Why animal medicines are so different

In this article, **Steve Dean** writes about some of the challenges presented in veterinary medicines

It may come as something of a surprise that although the quality requirements for veterinary medicines are similar to those for medicines for humans, the safety assessment required is more extensive. There are good reasons for this. First, medicines that remain in the bodies of farm animals may pose a health risk to consumers. This means that special data regarding the residues remaining in meat or dairy products are required and, for each medicine, a withdrawal or waiting period (the time from the use of a medicine at which the consumption of milk, eggs or meat from that animal will be safe) must be established. Second, those administering medicines to animals, or involved in mixing animal feeds containing medicines, also deserve protection. Third, veterinary medicines are often used in the countryside, with the possibility of contaminating the land. It is not surprising, therefore, to find that medicine residues, user safety and environmental safety are carefully assessed during the authorisation process for veterinary medicines.

Veterinary medicines, particularly medicines for pets, have several similarities to medicines used for humans. Similar anaesthetics, pain control therapies and antibiotics are used and even fluid therapy is a valued treatment. For pets, the conditions of use are also similar to those for humans, and veterinary clinics contain a variety of familiar hardware such as X-ray machines, laboratory analysers and ultrasound scanners.

It is when we move into the field, quite literally, of farm animals that the similarities become more tenuous. High levels of sterility in a loose box or in the middle of a 10-acre field are impossible and although sterile procedures will be observed around a surgical site, straw and muck will not be far away. Thus a caesarean section will often be conducted under local anaesthesia, with the cow standing up.

Some of the medicines used on farms are also similar to many of those used in human medicine but, clearly, if a veterinary surgeon is treating an animal weighing several hundred kilograms or an entire flock of sheep, the volumes required will be much greater. Injection doses of 30ml are not uncommon and if a cow is dehydrated it can require many litres of intravenous fluids. As a further illustration, to dose a flock orally to remove roundworms, a shepherd will typically require at least a litre of product for every 100 ewes, and the favoured pack sizes are multiples of five litres.

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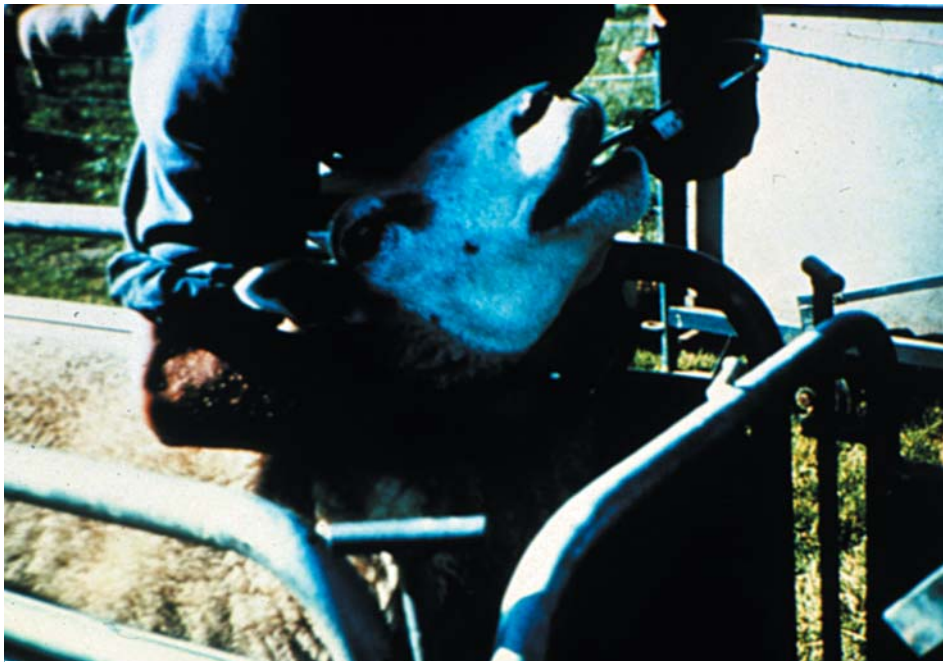

"Drenching" a sheep

Not all human medicines are suitable for animals. For example, the case for using the non-steroidal anti-inflammatory drugs (NSAIDs), popular in human medicine, is not a simple one in animals and experience has demonstrated the lethal potential of the human NSAIDs when used at the recommended label dose in dogs. As a result, some NSAIDs have been developed for veterinary use.

Animal compliance

Less dangerous for the patient, but just as problematic, is the use of tablets and capsules. Giving medicines in these forms requires co-operation from the patient and any parent that has tried to administer tablets to a reluctant child will testify how difficult this can be. The similarities, when compared to the treatment of a recalcitrant cat or dog are obvious — and the teeth and claws are dangerously sharper. This has led to some ingenious solutions for administration. For example, treating a flea-ridden dog or cat with a noisy, hissing spray was never a recipe for success and the patient would likely exit rapidly on the second occasion the owner reached for the spray-can. Consider, as well, bathing dogs or cats in pesticidal shampoos — never an inspiring prospect and not without concerns for the safety of the owner as a result of patient opposition.

One solution has been found in the development of low volume "spot-on" formulations, intended for application to the back of the animal's neck. From here the active ingredient may be either absorbed into the bloodstream or distributed throughout the animal's coat to achieve the desired death of resident parasites. For cattle, worm treatment, traditionally administered in an oral suspension, is a labour intensive business when treating an entire herd. Here too, formulations that permit the anthelmintic to be poured along the animal's back, have made administration easier.

Innovations in veterinary medicine

Even more revolutionary has been the development of sophisticated bolus technologies. These are weighted dosing devices, intended to reside in the second stomach of the ox (cattle have four stomach chambers). Boluses can release the medicine in a trickle dose, over several months, or even in five or more discreet pulses, automatically dosing an animal at intervals of three weeks.

Perhaps it is the major markets for farm animal medication where there is the greatest impetus for innovation. The size of the doses needed to treat large animals such as cattle, the need to treat large groups of animals at one time, particularly in the poultry and fish farming industries, and the over-riding need for farming to be economic, act as significant drivers for progress.

Fish and fowl

Fish and chicken farmers face the prospect of disease in large groups kept in close proximity. The financial margins in these industries are small and an outbreak of disease, and the associated cost of treatment, could easily lead to financial ruin. It is not surprising, there-

fore, to find that vaccines are major weapons in the farmer's battle to keep livestock healthy. However, vaccinating thousands of fish and fowl is a challenge. In some cases, there is no option but to handle each chick or fish smolt to administer these vaccines by injection. Nevertheless, it is clearly unreasonable for farmers to have to perform, and animals to be subjected to, this practice several times, so veterinary vaccines often contain multiple antigens to protect against several diseases within a single vaccination. Furthermore, to avoid excessive handling, some vaccines have been developed as aerosol sprays, enabling whole sheds of chickens to be immunised rapidly. Most of these vaccines are designed to protect against the respiratory diseases that are naturally transmitted in this way, but one novel vaccine aims to protect the birds against a parasitic disease (coccidiosis). The anti-parasitic is combined in a spray with a red food-dye, which attracts the birds to clean the droplets off their feathers. In this way, they ingest the vaccine and gain protection against infection.

Theres something in the water

A more traditional option for treating large groups of animals, involves the incorporation of the medicine in feed or drinking water. This reduces the animal handling requirement — an advantage where there are several thousand chickens to be treated — but presents challenges for achieving accurate dosing. One limitation is the lack of appetite in sick animals, so it is fortunate that most will still drink water. Then there is the issue of some animals in the group drinking or eating more than others; it is not unusual for the dominant members of the herd or flock to eat larger portions of the feed in the communal trough.

The dose calculation for a flock or herd is, therefore, a compromise, based on average consumption figures. This can raise difficult questions about the efficacy of the dose and, in the case of antimicrobials, about the effect under-dosing may have on resistance. Issues like these are required to be addressed during the authorisation process.

There is, of course, a myriad of other regulatory issues that require resolution before an authorisation is granted for any mass medication product. Just a few examples are solubility, palatability, whether it will obstruct the nipples in automatic drinking systems, its stability once dissolved in water or included in feed.

Accurate dosing

Even when using what may appear to be accurate administration methods, accurate dosing can be a challenge. Oral drenching guns (drenching is the term used when farm livestock are given oral doses of fluid medicines) are a good example. The dosing guns are commonly calibrated with sufficient accuracy to provide dose volumes in the range of 2.5 to 20ml. They are routinely used to supply medicine to large flocks of sheep and herds of cattle.

Each animal is handled and given a dose from the gun, which is automatically refilled through a connection to a "back-pack" of medicine, capable of providing several hundred doses. However, at each stage, dosing errors can occur due to practical constraints. First, although groups of animals will not be uniform in size, it is impractical to weigh every animal before drenching. The weight of each animal will be estimated, and this will be subject to error. Second, even if animals are weighed, it is not practical for the stockman to adjust the drenching gun for each individual.

The stockman has two choices: estimate the heaviest weight in the group and dose the whole group accordingly, or estimate an average weight and use this as a guide. Neither will be right. The former will overdose most of the animals and the latter will underdose 50 per cent and overdose 50 per cent. Fortunately, farmers tend to keep animals in groups of similar size so this is rarely a significant problem. However, occasionally, where a number of miscalculations add together, the consequences can be serious for the health of the animals.

Up to this point, horses have not been mentioned. Horses are unique animals in many ways, and this includes their medical treatment. Routine examinations and medication will be carried out in conditions similar to those of farm animals. However, horses are frequently examined and treated in specialised hospital conditions, comparable to those for pets, but on a suitably large scale. The high value of horses makes this a feasible and affordable option, especially because many are insured with private medical plans.

Fish

The relatively new industry of fish farming in the UK has presented more challenges to vets. An obvious way to treat fish is to add medicines to the water ("bath therapy") but this has some practical difficulties. Where fish are kept in large pens, with water flowing through, how can treatment be effective? For example, in Scotland, Atlantic salmon are farmed in large cages at sea and the unchecked flow of seawater through the mesh would soon remove any treatment from the water surrounding the fish. To solve this, tarpaulins are used to enclose the fish while treatments are administered — not a simple task to achieve in an open loch or at sea. Anti-parasitics are often applied in this way but diluting sufficient product in vast quantities of seawater is a problem of daunting scale. Treatment is further complicated by the need to consider the weather, because large cages at sea will be difficult to reach in poor conditions.

Medicines can sometimes be included in feed, but this is not an option for treating fish eggs. It may seem strange that fish eggs need treatment but they, too, are prone to infections and, where necessary, medicines will be added to the water that flows over the eggs or young fry.

More exotic species

So far, my discussion has revolved around the treatment of traditional domesticated animals. However, the number of exotic species being kept as pets in the United Kingdom is increasing. They include reptiles, rodents and birds. The market for medicines for these animals is not large and, therefore, the number of drugs that are authorised for use in these species is small. This means that most treatments will be adapted from those authorised for use in dogs, cats, cattle and the like.

There are also many species of farm animal that are not well served with medicines because of their low numbers. For example, few medicines are available for use in goats. Furthermore, a veterinary surgeon cannot assume that goats are just long-legged sheep — they react differently to many treatments.

Other species require special considerations due to large physiological differences from mammals. The avian respiratory system, for example, is significantly different from that of mammals, and birds require great care during anaesthesia. Similarly, reptiles are cold-blooded. Their body temperature varies greatly and this may mean that depot injections do not perform predictably.

There are also further problems for species related to traditional farm animals. Take the example of the pot-bellied pig, which has become popular as a pet. The law demands that all food animal species are treated only with medicines for which a withdrawal period can be set and, under legislation, pigs are considered to be food animals, even if there is no intent to ever use an animals for food. This limits the medicines that can be used to treat such a pet. All these factors make the choice of medicine challenging for vets.

Adding medicine to feed is a way of treating large numbers