RESPONSIBLE USE OF MEDICINES IN AGRICULTURE ALLIANCE

ruma

GUIDELINES

Responsible use of vaccines and vaccination in dairy and beef cattle production

A farm health planning initiative in partnership with DEFRA

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Introduction

As described in the companion RUMA guideline "Responsible Use of Vaccines and Vaccination in Farm Animal Production" all vaccines used in the EU have been registered for their current uses on the basis that they are effective and safe in animals and safe to the user. They help reduce the incidence of disease in animals by stimulating the immune system to provide protection. 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 animals do not become ill or signs are mild. This eliminates or reduces treatment costs, as well as preventing the reduction in growth, milk production or fertility that may otherwise result.

Several vaccines (for example those against salmonellosis, leptospirosis, ringworm) also act as a safeguard to human health by reducing the risk of zoonotic infection. This helps to ensure the health of those working with cattle by lowering disease levels. Health is essential for efficient performance and disease control is a key element of any successful management programme.

Treatment of disease is not as effective or as economical as prevention. Poor health status and subclinical disease can be a major cause of losses in all forms of dairy and beef production, including organic production. Many disease conditions can be avoided or minimised by using management practices that reduce exposure to disease, lower stress, and include good hygiene and biosecurity. Key management areas and the importance of an appropriate vaccination protocol are highlighted in these guidelines. Vaccination programmes are an important element in a comprehensive, well-planned herd health control strategy.

Cattle farmers and their veterinary surgeons will always aim to ensure that animals are kept in the best state of health and welfare. Whist this aim should never be compromised it is important to recognise that it is influenced by the profitability of the farming business.

The use of vaccines on all farms is usually under the supervision of a veterinary surgeon. It is, as described earlier, a legal requirement for farmers to keep a record of the administration of all vaccines and this record in a Medicines Book must be available for inspection. Farm assurance schemes' and Government inspectors audit compliance with the legislation. Farmers and veterinary surgeons have a shared responsibility to ensure that all medicines, including vaccines, are used correctly, efficiently and appropriately.

Principles of Vaccination

The aim of any vaccination policy in any species is to challenge the individual with a "controlled" dose of a potentially pathogenic organism (bacterium, virus, mycoplasma, fungus, etc) in order to stimulate an immune reaction that will prime the animal's immune system to respond quickly and effectively to any future field challenge. Thus, vaccination is designed **to prevent future disease – it will not necessarily prevent future infection.**

The immune system is highly complex. The ability to function to its potential can be compromised in several ways. Certain viruses, mycoplasmas, etc, can influence this response as can deficiencies in essential nutrients. Animals in poor bodily condition, lacking in essential micro-nutrients, stressed or suffering from concurrent disease rarely respond fully to invading pathogens or vaccines.

Vaccines work by stimulating the immune system without provoking disease. This is achieved by either inactivating the organism, by growing it in the laboratory in a succession of culture media (attenuation), and so when introduced into the body it provokes an immune response without causing disease. In the case of lungworm vaccine, husk larvae have been irradiated so that although they are still alive and active they do not complete their life cycle. Thus when given by mouth they go through all the life cycle except producing eggs and larvae. This stimulates the immune system but because of the controlled small number of larvae (1000 per dose) it does not provoke disease and the incomplete life cycle prevents other animals becoming infected by the vaccine. In some cases invading bacteria produce powerful toxins and these are treated chemically to inactivate them. This treated toxin is then used as a vaccine e.g. many clostridial diseases.

Usually the full response to a vaccine does not occur for about 14 days after administration of the initial course. Generally modified live viral vaccines provoke a satisfactory immune response with a single dose. Bacterial vaccines frequently require two doses to elicit a satisfactory response. This is referred to as a **primary course**. Timing between doses is fairly critical and a full response only occurs about 14 days after the second dose.

Adjuvants are added to some inactivated vaccines, these may be simple such as aluminum hydroxide, Quil A or in some cases an oil. These act by helping to present the antigen more directly to the immune system, slowing the dispersion from the injection site and some act directly by stimulating the immune response.
Vaccines work by mimicking the pathogen and so stimulating the immune response, but they fail to induce active disease because of inactivation or attenuation. Fit, well fed cattle respond well to vaccines; poor debilitated, parasitised animals and those suffering from disease do not.

The aim of each specific vaccination programme is to stimulate the particular responses most appropriate to the disease-causing organism concerned. It is also necessary to be aware of the response expected, as this may influence the speed of protection following vaccination.

Maternally Derived Antibody (MDA)

A correctly vaccinated dam will have circulating antibody (gammaglobulin) against the organism to which she has been immunised. The dam has the ability to concentrate certain antibodies in her colostrum. The amount of antibody depends on several factors including the nutritional state of the cow and the amount of circulating antibody. Also it depends on the breed and especially in high yielding cows the individual cow. Frequently the concentration in the colostrum exceeds that in the circulation. In the case of calves, antibody is absorbed for up to 24 to 36 hours but absorption starts to decrease after six hours. Thus the calf is protected against systemic disease, in particular those which strike in the first 21 days or so of life. MDA slowly fades; antibody to some infections persists longer than others. A common misconception is that immunity can be “boosted” by a dose of an appropriate vaccine to the calf. This is not the case as the gammaglobulins have been donated by the dam to the calf. As the calf has not been exposed and stimulated to produce these gammaglobulins they cannot be boosted.

In many species circulating maternal antibody seriously interferes with response to vaccines. In cattle there appears to be much less interference, certainly with the vaccines likely to be administered early in life. Generally, administration of vaccine can safely be delayed until the level of maternal antibody has waned.

Vaccination Classification

Vaccines may be classified according to the target species for disease control, by the disease or diseases they help control, type of vaccine or by their biological action e.g., attenuated live virus; killed; etc.

All vaccines aim to influence the animal's immune system and innate immune defence mechanisms in order to stimulate future protection against a disease or diseases. This is achieved by either administering a live, but attenuated (non-virulent or little virulence) form of the infectious organism**,** or by administering a killed version of the organism or a modified toxin. Killed vaccines are usually administered in combination with an adjuvant, a substance that helps and enhances the immunological effect of a drug. The purpose of the adjuvant is to stimulate a greater immune response (and therefore protective effect) to the killed or attenuated organism than would be the case without it.

As the vaccine relies on the animal mounting an adequate immune response it is important that the animal is not suffering any undue stress, caused by factors such as poor diet, housing or husbandry. The animal should be in good health and not suffering from any other disease. Sufficient time must be allowed to elapse between vaccinating and exposure to the natural infection.

Different vaccines may stimulate an immune response in different ways; therefore it is vital that the manufacturer's guidelines for timing of vaccination are closely followed. Many vaccines provide protection against a single disease (univalent). Unless authorised and otherwise stated on the Summary of Product Characteristics SPC or product literature, or following taking expert advice, these should not be administered alongside other vaccines, and should be used within their own defined programme. The mixing of vaccines should never be undertaken unless specifically authorised as the safety and efficacy of the combined product could be adversely affected.

Some vaccines provide protection against more than one strain or disease (multivalent). These vaccines have been specially developed to induce immunity against a number of pathogens or antigens and are highly effective at reducing diseases caused by a combination or range of pathogens. These vaccines must be used exactly as laid down in the Summary of Product Characteristics (SPCs) (data sheets) and must not be administered with any other vaccines or medicines unless the specific information has been obtained that such additions are acceptable and suitable.

The effect of some vaccination programmes can be monitored, depending on the organism and vaccine, by taking milk or blood samples (serology) and assessing the antibody levels thereby indicating the immune response mounted. This response is similar to that produced to natural infection with the disease organism and the two are usually indistinguishable. However, where it is important to be able to distinguish between immunity (antibodies) to vaccination and natural infection, if available, a marker vaccine should be used. At present, there are few cattle marker vaccines although a few are on the market for infectious bovine rhinotracheitis (IBR).

Marker vaccines can become important for herds with a designated "disease free status" and when trading with countries that are free from, or eradicating, these diseases. This is particularly of consequence since the lifting of the beef export ban as countries or regions undergoing eradication scheme(s) could seek derogations to prevent cattle importations unless there is at least some monitoring of some specific diseases such as IBR.

Methods of Administration

Vaccine Handling and Administration

- Clear instructions must be provided on the farm about the appropriate use and administration of vaccines and made available to all staff involved in vaccinating.
- Always follow the manufacturer's recommended instructions, including the administration routes and methods of administration, the schedule of vaccination and all safety precautions for the target species, user and environment including proper restraint of the animal.
- An animal medicines record book together with copies of relevant regulations and Codes of Practice **must** be kept on the farm.

Storage

Medicines must be stored according to the manufacturer's instructions. Most vaccines require refrigeration. Ideally a fridge specifically for storage of vaccines should be used. A poor alternative is that they may be stored in an airtight box in a fridge used for other purposes. The fridge should be kept clean and tidy and only sufficient vaccine suitably stored for the procedures to be undertaken in the near future. Where more than one vaccine batch is kept, ensure those with the shortest usage life are in front. Vaccines should be kept cool whilst used them on the farm by using e.g. cool boxes, polystyrene bottle sleeves.

As a general rule, unused or unwanted medicines must be disposed of according to manufacturer's instructions or returned to the veterinary surgeon or supplier for safe disposal.

Syringes

Disposable syringes are to be preferred. Where a large number of animals are to be vaccinated the use of vaccinator guns should be considered.

Needles

Always use a needle appropriate to the size of the animal being vaccinated, suited to the type of injection given subcutaneous (sc) or intramuscular (im) with as small a bore as possible practically. Needles must be sterile and sharp.

On no account should a needle be inserted into an animal and then reinserted into the bottle (this risks contaminating the remaining vaccine in the bottle). Where repeated doses are to be extracted from the bottle a single needle should be used in the bottle and different needles used to inject the animals.

Hygiene and Health

Due to their action on the animal's immune system, vaccines are most effective when they are used in healthy animals. Stock should not be suffering any illnesses or disease or from nutritional stress or any other stress. Most vaccines are contra-indicated for use in unhealthy animals.

The immunity stimulated by vaccination, for example, rotavirus to protect against calf scours, is passed on to newborn calves through the colostrum. Therefore at the time of vaccination the dam must be in good health to ensure she is able to mount a sufficient immune response to influence the colostrum produced.

Only vaccinate healthy animals – vaccination of a sick animal not only risks a failure of the vaccine but increases the possibility of adverse effects (especially with live vaccines). In general avoid vaccinating cows and heifers in the 14 days before calving when their ability to respond to vaccination may be compromised by the hormonal and other changes occurring at that time, as well as the excess stress perhaps might initiate abortion or a metabolic disorder. Vaccination of pregnant animals should be undertaken with extreme care and only products specifically authorised for this category should be administered.

As a general rule concurrent prophylactic treatments do not interfere with vaccination. In specific situations, the concurrent use of antimicrobials at the time of vaccination and for several days either side must be avoided and for some bacterial vaccines this is specifically contra-indicated as they can kill the vaccine organism. Other treatments such as with anthelmintics usually do not interfere with vaccination, **but always seek advice from a veterinary surgeon first before using any concurrent treatments.**

Multiple Vaccinations

A number of vaccines are available which provide protection for more then one disease at the same time (e.g., bovine respiratory syncytial virus (BRSV), parainfluenza-3 (PI3), infectious bovine rhinotrachetis (IBR) and bovine viral diarrhoea (BVD). There are also a number of instances where it is appropriate to vaccinate for more then one disease around the same time. Most vaccine licences state that a vaccine should not be administered simultaneously with another. This is principally the result of a lack of detailed information rather than a known adverse interaction. This general rule should be followed but in particular **on no account:-**

1) Should vaccines be mixed in the same syringes (simultaneous use).
2) Should two vaccines be injected into the same site, even if several days apart, unless professional advice has been sought to indicate that it is suitable (concurrent use).

Volume to be administered

The dose to be administered as stated on SPCs (data sheets) is carefully worked out and fully evaluated in trials that lead to full licensing. Therefore, the stated dose should always be applied. Using more than the stated dose may not improve the immune response, will risk adverse reactions and be economically wasteful. A failure to give an adequate dose may undermine the immune reaction and lead to failure of vaccination/expected protection. Likewise, where the stated regime requires a primary course of two doses of vaccine, a failure to respect the necessary interval (typically between two and six weeks is needed between doses but it is specific to each vaccine) or a failure to give the second dose at all, may lead to vaccine failure.

Part Used Bottles

All cattle vaccines are supplied in multiple dose bottles with the instructions that any unused vaccine should be discarded once the bottle is broached and the in use shelf-life expired. This is for a number of reasons:

1) Risk of the bottle becoming contaminated with bacteria, or other organisms.
2) Increased air in the bottle increasing the risk of oxidation damage to the antigen or carrier.
3) Temperature fluctuation between storage and use increasing product decay.
4) With live vaccines rapid death of the organism may occur once reconstituted.

Partial or completely empty bottles constitute pharmaceutical waste and must be disposed of along with needles and syringes (which constitute clinical waste) by incineration in approved equipment as described by the manufacturer in the SPC/product literature. Return of bottles to the supplier in a dedicated "sharps" container may be the best method of disposal. On no account should bottles, needles and syringes be disposed of with ordinary domestic or trade waste or on farm bonfires.

Timing of Vaccination

Vaccination should be carried out well before any field challenge is expected in order to allow sufficient time for the protective immunity to develop - usually two weeks after the course is completed. In the case of disease challenge to very young calves, adequate colostral antibodies (MDA) will only be available if the dam has been correctly vaccinated and boosted at the optimum time. Be sure to observe SPC recommendations regarding the use of vaccine at certain times in the animal's life (for example 'do not use in pregnant cows').

Safety

Some vaccines can cause serious injection site reactions if accidentally administered to humans. Always refer to the SPC (data sheet) if accidental administration occurs. **If there is any doubt, immediate medical advice should be sought and the SPC (data sheet) should accompany the person to the doctor or hospital.**

Adverse reactions

Any suspected adverse reaction (SAR) in either the animals vaccinated or the staff treating them, should be reported on the appropriate form (animal or human) to the Veterinary Medicines Directorate (VMD). Suspected Adverse Reaction Surveillance Scheme (SARSS) (yellow) forms can be found on the VMD's website at www.vmd.gov.uk. A report can be submitted either by the farmer or the attending veterinary surgeon. Ideally keep a copy of the VMD's suspected adverse reaction report or otherwise make a detailed note in the Medicines Book.

Withdrawal Periods

The current range of vaccines authorised for use in cattle in the UK have zero meat and milk withdrawal periods following application.

Recording

Accurately record date of administration, the identity of treated animals, the batch number, amount and expiry date of the vaccine used. Appropriate information should be kept on file of vaccines used (e.g. Summary of Product Characteristics (SPC) – product data sheet, package inserts or safety data sheets). Records must be kept for a period of five years after the treatment has ended even if the animal has been slaughtered.

Vaccine Failure

The majority of failures of vaccination regimes in cattle are the result of:-
a) Misdiagnosis of disease leading to incorrect vaccine choice.
b) The disease problem being multifactorial with other factors predominating and precipitating disease.
c) Misuse of vaccines including problems with storage, application and dosage.
d) Excessive challenge by field infection in situations of poor hygiene, ventilation etc.
e) Strain variants not covered by the vaccine used (e.g. *E. coli*)
f) Animal unable to produce a proper immune response (not immunocompetent) e.g. stressed, diseased, poor nutrition, etc.

Where a suspected vaccination failure occurs the failure should be reported to VMD under the suspected adverse reaction surveillance scheme (SARSS) as well as reporting it to the manufacturer/supplier.

Supply of Vaccines

All licensed cattle vaccines in the UK fall into one of two legal categories:-

1) POM-V - prescribed and used under the direction of a veterinary surgeon. They may only be supplied by veterinarians or pharmacists against a prescription issued by a veterinary surgeon. Veterinarians are only permitted to issue prescriptions for animals under their own care in this case.
2) POM-VPS - available either from the veterinary surgeon, pharmacist or Suitably Qualified Person (SQP). This is the former pharmaceutical merchant list (PML) category. Proper use and administration of these vaccines are non-the-less important. It is essential to understand the risk of the disease and the effect of vaccination, which animals to vaccinate and when.

The general rule is that for a product to be used in cattle in the UK it must have a UK or an EU-wide marketing authorisation (MA). UK marketing authorisation numbers begin with the letters Vm. However, under a process known as the ‘cascade’, a veterinarian may, when a suitable product is not available locally, make an application to use a product authorised in another country. Applications must be submitted to the Veterinary Medicines Directorate by a veterinary surgeon. If the product is authorised in another EU country the veterinary surgeon should make an application for a ‘Special Import Certificate’ (SIC), if from another country (outside EU) a ‘Special Treatment Certificate’ (STC) is required. Application must be made to the VMD in the prescribed format and a fee is payable for each certificate requested. This initiative has substantially improved access to vaccines which have small markets in different countries, and also been a great help in dealing with periods of inadequate supplies of a licensed product in one country, i.e. botulism and Johnes disease vaccines.

Another exception to the general rule relates to 'autogenous vaccines'. Autogenous vaccines can be successfully used to control bacterial diseases where:
a) no appropriate commercial licensed vaccine exists.
b) serotypes not included in commercial licensed vaccines are involved.
c) disease is occurring in age groups for which the commercial vaccine is not licensed and may have adverse effects e.g. pregnant animals.
d) disease is not being controlled by the commercial licensed vaccine(s).

Autogenous vaccines and their production must be licensed under Veterinary Medicines Directorate (VMD) regulations. Applications for an Autogenous Vaccine Authorisation (AVA) are processed within a set time period and the manufacturers are inspected before they can supply vaccines. Inspections are performed every two years to ensure the authorisation is still valid. It is the duty of the veterinary surgeon attending the animals to ensure that all the conditions of the licence are observed.

All autogenous vaccines are "tailor made" for each application, using a bacterial isolate from infected animals on a specific farm/unit. An example of an emergency vaccine would be one for *Campylobacter fetus* var. *venerealis.*

Responsible Use of Vaccines in Cattle Production

Responsible Use – Veterinary Surgeons

In all vaccination programmes, the best available information should be used to determine the correct regimes and protocol. The veterinary surgeon should perform post-mortem examinations, (serology), make farm visits, take samples and other relevant laboratory investigations where necessary. The aim is to ensure the need for a vaccine and that the correct vaccine is chosen.

Responsible Use – Farmers

Cattle farmers have a responsibility to safeguard the health of the cattle on their farm. Where appropriate, farmers may ask their veterinary surgeon to help them discharge this responsibility. Farmers can play a major role in ensuring the responsible use of vaccines by following the guidelines outlined in their farm assurance scheme. Advice should always be sought before undertaking a vaccination programme to ensure its suitability for the herd in question.

Disease Prevention

The best way to prevent disease is to prevent it from entering the farm. It is important to develop a preventative programme and consulting with those who have additional expertise and experience in the use of suitable products to prevent disease may be helpful..

Biosecurity

The biggest risk of introducing disease to a herd is through the introduction of new stock carrying the disease. The likelihood of an individual animal or a herd suffering a disease outbreak is a balance between the level of exposure and the immunity of the animal. Therefore, whether vaccinating or not, all herds would benefit from maintaining a stable population and reducing the number of new animals introduced. Maintaining the herd where no new animals are introduced and all replacements are homebred is the true definition of a

closed herd. When herds have adopted a disease eradication programme, maintaining a closed herd is vital.

For most farmers, maintaining a closed herd is not a viable option. “Open” herds include all herds that accept incoming stock e.g. replacement bulls. For these herds, vaccination may be the best way of reducing the financial and health impacts of introducing disease.

Responsible Use – Farm Assurance Schemes

The rationalisation of farm assurance schemes into a single umbrella scheme, Assured Food Standards, has simplified and standardised the requirements for cattle farmers. Food Assurance Schemes set out certain production standards in areas such as food safety and hygiene, environmental protection, animal welfare and inspections. For dairy farmers the standards Assured Dairy Farms (ADF) – formerly known as NDFAS – have been developed to address the concerns of all the interested parties in the milk supply chain. Consumers and retailers need to be assured that standards are being achieved to provide confidence about the production methods and the safety and quality of milk leaving the farm premises. Assurance schemes have a very important role to play in promoting the responsible use of medicines on farms, including vaccinations.

Major Cattle Diseases Controlled by Vaccination

Vaccine technology is the focus of research with improved health, welfare and production benefits of controlling disease as the objectives and this results in the continual development of new and improved vaccines.

For some diseases, particularly those that are due to viruses, no effective treatment is available and so vaccines are often the main form of control. For other diseases the time between infection, disease expression and death can be very short, meaning that the only viable means of protecting the herd is by vaccination e.g. blackleg.

The economic impact of almost every disease in cattle is such that disease prevention is far preferable to treatment. The following are the groups of disease for which a cattle vaccine or vaccines are available in the UK:

- Cattle viruses, such as BVD and IBR
- Cattle bacteria, such as *Salmonella* spp.
- Cattle parasites, lungworm (husk)
- Cattle fungi, ringworm
- Clostridial diseases such as blackleg
- Rabies, can affect all mammals including ruminants. UK is currently rabies-free
- Cattle pneumonia, such as *Mannheimia* spp. (*Pasteurella* spp), RSV, PI3 and IBR
- Calf enteritis such as rotavirus and *E. coli.*

Bovine Viral Diarrhoea (BVD)

Bovine Viral Diarrhoea (BVD) is caused by bovine viral diarrhoea virus (BVDV) and is widespread throughout the UK. Infection can result in infertility, reduced calf immunity leading to other infections (calf pneumonia – RSV, PI3 or IBR) or mucosal disease in calves. BVDV can also cause enteritis, which is usually mild, but is occasionally severe enough to cause death of adult cows.

BVDV infection of susceptible pregnant cattle almost invariably results in the transfer of the virus to the foetus. The outcome may be an aborted or stillborn foetus or the birth of a congenitally malformed calf, a weak, undersized calf or a clinically normal calf. Infection of susceptible cows at the time of breeding can cause early embryonic loss and repeat breeding.

Foetal infection with BVDV before 90 to 120 days gestation induces specific immune tolerance. Such calves are born persistently infected (PI) with BVDV and often shed large amounts of the virus for life while remaining antibody negative. They are frequently ill-thrifty and have a high probability of developing fatal mucosal disease, which commonly occurs between six and 18 months of age. Calves born from PI cows are always persistently infected. Calves born from susceptible pregnant cattle infected with BVDV after 90 to 120 days gestation are not persistently infected and have antibody to BVDV.

BVD is spread by PI animals in their nasal secretions and via semen from transiently infected bulls. Identification and removal of PI animals from herds is considered an important control strategy for the disease. Other control strategies include implementing strict biosecurity measures and increasing herd immunity through vaccination. Correct vaccination provides good protection for the dam and the unborn calf.

There are three vaccines available all containing inactivated strains of BVDV and two combined vaccines where inactivated BVDV is included with respiratory viruses (RSV, PI3 and IBR).

The BVD status of the herd can be established by ELISA testing of bulk milk or blood samples and the results of these tests can direct the control and vaccination strategy.

Infectious Bovine Rhinotracheitis (IBR)

Infectious Bovine Rhinotracheitis (IBR) remains a common cause of respiratory disease in both young stock and adult cattle in the UK. It is usually a highly infectious and contagious disease and is caused by bovine herpes virus 1 (BHV1).

The main sources of infection between animals are nasal discharge (or eye discharge), when it is affecting the respiratory system, and vaginal or preputial discharges, semen or foetal fluids and tissues when infection involves the reproductive tract.

Once an animal has been infected it often remains a carrier for life (latent infection). During periods of stress such as when moved or calving, starting a bull in work, bringing in for the winter, or animal becomes ill, shedding of virus may occur. The level of latent infection is variable but can be up to 10 per cent of clinically normal animals.

A survey of bulk milk antibodies in 341 UK dairy herds in 1998 showed 67% of herds were seropositive. Another survey (2000-2003) showed that up to 32% of samples from calves were seropositive for IBR.

The most common form of the disease is a severe upper respiratory tract disease, which may progress to a fatal pneumonia. In the reproductive form reduced fertility, increased abortions, a drop in milk yield and inflammation of the vulva/prepuce can occur. In most outbreaks, the respiratory and reproductive forms are not seen together.

Live IBR vaccines are available. They are given by intranasal inoculation (or by im injection) and should be administered 24-48 hours after entry to the farm. Ideally, calves should be vaccinated 10 days prior to any movement.

Gene-depleted live and inactivated vaccines (so called marker vaccines) for the control of IBR are also available. The immunity produced allows differentiation from that initiated by the wild IBR infection. This means the vaccination can be used in an IBR eradication campaign.

Several countries within Europe have successfully eradicated BHV1 infection (IBR), including Austria, Denmark, Finland, Norway, Sweden and Switzerland. An EU-approved national compulsory eradication scheme is being undertaken in Germany. Control programmes are being pursued in the Netherlands, Belgium and France. A programme for the monitoring, screening, eradication and accreditation of freedom from IBR is being undertaken in UK herds by Cattle Health Schemes which are regulated by the Cattle Health Certification Standards (CHeCS). CheCS is the accreditation body for the Cattle Health Schemes operating in the UK and ensures that all suppliers of schemes work to common standards and best practice. It operates for other non-notifiable diseases including BVD, Johne's Disease and leptospirosis.

In addition as many European countries are, or become, IBR free, animals exported from the UK to the EU will generally have to come from IBR Accredited-free herds.

Also, the production of semen is governed by EU rules affecting bulls on approved EU bull studs. This means that these animals must have **no** antibodies to IBR – i.e. following infection with wild BHV1 or following use of any IBR vaccine (conventional or marker vaccine).

Salmonellosis

Salmonellosis can affect most species including cattle, sheep, pigs and poultry as well as humans. Many species of Salmonella can cause disease in cattle including *S. dublin*, *S typhimurium*, *S. newport*, and *S. arizona*. The two commonest forms in cattle in the UK are *S. dublin* and *S.typhimurium*, and especially *S. dublin* can be endemic in a herd. Recent estimates would suggest that approximately 20 per cent of UK cattle herds may be infected with salmonellosis at any one time, although obvious disease is a much rarer event. The disease is usually introduced by infected cattle, a wildlife vector or contaminated water source. Identification of *Salmonella* spp. infection in the UK in food producing animals is reportable, i.e. must be reported to the relevant authorities.

In cattle the majority of cases are self-limiting intestinal infections although occasionally there may be a high mortality even when animals are treated. A feature of salmonellosis is that some strains have developed resistance to one or more antibiotics. In calves the

disease typically causes diarrhoea, enteritis and/or septicaemia. In adult cattle it can cause a number of diseases including enteritis and abortion.

An inactivated vaccine containing *S.dublin* and *S.typhimurium* is available in the UK and can be used in the face of a disease outbreak. Vaccination can help reduce the spread of disease and reduce the shedding of infection by infected cattle.

When the disease has been confirmed, all at-risk stock not showing overt clinical salmonellosis can be vaccinated. Calves can be vaccinated from 21 days of age and a second dose must be given after 14-21 days. Adult cattle require two doses 21 days apart. For pregnant cows, this primary vaccination course can be given irrespective of their reproductive status. All cows that have not calved within eight weeks of the second dose should be revaccinated three to four weeks before calving. Vaccinated cattle should receive a booster dose at least two weeks prior to each period of risk or at intervals of not more than 12 months.

Control of salmonellosis in cattle involves the use of strict hygiene measures, antibiotics and vaccinations, either singly or in combination. To prevent the introduction of salmonellosis into herds it is necessary to provide animals with uncontaminated feed and water, to control ingress of rodents and birds and limit human contact. Vaccines have an important role to play in the control of bovine salmonellosis, but they should not be used as a substitute for good husbandry and hygiene.

Lungworm (Husk)

Lungworm (*Dictyocaulus viviparus*) is a parasite of cattle and typically affects young cattle during their first season at grazing. In certain situations, infection is also found in older cattle and it has been recognised as a cause of milk drop, respiratory signs and occasional deaths in dairy cows.

The parasite has a complicated life cycle, the speed of which is affected by temperature and moisture levels. The prevalence of infection will, therefore, depend on the time of year. Disease is typically seen in mid summer to autumn in cattle in their first year of grazing. The range of signs is from occasional cough to severe respiratory disease and death, and is a reflection of the number of infective larvae ingested during a relatively short period of time.

A live attenuated oral vaccine is available which provides excellent protection against this disease. Each dose comes in a bottle that should be shaken well and the contents then given orally. Calves should be at least eight weeks old when dosed and second dose is given four weeks after the first. Calves should not be exposed to any potential source of lungworm infection for at least two weeks after the second dose. During subsequent grazing seasons exposure to lungworm infection reinforces this initial immunity. Vaccinated stock should not be grazed with unvaccinated animals or follow behind unvaccinated stock in a grazing system since any increase in pasture lungworm burden may cause an overwhelming of immunity. Only healthy calves should be vaccinated. Careful consideration should be given to calves suffering from respiratory disease before dosing. It is advisable not to use any other live vaccine for a period of two weeks either side of vaccination.

Ringworm

Ringworm is a fungal infection of hair and skin keratin caused by *Trichophyton verrucosum*. The incidence is considered to be high and it is particularly common in young stock between two and seven months of age and during the autumn and winter months of the year. Adult cattle are quite frequently infected.

Animals kept in close contact with one another, e.g. under intensive management systems, are particularly at risk. Although not giving rise to serious debilitating signs, the effect of ringworm is on the value of the animal or its hide.
The disease is usually non-pruritic in cattle. Lesions are greyish-white and have an ash-like surface. There can be hair loss and, if the skin is itchy, it can lead to reduced weight gain in growing cattle.

Ringworm infection is generally considered to be self-limiting and the course of the disease is usually one to four months, although in some cases a period as long as nine months has been necessary for resolution to take place.

A vaccine prepared from a live attenuated strain of *T. verrucosum* is available. It can be used to reduce clinical signs of ringworm (prophylactic dose) or to shorten the recovery time of infected cattle showing clinical signs of ringworm (therapeutic dose). The prophylactic dose is 4 ml and the therapeutic dose 8 ml, both are administered by im injection. Calves as young as two weeks of age can be injected. Two doses at an interval of 10 to 14 days are recommended. Initially the whole herd should be vaccinated and then, in a closed herd, only the young calves need subsequently to be vaccinated. Onset of immunity occurs three weeks after completion of the course. All new animals introduced to the herd should be given a full vaccination course. Once vaccinated, booster doses are not required. Occasionally a small crusty lesion may develop at the site of injection. Cattle infected with or exposed to ringworm should not be vaccinated with the prophylactic dose as such animals can develop very severe signs of ringworm. Vaccination can help reduce the impact of the disease in herds with a history of a problem.

Ringworm can infect man and cause serious skin lesions.

Clostridial Diseases

The clostridial organisms are common and responsible for many serious diseases in cattle.

Causative organism	**Disease**
C. chauvoei	Blackleg Postparturient gangrene
C. septicum	False blackleg
C. novyi type B	Black disease
C. haemolyticum type D	Bacillary haemoglobinuria
C. tetani	Tetanus
C. botulinum type C and D	Botulism
C. perfingens types A, B, C and D	Enterotoxaemia
C. sordelli	Sudden death
Mixed species of *Clostridium*	Gas gangrene

These bacteria are principally found in the environment, particularly the soil. Some areas appear to harbour greater numbers of organisms than others. The organisms produce toxins that cause severe tissue damage, and infection quickly leads to disease, often with death before the animals have been noticed to be ill. For this reason protection through vaccination is the best way of controlling the diseases.

There are two polyvalent vaccines available, one containing *C. chauvoei, C. septicum, C. novyi* and *C. tetani* and a second (10-valent) vaccine containing *C. perfringens* types A, B, C and D, *C. chauvoei, C. novyi, C. septicum, C. tetani, C. sordelli* and *C. haemolyticum*. Animals should receive two doses with an interval of not less than six weeks. Booster vaccination must be given at six-monthly intervals for continuous protection, but where there is no period of risk in the winter, an annual booster vaccination is sufficient. A univalent C. *chauvoei* vaccine can be used in calves over three months old with two initial doses three to four weeks apart. Booster vaccination should be no more than 12 months apart and ideally given two to three weeks before a period of risk.

Tetanus

Tetanus is a severe, often fatal, disease of all species of livestock. The disease is produced by the toxin of the bacterium *Clostridium tetani* and is characterised by hyperaesthesia, tetany and convulsions. The organism exists in the soil and cattle are usually infected through wounds or lesions.

In areas were tetanus infection have been identified, vaccination is often the most appropriate way of reducing disease risk.

Two polyvalent vaccines are available, one containing *C. chauvoei, C. septicum, C. novyi* and *C. tetani* and a second (10-valent) vaccine containing *C. perfringens* types A, B, C and D, *C. chauvoei, C. novyi, C. septicum, C. tetani, C. sordelli* and *C. haemolyticum.*

A monovalent tetanus toxoid vaccine, which is prepared from purified tetanus toxin treated with formalin, should only be used where a tetanus threat is suspected or has been experienced. Animals can be vaccinated from three months of age and should receive two doses with an interval of four to eight weeks. Booster vaccinations must be given at intervals of about 12 months.

Rabies

Rabies is an invariably fatal neurotrophic disease of all warm-blooded animals, i.e. mammals. The virus is excreted in the saliva and transmitted by the bite of an infected animal. Clinical signs are irritability, mania, hydrophobia and paralysis. It is usually fatal, although a few recoveries have been documented. The UK is currently free of rabies.

A vaccine is available and is advised from six months of age. Following the primary dose a booster is given annually. Calves can be vaccinated from two months of age but require a booster at six months of age.

Bovine Respiratory Disease (BRD) Complex

Bovine Respiratory Disease (BRD) is a multifactorial disease which can be triggered by various stresses such as transport, housing, the weather, general cattle handling or immunosuppression by Bovine Viral Diarrhoea virus (BVDV). These stresses lead to infection by primary pathogens which cause lung damage and disease. The primary pathogens include Bovine Respiratory Syncytial Virus (BRSV), Parainfluenza-3 virus (PI3), Infectious Bovine Rhinotracheitis (IBR) or *Mycoplasma bovis* and some other mycoplasmas as well as bacteria such as *Mannheimia* (*Pasteurella*) *haemolytica, Pasteurella multocida and Haemophilus somnus.*

Following this the damaged lungs are invaded by secondary bacterial pathogens. The principal organism is *Mannheimia haemolytica* which causes severe lung damage, pneumonia and even death. *Arcanobacterium* (also previously called *Actinomyces* and *Corynebacterium*) *pyogenes* and *Fusobacterium necrophorum* also are present in abscesses and other lesions in many affected lungs.

BRD principally affects calves and young growing cattle. Protection against these diseases prior to periods of risk such as weaning, housing or transportation is an important factor in controlling the disease. Attention to detail in management strategies, proper biosecurity and appropriate housing will help reduce the disease incidence. Vaccination will help where these situations are not optimum. As the disease is multifactorial, preventive measures include attention to management factors as well as possible vaccination.

Before embarking on a vaccination programme it is important to ensure that the pathogens on the farm are properly identified so that the programme can be introduced correctly. Such regimes will usually work well on farms housing just home-produced cattle. However, there is a particular problem for farmers who continually buy in batches of calves as the pathogens introduced with each group are likely to be different. Thus, it is very difficult to create a suitable vaccination policy to prevent pneumonia, unless several vaccines are used to cover most of the major pathogens. Such a policy is obviously costly and at times very wasteful as it will result in immunisation for diseases that are not present. This has led to the suggestion that in such units it is best to make a diagnosis as to the likely cause of enzootic pneumonia in the first animal(s) to be affected. If the cause is identified as being predominantly viral then, following veterinary advice, vaccination of calves in the face of an outbreak can be helpful.

Neonatal Diarrhoea

Neonatal calf diarrhoea is a multifactoral disease complex involving management and infective factors. Several bacteria, viruses and protozoa are associated with the disease, for example, enterotoxigenic *E.coli, Salmonella* spp., rotavirus, coronavirus and cryptosporidia. Pathogenic infections with *E. coli* are most common in the first four days of life whereas rotaviruses are most pathogenic from seven to 14 days and coronavirus causes disease from seven to 21 days.

As these diseases occur shortly after birth, there is insufficient time to vaccinate the calf and produce an immune response. Thus, the only way to achieve protection is to vaccinate the cow so that there are high levels of antibodies in the colostrum and, provided the management is right, the calf will receive excellent MDA protection.

Vaccines are available and very successful in practice; they contain inactivated strains of bovine rotavirus with coronavirus and *E. coli* K99 antigens.

Depending on the vaccine the pregnant cow is vaccinated with one or two doses between eight and three weeks of the expected calving date. Calf protection is dependent upon the animal receiving adequate (three litres) colostrum within the first six hours of life. They must continue to receive colostrum or milk from vaccinated cows for the first two to three weeks. This allows further exposure to antibodies to help deactivate the pathogens in the gut. An annual booster is recommended.

Successful control of an outbreak depends on identifying the important factors causing the disease and correcting them. Management problems identified need to be corrected and the identification of the infectious agents involved is important as it allows a logical approach to disease control. Appropriate advice on nutrition, colostrum feeding, vaccination, hygiene and the use of antibiotics can only be given when it is clear which infectious agents are present and what their contribution is to the disease process..

Leptospirosis

Leptospirosis in cattle is caused by the organisms collectively referred to as *Leptospira hardjo*. There are two serotypes - *Leptospira interrogans* serovar *hardjo* (*L. hardjo prajitno)*, and *Leptospira borgpetersenii* serovar *hardjo (L. hardjo bovis)*. Up to 50 to 60 per cent of British farms may be infected.

The bacteria are present in the reproductive tract and kidneys and spread of infection is from cow to cow via urine, foetuses and uterine discharge, and from bull to cow via infected semen. The main source of infection is via carrier cows or infected calves. The organisms often pass into streams and other water sources so these can also be a source of infection.

The disease can cause a “milk drop syndrome” (severe or mild) in cattle. In the severe form there is a sudden drop in milk yield affecting all four quarters with pyrexia. The udder secretion becomes thickened and clotted. The udder itself is not swollen or inflamed but tends to be flaccid. The condition usually resolves over seven to 10 days. In the mild form many cows are infected and show only a slight drop in milk yield.

Leptospirosis can cause infertility and abortions which usually occurs six to 12 weeks after the dam is infected. Abortion can occur on its own or be preceded by the milk drop syndrome. Most cases of abortion occur during the second half of pregnancy. If infection occurs late in pregnancy the birth of weak calves can also result and calves born to infected animals are often sickly. There may also be some apparent infertility in the herd.

Humans can be infected but they must be exposed to concentrated infection, i.e., contact via urine during milking. Although infection is present in the milk it quickly dies off once taken from the udder. Meat does not carry infection. Leptospirosis in humans causes a usually treatable meningitis, provided the cause is diagnosed.

There are two leptospiral vaccines available which contain either *Hardjo bovis* or *Hardjo prajitno* strains. Cross protection has been shown between *Hardjo prajtino* vaccine and the *Hardjo bovis* strain. Both vaccines will control abortion and improve fertility in endemic herds. Vaccination involves two initial doses separated by a four to six week interval. If cattle are young when vaccination commences then two doses are required after five months of age as MDA may interfere with the immune response. An annual booster is

recommended but two vaccinations a year may be required in herds that calve in the autumn. Vaccination does not affect animals that already have milk drop syndrome. However, vaccination does help prevent abortion but infected cows may still excrete leptospira.

Coliform Mastitis

Coliform mastitis, caused by many different strains of *E.coli*, can affect dairy cattle at any time during the lactation but is more common among housed cows. A dramatic form is peracute mastitis around calving. Around 50% of peracute cases die.

The primary source of infection is bovine faeces so appropriate management of the environment and housing and attention to detail in the parlour is required.

Vaccination can also help by boosting the cow's immunity in the period, just prior to calving, the greatest period of risk. The vaccine works by promoting an immune response to J-5 a core antigen found in most coliform bacteria.

Three doses of vaccine are recommended. The first dose is given to cows at drying off and heifers two months prior to calving. This is followed by a second dose four weeks later and a third dose two weeks after calving. The protection afforded by this regime increases with each inoculation and is 10 per cent, 30-40 per cent and 60-80 per cent respectively.

The vaccine does not totally prevent intramammary infection in the first 100 days of lactation, but it does significantly reduce the severity of clinical signs. It is best considered as an aid to the control of coliform mastitis, but will never be a substitute for good dairy cow management. Herd vaccination has been shown to be profitable when more than one per cent of cows in the herd are affected with clinical coliform mastitis.

Vaccinating dairy cows has shown to reduce both the incidence and severity of infection; however, a vaccine should be used in conjunction with appropriate mastitis management.

Louping-ill

Louping-ill is an acute viral disease of the central nervous system that primarily affects sheep. Infection is transmitted by ticks. Thus louping-ill is confined to areas where the vector tick, *Ixodes ricinus*, is prevalent. Clinical signs vary from sudden death to transient ataxia.

Vaccination starts with two doses given at an interval of not less than three weeks and not more than six months apart, and then annual boosters. The initial course should be completed at least two weeks before exposure and in pregnant cows before the last month of pregnancy. Vaccination of the dam will result in the transfer of antibodies in the colostrum which provide protection of the calf in the first few months.

The louping-ill vaccine is an oil emulsion preparation. It is viscous when cold and should be gently warmed before use to facilitate easier administration. The dose is 1ml given subcutaneously (sc). In the case of accidental self injection, medical advice must be sought immediately, with the SPC (data sheet) being taken to the hospital or medical surgery with the patient.

Appendix 1

Vaccination Example Protocols

In all vaccination programmes, the best available information should be used to determine the correct regimes and protocol. It is important that the recommendations of the manufacturer are followed when designing a vaccination schedule for animals. The aim is to ensure the need for a vaccine and that the correct vaccine is chosen. Advice should always be sought before undertaking a vaccination programme to ensure its suitability for the herd in question.

Table 1. Suggested Vaccination Regime for young growing calves

Age	Disease	Age of Vaccination + schedule	Comments
> 2 weeks	BRD complex (RSV, PI3, *Mannheimia*)	Two doses 3 to 4 weeks apart.	Usually part of a combination vaccine.
> 2 weeks	Ringworm	Two doses 10 to 14 days apart.	
> 3 weeks	Salmonella	Two doses 14 to 21 days apart.	
> 12 weeks	BVD	Two doses 3 to 4 weeks apart.	Usually part of a combination vaccine.
Prior to 1st grazing season	Lungworm	Oral vaccine. Double dose to be given month apart with second dose 2 weeks prior to first turnout	

Table 2. Suggested Vaccination Regime for dairy replacement heifers.

Age	Disease	Age of Vaccination + schedule	Comments
Prior to first service/going to bull	Leptospirosis	Primary dose plus booster 4 weeks later.	
Prior to breeding	BVD	Annual booster	
Prior to breeding	IBR	Annual booster	
Prior to calving	Coliform mastitis	Three dose programme. Dose 1 – 8 weeks prior to calving. Dose 2 – 4 weeks prior to calving. Dose 3 – within 2 weeks after calving	
Prior to calving	Neonatal diarrhoea	One dose or two doses 2 - 5 weeks apart. Both doses to be given to complete course 2 - 3 weeks prior to calving	
Prior to calving	Clostridial diseases and/or tetanus	Annual booster	

Table 3. Suggested Vaccination Regime for dairy cows.

Age	Disease	Age of Vaccination + schedule	Comments
Prior to turnout	Leptospirosis	Annual booster.	
Prior to breeding	BVD	Annual booster	
Prior to housing	IBR	Annual booster	
Prior to drying off	Coliform mastitis	Three dose programme. Dose 1 – 8 weeks prior to calving. Dose 2 – 4 weeks prior to calving. Dose 3 – within 2 weeks after calving	
Prior to drying off	Clostridial diseases and/or tetanus	Annual booster	
2 – 6 weeks prior to calving	Neonatal diarrhoea	Annual booster	
3 – 4 weeks prior to calving	Salmonellosis	Annual booster	

Table 4. Suggested Vaccination Regime for suckler cows.

Age	Disease	Age of Vaccination + schedule	Comments
Prior to turnout	Leptospirosis	Annual booster.	
Prior to breeding	BVD	Annual booster	
Prior to housing	IBR	Annual booster	
Prior to drying off	Clostridial diseases and/or tetanus	Annual booster	
> 4 weeks prior to calving	Louping-ill	Annual booster	
2 – 6 weeks prior to calving	Neonatal diarrhoea	Annual booster	
3 – 4 weeks prior to calving	Salmonellosis	Annual booster	

The Responsible Use of Medicines in Agriculture Alliance (RUMA) was established in November 1997 to promote the highest standards of food safety, animal health and animal welfare in British livestock farming.

A unique initiative involving organisations representing every stage of the food chain, RUMA aims to promote a co-ordinated and integrated approach to best practice in the use of animal medicines.

RUMA membership spans the food chain and includes organisations representing interests in agriculture, veterinary practice, the pharmaceutical industry, farm assurance, training, retailers, consumers and animal welfare interests.

RUMA
Acorn House,
25, Mardley Hill,
Welwyn,
Hertfordshire,
AL6 0TT

Tel/Fax: 01438 717900
Email: info@ruma.org.uk
Website: www.ruma.org.uk

RUMA is made up of the following organisations:

Agricultural Industries Confederation (AIC)

Animal Health Distributors Association (AHDA)

Animal Medicines Training Regulatory Authority (AMTRA)

Assured Food Standards (AFS)

British Poultry Council (BPC)

British Retail Consortium (BRC)

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Linking Environment and Farming (LEAF)

Meat and Livestock Commission (MLC)

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