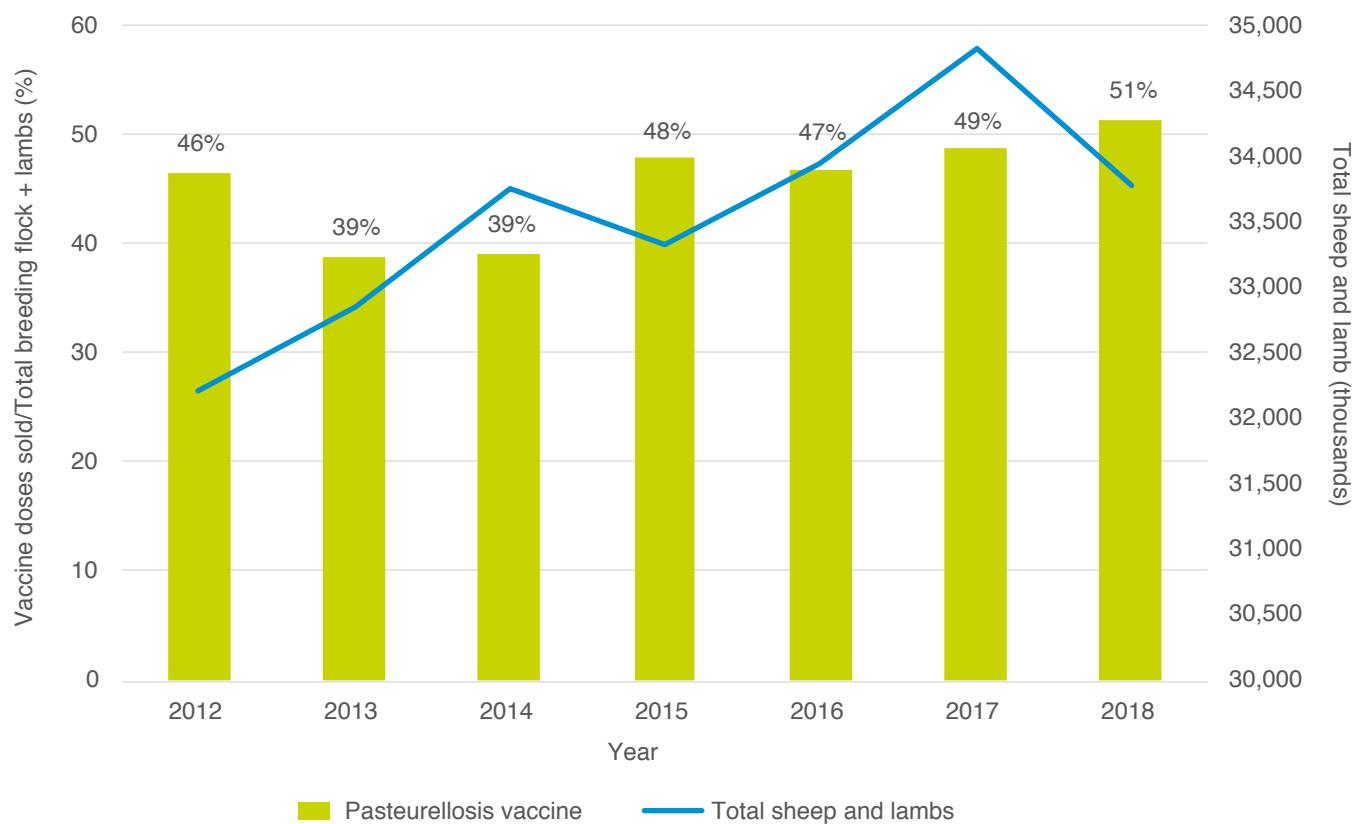
## Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack. For Covexin 8, a higher dose is used as the first dose in the primary vaccination course. It has been assumed that 20% of all doses of Covexin 8 are used in primary vaccination courses and that half of these are administered at the higher dose level. Bravoxin and Covexin 8 are also licensed for use in cattle. It has been assumed that 80% of the use of these vaccines is in sheep and the remainder in cattle. A small amount of clostridial vaccine is also used in pigs but this is not considerable.

**Denominator:** The common industry recommendation is to vaccinate lambs with a primary course of clostridial vaccine, unless they are destined for slaughter before 12 weeks of age and their mother was given a booster vaccine in late pregnancy. It is recommended that all adult sheep should be given a primary course and receive an annual booster. The total number of clostridial vaccine doses that would be required by the national UK flock has been estimated based on the assumption that all lambs in flocks in June should receive 2 doses of clostridial vaccine and that the total breeding flock and all rams should get 1 annual booster vaccination.

## Vaccination uptake

Clostridial vaccine uptake dropped from 61% of the estimated vaccine doses required in 2012, to 52% in 2013 – the lowest level of uptake over the period 2012–2018. In the 5 years since 2013, there has been a steady increase in uptake, with a high of 68% in 2018.



## Pasteurellosis

Bacteria previously identified as being *Pasteurella* species have been reclassified; the main species causing disease in sheep are now called *Mannheimia haemolytica* (previously *P. haemolytica*) and *Bibersteinia trehalosi* (previously *P. trehalosi*). *M. haemolytica* commonly causes either septicaemia in young lambs or pneumonia in all ages of sheep, but especially in lambs. *B. trehalosi* is most commonly associated with septicaemia in older lambs. Pasteurellosis is one of the most common causes of death in growing lambs in Great Britain (GB)<sup>8</sup>, despite there being effective vaccines that offer protection against disease caused by both *M. haemolytica* and *B. trehalosi*.

**The cost:** £7–15m per year of acute enzootic pneumonia to the GB national flock in 2015.<sup>9</sup>

Most of the vaccines marketed in the UK for the control of pneumonic and/or systemic pasteurellosis are in combination with vaccines for clostridial diseases:

- **Heptavac P Plus** is a multivalent clostridial vaccine for sheep that can also aid in the control of pneumonic and systemic pasteurellosis. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered at intervals of not more than 12 months. To provide passive protection for lambs via the colostrum, it is recommended to give a single booster dose to the dam between six and four weeks before parturition, provided that she received a full primary vaccination course before pregnancy

Figure 7. Pasteurellosis vaccine uptake

- **Ovipast Plus** is a vaccine for the active immunisation of sheep as an aid in the control of pasteurellosis caused by *M. haemolytica* and *B. trehalosi*. It may be used as an aid in the control of pneumonic and systemic pasteurellosis. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered at intervals of not more than 12 months. In adult breeding ewes, these yearly booster injections should be given during the pre-lambing period, 4–6 weeks pre-lambing, as an aid in the control of pasteurellosis in their lambs
- **Ovivac P Plus** is a multivalent clostridial vaccine for sheep that can also aid in the control of pneumonic and systemic pasteurellosis. The primary vaccination course is 2 doses of vaccine separated by a 4–6 week interval. A booster dose should be administered at intervals of not more than 12 months

## Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

**Denominator:** The common industry recommendation for farms on which pasteurellosis is an issue is to vaccinate lambs with a primary course of pasteurella vaccine, unless they are destined for slaughter before 10 weeks of age and their mother was given a booster vaccine in late pregnancy. On such farms, it is recommended that all adult sheep should be given a primary course and receive an annual booster. The total number of vaccine doses that would be required to protect the national UK flock from pasteurellosis has been estimated based on the assumption that all lambs in flocks in June should receive 2 doses of vaccine and that the total breeding flock and all rams should get 1 annual booster vaccination.

## Vaccination uptake

The uptake of vaccines to provide protection to sheep from pasteurellosis follows a similar trend to that of clostridial vaccines. This is not surprising given that the main vaccines used are combination clostridia–pasteurellosis vaccines. Uptake dropped from 46% of the estimated vaccine doses required in 2012, to 39% in 2013 – the lowest level of uptake over the period 2012–2018. Uptake recovered to 48% in 2015 and reached its highest level, 51%, in 2018.

## Abortion

Control of enzootic abortion is 1 of 3 hotspot areas for the reduction of antibiotics in the sheep industry, as identified in the RUMA Targets Task Force Report 2017. Reduced abortion can be achieved by improving the uptake of existing effective vaccination strategies.

The 3 main infectious causes of abortion, which have been consistent over the last 5 years, are:

- **Enzootic abortion of ewes (EAE) caused by *Chlamydia abortus***
- **Toxoplasmosis**
- **Campylobacter spp.**

Although the epidemiology of these three infections are very different, any one of them can cause outbreaks of abortion in flocks. In an outbreak, up to 40% of ewes may either abort or produce weak, poorly viable lambs.

**The cost:** £11–48m per year in 2005<sup>3</sup> for enzootic abortion to the national flock

Effective vaccines against EAE and toxoplasmosis are available:

- **Enzovax** is a live vaccine for the active immunisation of susceptible breeding female sheep against *C. abortus* infection. Sheep should receive 1 dose of vaccine as a primary vaccination. Shearlings and older ewes should be vaccinated during the 4-month period before mating; ewe lambs intended for breeding may be vaccinated from 5 months of age. Vaccination must take place at least 4 weeks before mating. Revaccination is recommended every 3–4 years depending on farm management practices and conditions
- **Cevac® Chlamydia** is a live vaccine for the active immunisation of susceptible breeding female sheep against *C. abortus* infection. Sheep should receive 1 dose of vaccine as a primary vaccination. Shearlings and older ewes should be vaccinated during the 4-month period before mating; ewe lambs intended for breeding may be vaccinated from 5 months of age. It may be useful to perform a booster vaccination after 3 lambings or 4 years
- **Mydiavac** is an inactivated vaccine for the active immunisation of susceptible breeding female sheep against *C. abortus* infection. Sheep should receive 1 dose of vaccine as a primary vaccination. Animals should be vaccinated approximately 1 month before tupping, or from 4 weeks after the ram is removed. It is recommended that the vaccination should be repeated 771 days after the initial vaccination
- **Toxovax** is a live, concentrated vaccine containing tachyzoites of the S48 strain of *Toxoplasma gondii*. Sheep should be given a single dose at least 3 weeks before mating. Shearlings and older ewes should be vaccinated during the 4-month period before mating; ewe lambs intended for breeding may be vaccinated from 5 months of age. Vaccination must take place at least 4 weeks before mating. Revaccination is recommended after 2 years, as a single dose at least 3 weeks before mating

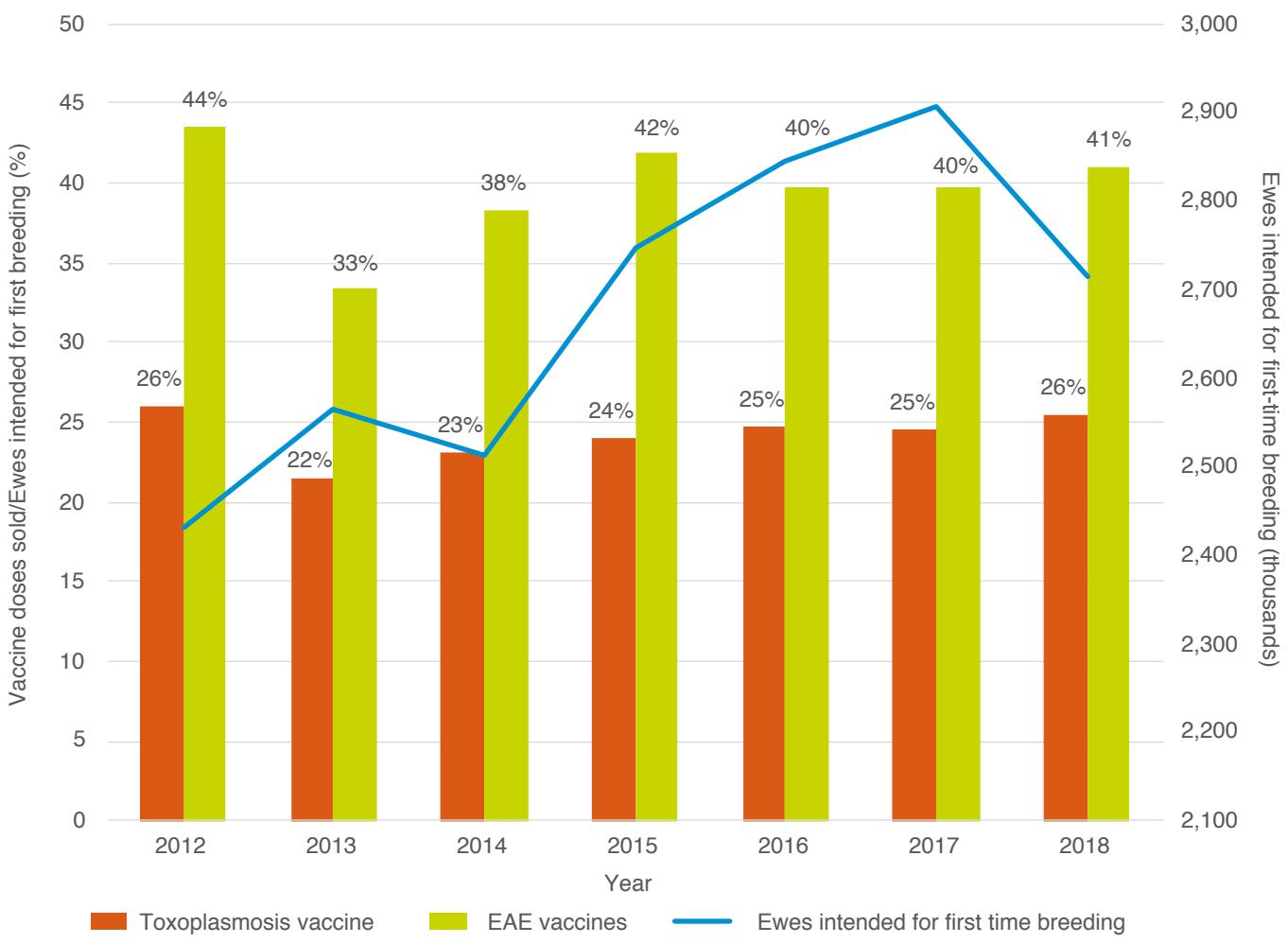


Figure 8. Toxoplasmosis and EAE vaccine uptake

## Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

**Denominator:** The common industry recommendation is to vaccinate all breeding females before the first joining with the ram. Although revaccination is recommended after 3–4 years, it is not considered that a considerable amount of vaccine is used in this way. The total number of vaccine doses that would be required to protect the national UK flock from EAE and toxoplasmosis has been estimated based on the assumption that all ewes intended for first-time breeding in June should receive a dose of vaccine.

It is accepted that this denominator is probably an underestimation of the actual number of ewes that should receive vaccination, but it was chosen for both simplicity and repeatability.

## Vaccination uptake

The estimated proportion of ewes intended for first-time breeding that were vaccinated for EAE was highest at 44% in 2012. This dropped to 33% in 2013, recovered to 42% in 2015, dropped back slightly to 40% in 2016 and 2017 and was 41% in 2018.

The estimated proportion of ewes intended for first-time breeding that were vaccinated for toxoplasmosis was 26% in 2018, as it was in 2012. The uptake of toxoplasmosis vaccination dropped to an estimated 22% in 2013 before recovering.

Some of the decrease in abortion vaccine sales could be attributed to vaccine supply issues. The manufacture of these live vaccines is known to be complicated and the timing for administration is generally concentrated over a short time period, just before the breeding season. In recent years, there have been several occasions when whole batches of vaccine have failed quality control and supply has been limited at key times of the year.

## Lameness

Lameness in sheep flocks is one of the most common and persistent disease problems, with scald, foot rot (caused by *Dichelobacter nodosus*) and contagious ovine digital dermatitis (caused by treponemes) being common causes. It is unrealistic to expect that a flock will never have lame sheep, but it is important that the infectious nature of lameness is fully understood so that careful control might prevent the number of cases from escalating.

**The cost:** £24m per year<sup>3</sup> (foot rot) and a 10% lameness prevalence reduces profitability by £6–14 per ewe.<sup>10,11</sup>

The Five Point Plan<sup>1</sup> is the current sheep industry-accepted standard for lameness control. It usefully summarises the tools that are available for lameness control in sheep flocks.

1. Cull badly or repeatedly affected animals.
2. Quarantine incoming animals.
3. Treat clinical cases promptly.
4. Avoid transmission of infection on farm.
5. Vaccinate against foot rot biannually.

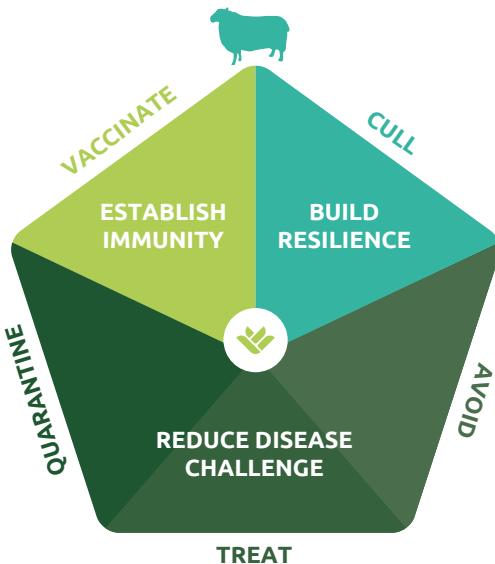


Figure 9. The Five Point Plan

Lameness poses a considerable animal welfare and economic challenge to the sheep sector.<sup>12</sup> Most of these costs are attributed to reduced flock performance, but some are associated with the time spent catching and

treating lame sheep. A report published by the Farm Animal Welfare Council (FAWC)<sup>13</sup> estimated that about 3 million sheep or 10% of the national flock are lame at any one time.<sup>10,11</sup>

With two-thirds of antibiotics used on sheep farms considered to be used in the control of infectious lameness<sup>14</sup>, improved lameness control is one of three hotspot areas for the reduction of antibiotics in the sheep industry, as identified in the RUMA Targets Task Force Report 2017.<sup>14</sup> This target is to be achieved by increasing awareness and uptake of the Five Point Plan. One way to measure uptake of the Five Point Plan is to measure usage of foot rot vaccination. The common industry recommendation is that vaccination should be considered in flocks that have lameness levels caused by foot rot of over 2%.<sup>16</sup>

Only 1 foot rot vaccine is available:

- **Footvax** is a vaccine for the active immunisation of sheep as an aid to the prevention of foot rot and reduction of lesions of foot rot caused by serotypes of *D. nodosus*. The primary vaccination course is 2 doses of vaccine separated by a 6-week interval. Vaccination programmes should be tailored to meet individual flock requirements, which will vary from season to season according to the actual or likely incidence of foot rot. A booster dose should be administered at intervals of not more than 12 months

### Assumptions

**Numerator:** The number of doses of vaccine administered has been calculated by multiplying the number of packs sold by the number of doses per pack.

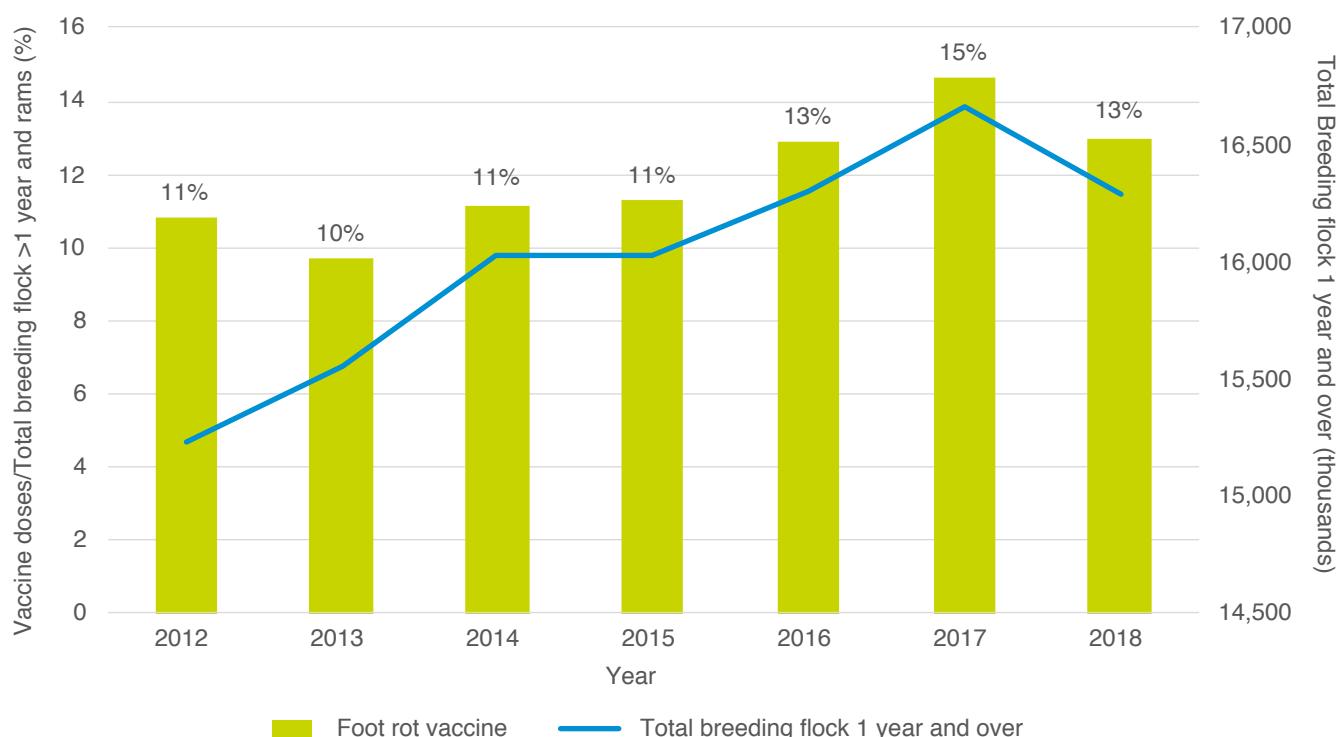


Figure 10. Foot rot vaccination uptake

**Denominator:** Although there are flocks for which lameness is well controlled and foot rot vaccination is not necessary, for the purposes of this report it was decided that for a denominator, all ewes intended for first-time breeding should receive 2 doses of vaccine as a primary course and that older ewes would be vaccinated at least once a year. Rams appear to be particularly susceptible to infectious lameness and, since the mobility of rams is critical to their breeding performance, it was considered that all rams should be vaccinated for foot rot twice a year. The total number of vaccine doses that would be required to help prevent foot rot in the national UK flock has been estimated based on the assumption that all ewes intended for first-time breeding and all rams should receive 2 doses of vaccine and that all ewes intended for further breeding or slaughter receive an average of 1 dose. Ewes that are culled without being vaccinated are likely to be balanced by those ewes receiving additional doses in times of higher risk.

### Vaccination uptake

The estimated proportion of the target population that was vaccinated averaged 11% between 2012 and 2015. This rose to its highest level of 15% in 2017 and dropped back to 13% in 2018, though the very dry summer may have meant that farmers took a decision not to vaccinate due to lower risk factors for disease spread in dry underfoot conditions. Achieving the RUMA target to increase uptake of the Five Point Plan to control lameness, measured by an increase in foot rot vaccine sales of 5% per year over 5 years, remains a challenge, although this was previously achieved between 2013 and 2017.

### Summary

The total number of sheep vaccine doses sold, which are monitored in this report, increased by 16% between 2012 and 2018. The volume of vaccine sold dropped by 13% between 2012 and 2013 though by 2018, the volumes sold were 34% higher than 2013. This does not count clostridial and pasteurellosis vaccines separately – in most cases, these vaccines are sold as a combination vaccine.

The proportion of abortion vaccines given to first-time breeding ewes increased from 2013 to 2015 and, since then, have remained largely static at 1 in 4 replacement ewes vaccinated against toxoplasmosis and 2 in 5 replacement ewes vaccinated against enzootic abortion. In 2018, sales of foot rot vaccines dropped back to 2016 levels, having peaked in 2017, though, as discussed, the dry conditions may have contributed to this.

Although the RUMA targets aimed for the use of both foot rot and enzootic abortion vaccines to increase, there were some manufacturing and supply issues in 2018 and considerable uncertainty within the sheep sector – both of these could have caused a decrease in vaccine sales.

The number of doses of vaccines sold for clostridial diseases and pasteurellosis were the highest of the entire period and over one-third higher than in 2013. Pasteurellosis is thought to be responsible for a considerable, but unknown, proportion of the antibiotic use in sheep. Given the focus on responsible use of antibiotics, it is good to see increased uptake for these vaccines.

Table 2. Vaccine uptake in sheep between 2012 and 2018

Vaccine uptake in sheep	2012	2013	2014	2015	2016	2017	2018
<b>Sheep and lambs</b>							
Total number	32,214,916	32,856,476	33,743,346	33,336,590	33,942,509	34,831,991	33,780,817
Clostridial vaccine (%)	61	52	53	62	62	64	68
Pasteurellosis vaccine (%)	46	39	39	48	47	49	51
<b>Ewes intended for first-time breeding</b>							
Total number	2,430,862	2,563,725	2,511,330	2,745,937	2,843,833	2,907,449	2,713,993
Toxoplasma vaccine (%)	26	22	23	24	25	25	26
EAE vaccines (%)	44	33	38	42	40	40	41
<b>Breeding flock 1 year and over</b>							
Total number	15,229,456	15,561,296	16,026,113	16,023,715	16,303,891	16,669,431	16,285,553
Foot rot vaccine (%)	11	10	11	11	13	15	13
<b>Doses of vaccine sold</b>							
Total	33,304,866	28,785,486	30,456,271	35,018,208	36,058,143	38,371,472	38,678,889

As highlighted earlier, it should be noted that sales from wholesalers do not necessarily equate to use in that year; estimates of vaccine uptake are necessarily crude because there will have been some use of vaccines in animals outside the denominator population against which vaccine uptake was measured. However, it is still a useful measure of the likely level of protection in the target group.

The analysis includes no estimates about how effectively these vaccines are used in sheep, though it would not be unreasonable to expect that deviations from recommended regimes and storage conditions would be equivalent to findings within the cattle sector. Additional specific evidence of poor vaccine administration compliance has been demonstrated in the sheep sector in the use of the orf vaccine.<sup>17</sup>

Vaccines are important in helping the sheep sector to meet the industry targets to use antibiotics more responsibly. With this in mind, it is good to note that analysis of the sales data has shown that the sale of vaccines within the sheep sector increased in 2018.

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