Sea Mammal Research Unit

THE INTERVET GUIDELINES TO VACCINATING WILDLIFE

Prepared by

Ailsa Hall & John Harwood

Natural Environment Research Council
Sea Mammal Research Unit
High Cross, Madingley Road, Cambridge

1991

research sponsored by:

Intervet

Summary

The death of nearly 18,000 seals in the North Sea during 1988 highlighted the vulnerability of wild animals to disease. Vaccination programmes have been extraordinarily effective in reducing, and sometimes eliminating, the effects of diseases in man. So it was inevitable that there have been calls that vulnerable wildlife populations should also be vaccinated. However, any proposal to vaccinate wildlife against an infectious disease raises a number of fundamental questions. These guidelines describe the questions and provide a framework for identifying those which should be addressed before any large-scale wildlife vaccination programme is instigated.

There are four sets of questions: is disease really a problem for the population under consideration; what would the benefits of a vaccination programme be; what are the risks associated with such a programme; and is a suitable vaccine available and useable? Because vaccination programmes can have harmful as well as beneficial results, it is important that the aims, chances of success and possible risks are carefully specified so that some form of cost-benefit analysis can be performed before the programme is begun. The availability of a suitable vaccine and the outcome of trials have to be considered, as well as the timing of the disease outbreak and the accessibility of the population. Finally the practical difficulties and costs of implementation also have to be explored.

Wildlife vaccination has, until now, been undertaken as crisis management. Decisions made in crisis are not always wise ones. These guidelines are intended to provide a ready made checklist of points which should be considered when difficult decisions have to be made. Our analysis of past and potential incidents where vaccination has been considered or implemented indicates that its role in species conservation is probably limited to situations where there is a clearly defined threat to a small population, and where vaccine can be administered with minimum disturbance. Alternatives to vaccination, such as reducing contact between infected and uninfected animals and limiting stress to the population, may be more effective in some cases.

Acknowledgements

Mr J Barker BVet Med, MRCVS; Mr D Clarke MA, VetMB, MRCVS, DVR; Dr J Cooper DTVM, FIBiol, FRCVS; Dr A Greenwood MA, VetMB, MIBiol, MRCVS; Dr B Hastings DVM; Dr S Mayer BVSc, MRCVS; Dr W Plowright CMG, FRCVS, FRS; and Dr G Smith MRCVS, DVR kindly discussed the issues involved in wildlife vacination with us, and provided helpful and constructive comments on the draft guidelines

Intervet UK Ltd

Preparation and printing of these guidelines was made possible by animal health specialists Intervet UK Ltd, a leading British manufacturer of products for the veterinary profession, including vaccines for small and large animals.

TABLE OF CONTENTS

Introduction

These guidelines are arranged in three sections. The first provides a general overview of the problems likely to be encountered in reaching a decision about the advisability of a vaccination programme for a wildlife population. It is written in a non-technical way and is intended to provide a very general understanding of the complexity of the problems. The second section describes the problems and approaches in more detail and in more technical language. It uses a set of decision trees to show what information is required to assess particular problems and how a decision may be arrived at. In the final section a number of case studies are described. There are two studies where vaccination was actually carried out and one where vaccination was seriously considered but not implemented. In each case the reader is taken through the appropriate decision trees to see how the decisions made at the time compare with those which would have been made if these guidelines had been available.

I. An Overview of the Problems

During the spring and summer of 1988, large numbers of dead common (*Phoca vitulina*) and some grey (*Halichoerus grypus*) seals were washed up around the North Sea and British coasts, causing concern and distress to the public and the scientific community alike. During the autumn the cause of the deaths was identified as a previously unrecognised virus, phocine distemper, which produces symptoms similar to those seen in dogs infected with canine distemper. As the death toll mounted to more than 18,000, the general public was understandably concerned that some European seal populations might be completely exterminated.

The epidemic eventually died out in early 1989 leaving many common seal populations in the southern North Sea reduced to half their former size but many Scottish populations virtually unaffected. What can be done to prevent this happening again and to ensure that other wildlife populations at risk from similar diseases are protected? One measure widely advocated in the media during the seal epidemic was vaccination. Once a vaccine had been developed and tested, as was the case towards the end of 1988, it was surely possible to protect the remaining seal population. Humans, livestock and pets are all regularly and successfully immunised against many killer infections, why not wildlife ?

The answer is not simple. Even for humans vaccination is not without risk; among wildlife it can have adverse and potentially devastating effects. These are quite apart from the practical difficulties involved in administering a vaccine to wild animals. The aim of these guidelines therefore, is to outline the various questions that need to be asked before a wildlife vaccination programme is undertaken

The objectives of a vaccination programme need to be clearly defined. Potential objectives can be conveniently divided into those directed at the health of individuals and those concerned with the population as a whole. In terms of the welfare of a particular wild animal, vaccination can be a life-saving procedure. The decision to vaccinate individual wild animals, particularly those brought into rescue centres and animal hospitals, is essentially a humanitarian one and is beyond the scope of these guidelines. By contrast, mass vaccination, which is carried out on an entire population, needs very different considerations. These considerations are the principle subject of the guidelines.

General Considerations

Unfortunately, there is very little baseline information on the occurrence of disease in wildlife. What are the diseases which occur "naturally" in a particular species? Often we simply do not know. Usually information has only been gathered in a systematic way.when an infectious or toxic agent causes visible, high numbers of deaths, over a short period of time. Even during a disease epidemic, the rates of infection or mortality are often difficult to establish and the resulting estimates may be unreliable.

Vaccination is normally only considered when unnaturally high mortality occurs in a population, but what is an "unnaturally high" level? We still do not know enough about how diseases regulate wildlife populations, and thus how important they are in the sustainability of a particular species or population.

It is important to define the reasons for considering vaccination at an early stage. It is not defensible to carry out any immunisation programme without specifying its purpose. The primary purpose may be simply "to reduce suffering", if this is so it should at least be stated at the outset. Other aims might be: to ensure that the mortality rate in a small or endangered population does not become so high that the population's future is in jeopardy; or to reduce the rate of spread of disease, either within the population or to another group or species. However, vaccination as a preventative measure may be impossible because the first evidence that disease is a threat will be the occurrence of an epidemic.

Of course a vaccine against the threatening infection must be available before vaccination can start. Given the current advanced technology in vaccine development this may seem an easy objective to meet. However, it is unlikely that a vaccine specific for the disease and the species of interest will already be on the market. Wildlife vaccines are generally only available against diseases which are a threat to human or livestock populations (most notable is the rabies vaccine for wild fox populations which are carriers of the disease - Baer, 1988) or for some zoo animals. It may be difficult to persuade a company to invest in developing a vaccine purely in the interests of a wildlife species, particularly one which may not be very appealing, for example a rodent.

Although a vaccine for a related species and/or disease may be available (for example canine distemper vaccine for dogs was tested against phocine distemper in seals), properly designed trials must be carried out on the species itself and trials on other animals with which it may come into contact. It is important to ensure the vaccine does not introduce a new disease into the ecosystem. Extrapolation of laboratory results to the wild situation is fraught with danger.

All these considerations must be addressed before the risks associated with the vaccine and vaccination itself are assessed.

Assessing the Risks

The next step is to determine what level of vaccine protection is acceptable. As with humans, not all animals will react in the same way to the vaccine. Only a fraction of those vaccinated will respond positively and thus be protected. Serological testing (looking for antibodies in the blood) or even challenge testing (exposing an animal to the agent to see if it contracts the disease) are the only reliable methods for evaluating this response. Again, laboratory results will not necessarily reflect the pattern that will be seen in the field.

Side effects or other physiological dangers may be associated with the vaccine. The rate at which these occur must also be investigated. The vaccine itself may be subject to "interference". For example, if an animal is vaccinated against a disease within the first few weeks of life, it may already have protection from its mother via maternal antibodies . Antibodies are blood proteins which react to foreign substances, called antigens, and which afford some protection against infection. Maternal antibodies are transferred from mothers to their young during lactation. They are short-lived but they may prevent a vaccine from stimulating antibody production.

Vaccines now come in many forms and one appropriate for the particular situation in which it is to be administered must be chosen. Similar decisions have to be made about the type of vaccine. There are various categories, all of which stimulate the immune system, the body's principal defence against disease: "inactivated" or killed vaccines; "attenuated" or live vaccines, which have been treated in some way which prevents them causing disease but which can still stimulate an immune response; and genetically manipulated vaccines, in which the section of the organism responsible for initiating immunity is transplanted into an innocuous "carrier" organism (eg Blancou *et al.*, 1986). The safety of the genetically manipulated vaccines has not been widely accepted yet, and some scientists still have misgivings about the risk that they may recombine with naturally occurring viruses.

Live vaccines can carry a high risk, particularly when used on a rare species. Although they may not produce disease in related, more common species they may cause serious infection in the rarer species. This was demonstrated with disastrous consequences when a canine distemper vaccine, used successfully on European ferrets, was given to six endangered Black-footed ferrets (*Mustella nigripes*)

in the US which had been captured for conservation breeding. All four females perished and it was feared that the species had been exterminated. This case history is described in more detail in Section III. Fortunately another population was discovered in the early 1980's in Wyoming.

Administering vaccine on a large scale may well be detrimental to a wild population, and can cause more problems than it solves. Many wildlife species are extremely sensitive to disturbance and the act of catching individuals to give a vaccine may cause as many deaths as the disease itself. Stress may also allow other diseases which had lain dormant within the population to express themselves. These problems are particularly acute if an inactivated vaccine is used because two or three doses may be needed to ensure protection. Catching wild individuals once is often hard enough, catching the same individual two or three times is often impossible.

These risks must be weighed against the expected benefits from mass vaccination. It is important to be sure that the objectives of the programme can be achieved, but it is also important to recognize the long-term commitment involved in a vaccination programme. Once the path of vaccination has been decided upon, each new generation must be vaccinated because it will be susceptible to the disease. If vaccination is discontinued, the population may be more vulnerable to the disease than it was before.

II. A Detailed Evaluation of the Need to Vaccinate

Introduction

This section deals with the epidemiological, ecological and veterinary issues that are central to any decision concerning the mass vaccination of wildlife. Its aim is to provide a framework in which the relative importance of these issues can be evaluated for specific cases where artificial immunisation is being considered seriously.

The relative importance of the different issues will depend on the particular circumstances of the case under consideration; we have not attempted to document all eventualities. Our objective is to identify a key set of issues which should be considered in most cases. The amount of detailed consideration given to each set of issues will depend on the situation.

Key Questions

We have identified five key sets of questions and constructed decision trees to help address them. They are: what is the potential effect of disease on the population; what are the overall aims of the proposed vaccination programme; what is the availability and trial status of a possible vaccine; what are the risks associated with that vaccine; and how should a vaccination programme be designed?

These questions need not be addressed in the order in which they are presented here, nor are they mutually exclusive. For example, in many cases the practicality of administering a vaccine is likely to be the single most important constraining factor and the decision tree appropriate to the design of a vaccination programme should be examined first. Other situations might call for the availability of a suitable vaccine to be determined first, particularly where unusual or macroparasitic diseases are in question. Where there is mounting public pressure for a "fire-fighting" response to a perceived problem, evaluating the importance of the disease may be superfluous.

The Need for Well-defined Aims

Any prophylactic immunisation programme is a compromise between immunisation efficiency and convenience of administration. However, in the case of wildlife vaccination, we believe that it is particularly important to define the overall aims of the programme before too much attention is focussed on practical aspects. The tacit assumption that immunisation can only benefit a population is a dangerous one, particularly when dealing with free-living animals. A comprehensive risk assessment, of the kind we advocate here, should ensure that the potential dangers associated with the vaccine and vaccination are recognised from the outset.

Once the aims of the vaccination programme have been established a feasibility study, covering practical points, administration and financial considerations, should be conducted. The cost of developing a suitable vaccine, if none already exists, may well prove prohibitive.

A detailed cost-benefit analysis is a key component of any large-scale immunisation programme. However, whilst the cost of such a programme is relatively easy to establish, the benefits from maintaining a disease-free wildlife population are more difficult to quantify in monetary terms.

Epizootiological Considerations

The effectiveness of wildlife immunisation cannot be evaluated solely in terms of the protection of individuals from disease. The effect of immunization on the population as a whole is paramount. Population size provides a good indication of the vulnerability of the population to disease and hence of the need for a vaccination programme. High additive mortality due to disease in a small population may result in a substantial loss of genetic variability and increased vulnerability to extinction from chance events. Both will prejudice the population's future. A reliable estimate of total population size is required, not only to evaluate the benefits of immunisation but also the costs.

The aim of many vaccination programmes is to establish "herd immunity" where the proportion of immune animals is sufficiently high that the probability of the disease being transmitted from infected to susceptible animals falls below some threshold value. It is therefore necessary to establish by how much the probability of transmission will decline as the density of susceptible animals is reduced by immunisation, and how many animals must be handled to achieve the required threshold density. In practice it will be impossible to determine this directly and some mathematical modelling exercise based on analogy with related, better studied diseases will be required.

Age-specific susceptibilities to the disease in question and the effects of acquired immunity are also likely to be important features. In essence a vaccine programme must be designed within a proper epizootiological framework if its potential effectiveness is to be evaluated properly.

The time when a vaccine is administered is also critically important. Administering a vaccine to an individual after it has been exposed to infection rarely alters the course of the disease. If an immunisation programme is delayed until after the disease became epizootic, then a significant proportion of vaccinated animals will already be infected and it will be impossible to assess the impact of the programme with any precision.

Vaccine Evaluation

Evaluating the efficacy of the vaccine itself poses considerable problems. An experimental model must be used if, as is likely, it cannot be tested on the target species The disease observed in the experimental model may not resemble that seen in the target species. Often no suitable model is available. Furthermore, the ability of the vaccine to induce antibody formation or cellular sensitivity does not

necessarily mean that it will confer immunity under field conditions. Physiological and behavioural differences between the experimental and target species must be considered.

The Decision to Vaccinate

Some controversy will always surround any proposal to immunise wild populations. The final decision may well be a political one in response to overriding public pressure, rather than the result of a real concern about public or livestock health issues. However, it may be presented in the guise of ecological principles.

Certainly ecological problems cannot be ignored. As anthropogenic pressures on wildlife increase, many species will become confined to ever smaller land areas. The resulting increase in density and stress will increase the occurrence and risk of both acute and chronic disease.

In future, guilt may be another motive for considering mass wildlife vaccination. If an epizootic is obviously of anthropogenic origin, the author of the outbreak may feel obliged to minimize its consequences! However, if such intervention is to be successful it will require a level of epizootiological knowledge which we do not possess at present.

Alternatives to Vaccination

Even if a disease is clearly identified as a threat to an endangered species or remnant population, to what extent is human intervention in a "natural" process acceptable? Such philosophical questions are difficult to answer because we know so little about the long term effect of disease on wildlife populations.

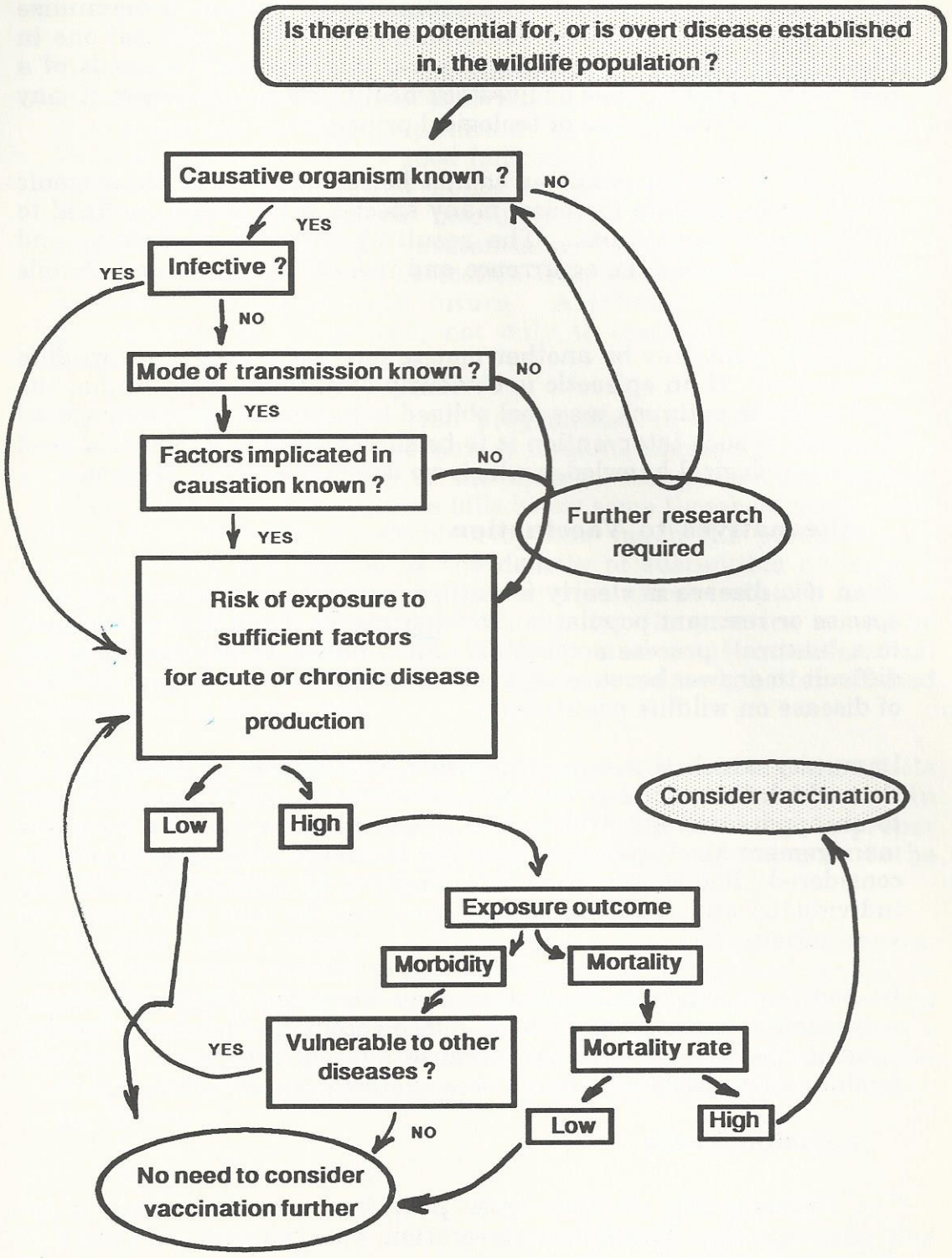
Immunity which is acquired naturally will always be preferable to that which is artificially induced. Vaccination is usually a reaction to an apparent crisis. But even in these circumstances, alternative management strategies to reduce the incidence of disease should be considered. Reducing contact rates between susceptible and infective individuals, and reducing social stress may be just as effective as vaccination.

In addition, mass immunisation may leave the population more vulnerable to disease than before. Once vaccination has been decided upon it has to be continued, because subsequent generations will produce new susceptible individuals who will require protection.

Decision Trees

The following five decision trees provide a structured format for evaluating the available information concerning a number of different aspects of vaccination programmes. We hope they are self-explanatory but each is followed by a page of notes which expand on the questions in the tree.

THE POTENTIAL EFFECT OF THE DISEASE



THE POTENTIAL EFFECT OF THE DISEASE

Is there the potential for disease (or is overt disease already established) in the wildlife population? If this criterion is fulfilled, the question of artificial immunisation may arise.

Causative organism known ? If the parasite has not been identified, further research will be required until it can be isolated or narrowed to within a particular genus. This would certainly be important if the organism is liable to mutation through antigenic drift and antigenic shift making the development of a life-long vaccine particularly difficult.

Infective ? If the organism is infective, i.e. easily transmissible from host to host, some subsequent questions may be irrelevant. A susceptible animal may only need to come into remote or secondary contact with a source and the risk of infection and subsequent disease will be high. The organism may therefore be a very strong factor in disease causation and to investigate the interaction of associated factors would perhaps be unnecessary.

Mode of transmission known ? Conversely, if the organism is uninfective (an assessment of infectivity will have to be made in conjunction with microbiologists and parasitologists), the mode of transmission may be important in determining the rate of spread of disease and therefore the most appropriate means of control; i.e if transmission is direct (inhalation, ingestion etc.) or indirect (via vectors or fomites) where, for example, the relative abundance of vectors or intermediate hosts would be important.

Factors implicated in causation known ? There may be other important physical, environmental and psychological factors which will initiate an outbreak of disease. Stress through transportation is known to precipitate disease in some domestic animals, for example *Chlamydia psittaci* infection in ducks. Various factors will be involved in the disease process, acting in conjunction with the organism. Animals may be asymptomatic carriers until sufficient individual 'causes' occur simultaneously, producing disease.

Risk of exposure to sufficient factors for disease production Some assessment of the risk of exposure to the parasite and any precipitative factors thought to be involved in the production of disease, must be made. Parameters considered might include population density, density of infective stages, rate of contact between host and infective stages, environmental conditions, behaviour of potential hosts, susceptibility of host in terms of genetic make-up, immune response, nutritional status, previous infection etc.

If the risk is deemed to be 'low', either in the short term (acute disease) or long term (chronic disease) there may be no need to vaccinate, since the probability of the disease spreading to a large proportion of the population will be sufficiently small. If, conversely, it is highly likely that exposure will occur, further information is required.

Exposure outcome Two possible outcomes are considered, morbidity (disease) or mortality (death).

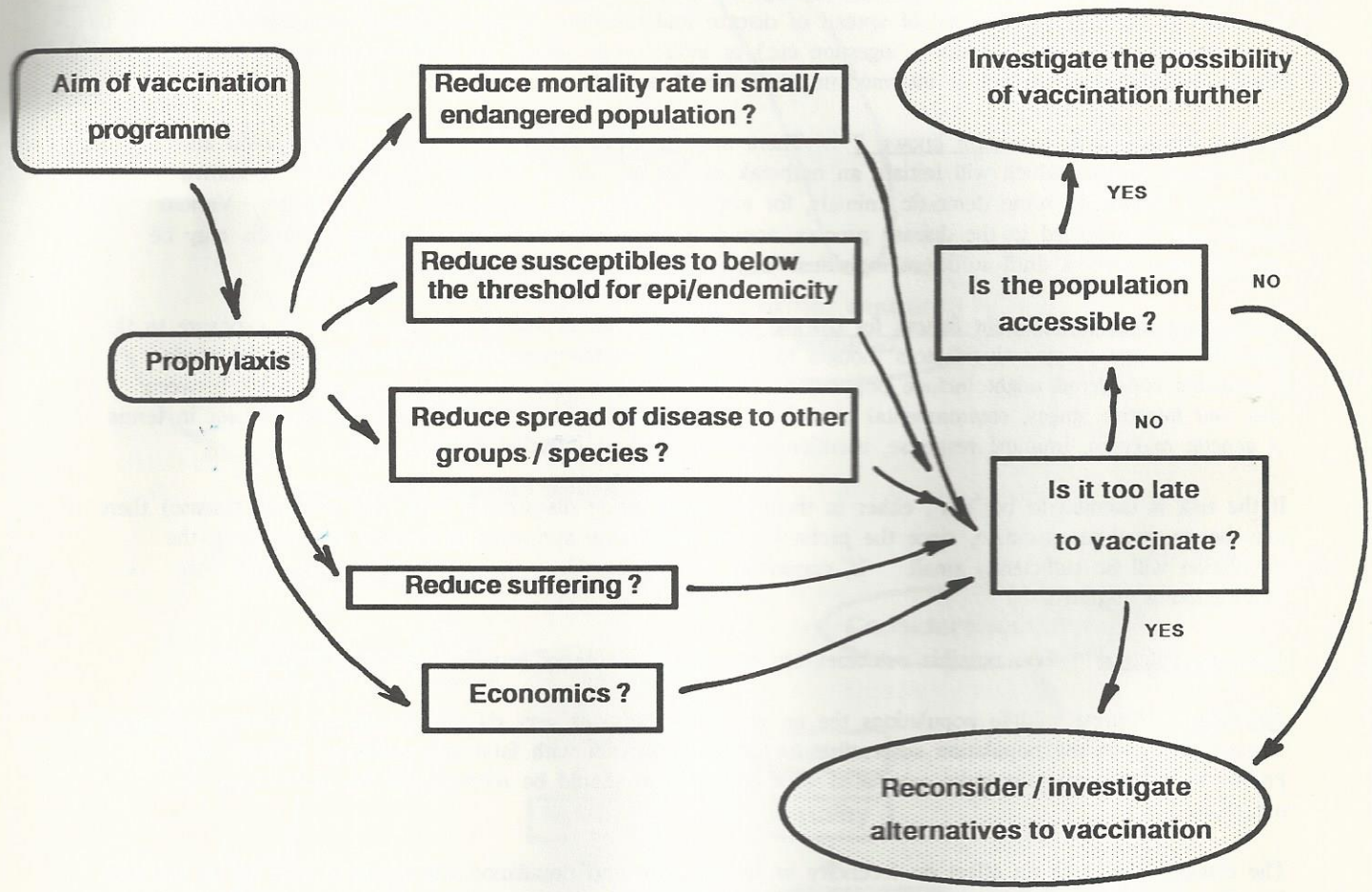
Morbidity Among wildlife populations the impact of morbidity is very difficult to assess. Immuno-suppressive disease may leave the population susceptible to further parasitism with fatal consequences. Where this is known to be the case, the risks associated with opportunism should be reconsidered for each causative organism.

The disease may have an effect on fecundity or reproduction and population survival may thus be in jeopardy. Its effect should be considered in terms of the likelihood, size and impact of a reduced reproductive rate. If no long-term effects are seen and animals recover following infection, there would be no need to vaccinate. There could be other implications for an individual's prolonged survival, but little effect on population dynamics or abundance will be seen.

Mortality The most important exposure outcome for population survival would be death.

Mortality rate Some indication of the rate of mortality, that is the proportion of the population dying from the disease in a specified period of time, would be advantageous. Where possible some idea of age-specific rates would be important, particularly where a disease is known to infect, preferentially, a proportion of the population. The mortality rate may be low and vaccination considered unnecessary.

THE OVERALL AIMS OF A VACCINATION PROGRAMME



THE OVERALL AIMS OF A VACCINATION PROGRAMME

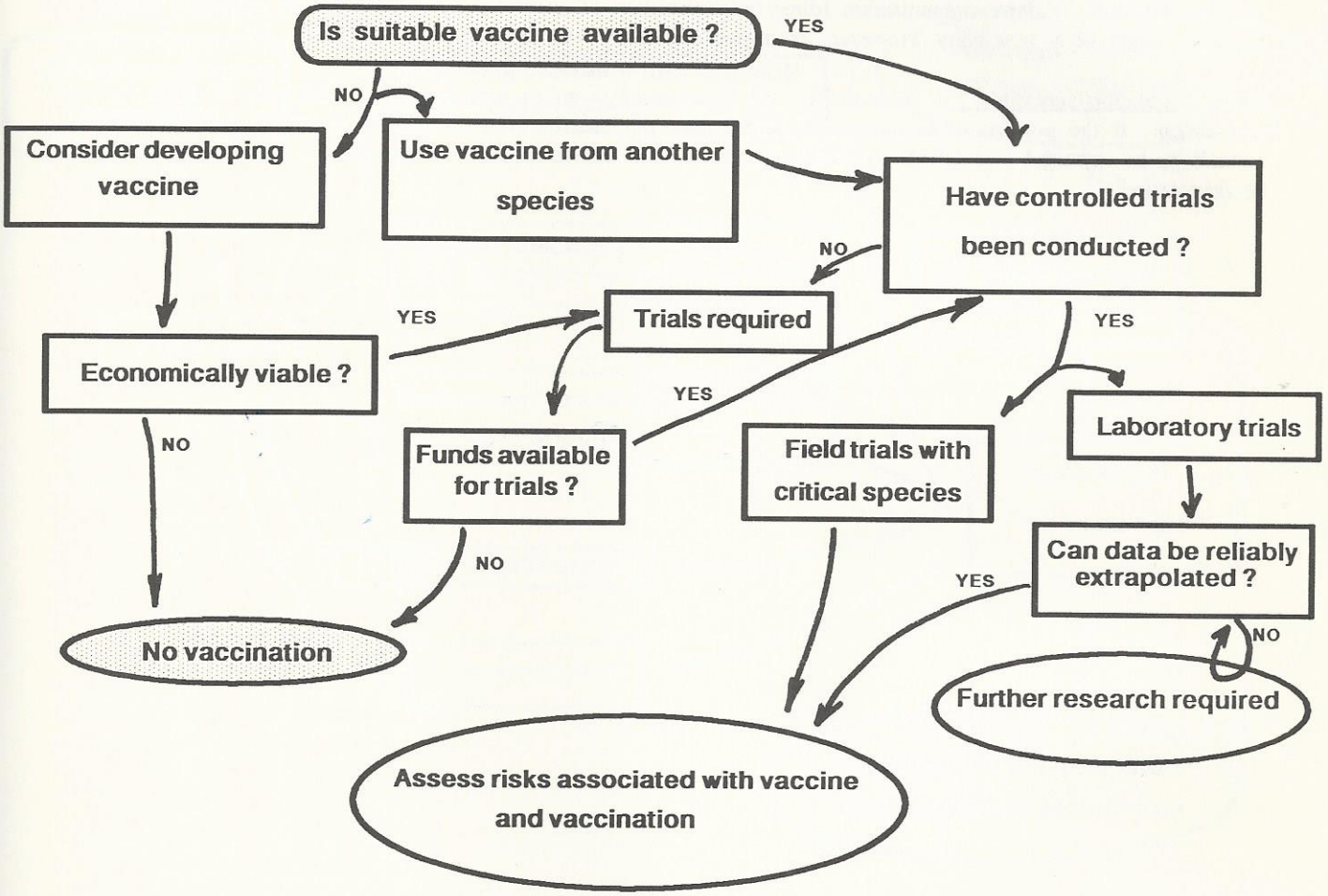
Aim of the vaccination programme This stage of the decision tree considers the reasons for chosing to vaccinate a population. Any vaccination programme will necessarily be a preventive measure, but within this definition will be various reasons for continuing the policy.

Aims might be to reduce the mortality rate in a remnant population or among an endangered species in the hope of preserving the remaining individuals; or because such populations and species are at risk from secondary infection through contact with a 'carrier' population. Large scale vaccination might reduce the number of susceptible individuals in the population to below some threshold which prevents the infection from becoming established. Finally, due perhaps to public pressure, there may be a perceived need to reduce the animals' suffering even if it is too late to prevent endemicity. Economic considerations will also come in, particularly if the wildlife population threatens to contaminate livestock.

Timing: Is it too late to vaccinate ? This is a vital consideration in view of the fact that active immunisation is only effective in an individual which has not yet been exposed to the disease or whose antibodies have waned. It will rarely alter the course of an infection once contracted. If the disease has established itself in the population it might be impossible to recognise the remaining susceptible individuals requiring vaccination, regardless of stage of infection. Passive immunisation (direct administration of antibodies) following known exposure, where available, might be a possibility. However, its degree of success will vary between individuals.

Is the population accessible ? Accessibility will be a major factor in determining the feasibility of mass vaccination. If the population is inaccessible to humans, particularly if administration of the vaccine required animals to be captured (see later), the consequences of such interference on the population may in themselves be devastating.

THE AVAILABILITY AND TRIAL STATUS OF A POTENTIAL VACCINE



THE AVAILABILITY AND TRIAL STATUS OF A POTENTIAL VACCINE

Is a suitable vaccine available ? This is a fundamental stage in the decision process. Where an imminent epizootic has been predicted, among for example an endangered population, this may bring forth various resources to enable a vaccine to be developed. In many other circumstances the motivation to develop a new vaccine may not be so strong. Often developmental costs will be prohibitively high.

If a species-specific vaccine is already marketed, the next stage would be vaccine trials. However, it is more likely that a vaccine developed for another species will have to be used.

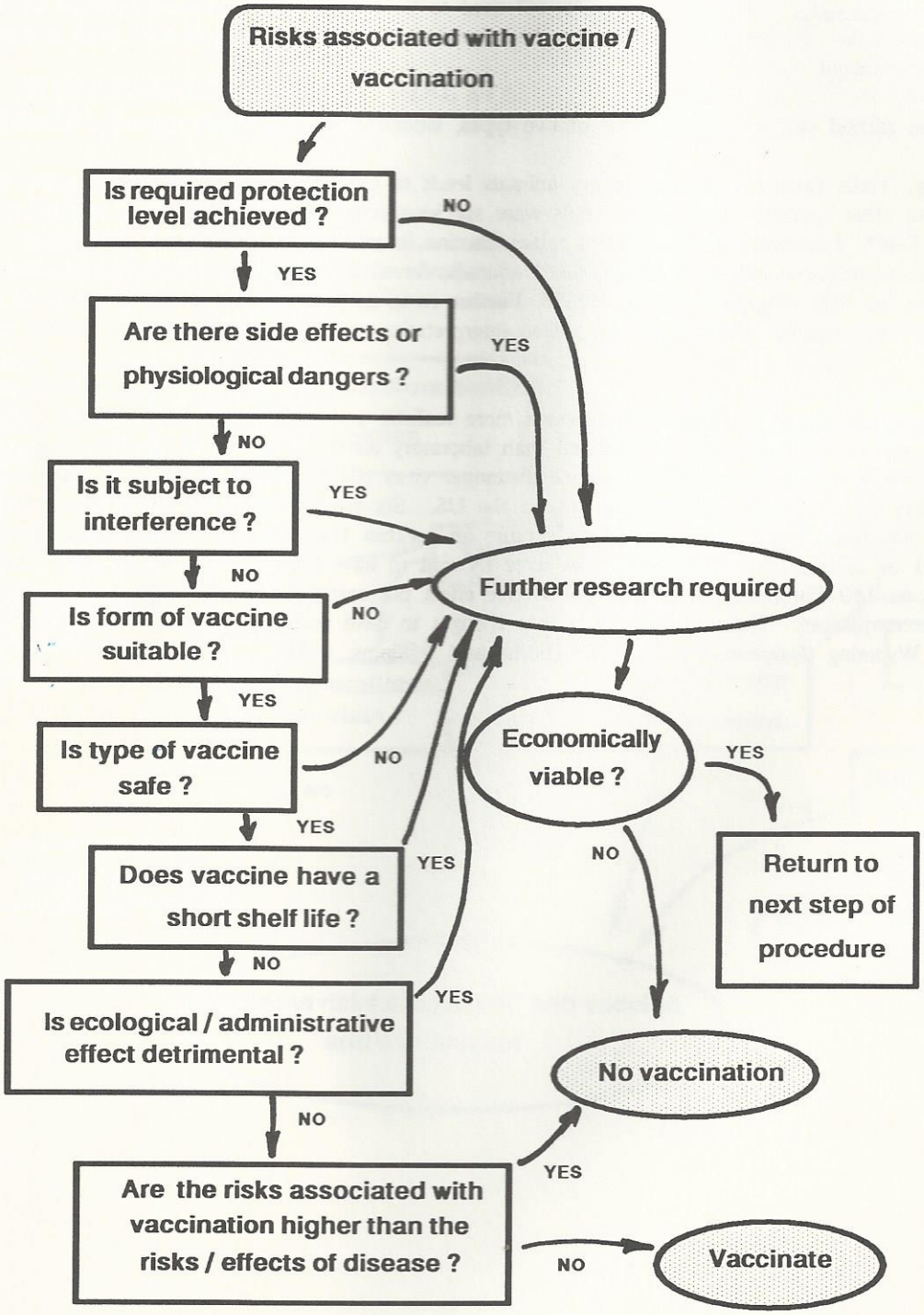
Have trials been conducted ? Experimental trials will need to be designed and carried out before the vaccine can be used in the wild. If these have not already been conducted, the cost implications of such a programme will have to be considered.

If they have been carried out, they will be one of two types, laboratory or field (both requiring controls).

Laboratory Trials Trials carried out on laboratory animals leads to the question, how reliably can the results be extrapolated to other species? Even if the trials were species-specific, could the laboratory model be extended to the field? For example, recombinant rabies vaccine in racoons demonstrated a discrepancy between the immune response induced in immobilised animals, force-fed vaccine, and those auto-inoculating or consuming bait in the field (Rupprecht et al, 1989). Further research to assist the assessment may be required depending on the trial outcome, but careful and skilled interpretation must be employed before further steps are taken.

Field trials with critical species Field trials although more realistic and likely to be species-specific, are rather more qualitative and less experimentally constrained than laboratory tests. The critical species is important as demonstrated by the use of a live attenuated canine distemper virus (CDV) vaccine among the endangered population of black footed ferrets (*Mustela nigripes*) in the US. Six were taken into a wildlife research centre for conservation breeding. All were vaccinated on capture and within 1 or 2 days 4 females had clinical signs of CDV and died 1 or 2 days later. The two males were thought to have been immune in the wild. The vaccine had been tested on 150 European ferrets with no adverse effect but extrapolation to a rare more exotic species had disastrous consequences. The population was thus thought to have perished but was rediscovered in the early 1980's in Wyoming (Carpenter et al, 1976; Thorne and Williams, 1988)

ASSESSMENT OF THE RISKS ASSOCIATED WITH THE VACCINE AND VACCINATION



ASSESSMENT OF THE RISKS ASSOCIATED WITH THE VACCINE AND VACCINATION

Risks associated with vaccine/vaccination The following questions should be empirically answered before consideration is given to vaccinating in the field.

Is the required protection level achieved ? Does the vaccine work ? Does it in any individual at risk, induce a sufficient and appropriate response, preventing them from contracting the disease ? This may be ascertained by serological testing where raised antibody titres are measured as markers of immunity. However, sacrificing animals by exposure to the parasite may be the only effective way of accurately determining the efficacy of the vaccine. It may also be necessary to use immune stimulants in conjunction with the vaccine. Establishing a dose-response relationship may be required in the species of interest and re-design of the vaccine may be required so that an effective immune response is elicited. For example, live attenuated rabies vaccine tested on racoons (*Procyon lotor*) indicated the dose required to initiate a response was several fold in excess of that previously reported as minimally protective in free-ranging foxes (Rupprecht et al, 1989).

Determining the uptake and administrative success rate for methods involving auto-inoculation or darting with injectable vaccines may be very difficult in the field.

If the required response is not induced, further research may be needed or a decision taken to abandon the project at this stage.

Are there side effects ? The vaccine should be thoroughly tested to ensure any observed and continuing side effects are not in themselves detrimental to the vaccinated individual.

Is it subject to interference ? This 'interference' may be from, for example, passive maternal immunity or other sub-clinical infection which prevents an antibody response by, for example, blocking the relevant antigenic receptor sites. Redevelopment of the vaccine may counteract this but only serological and challenge testing will indicate if interference is occurring.

Is the form of the vaccine suitable ? Oral and injectable forms may be available although often only one type will be viable in a given situation. Oral forms such as bait or aerosols will be dispersed into the environment and may affect unintentional species. Since oral vaccines can cover large geographical areas and thus dispersed populations, more easily than injected vaccines, these are more likely to be considered for wildlife populations.

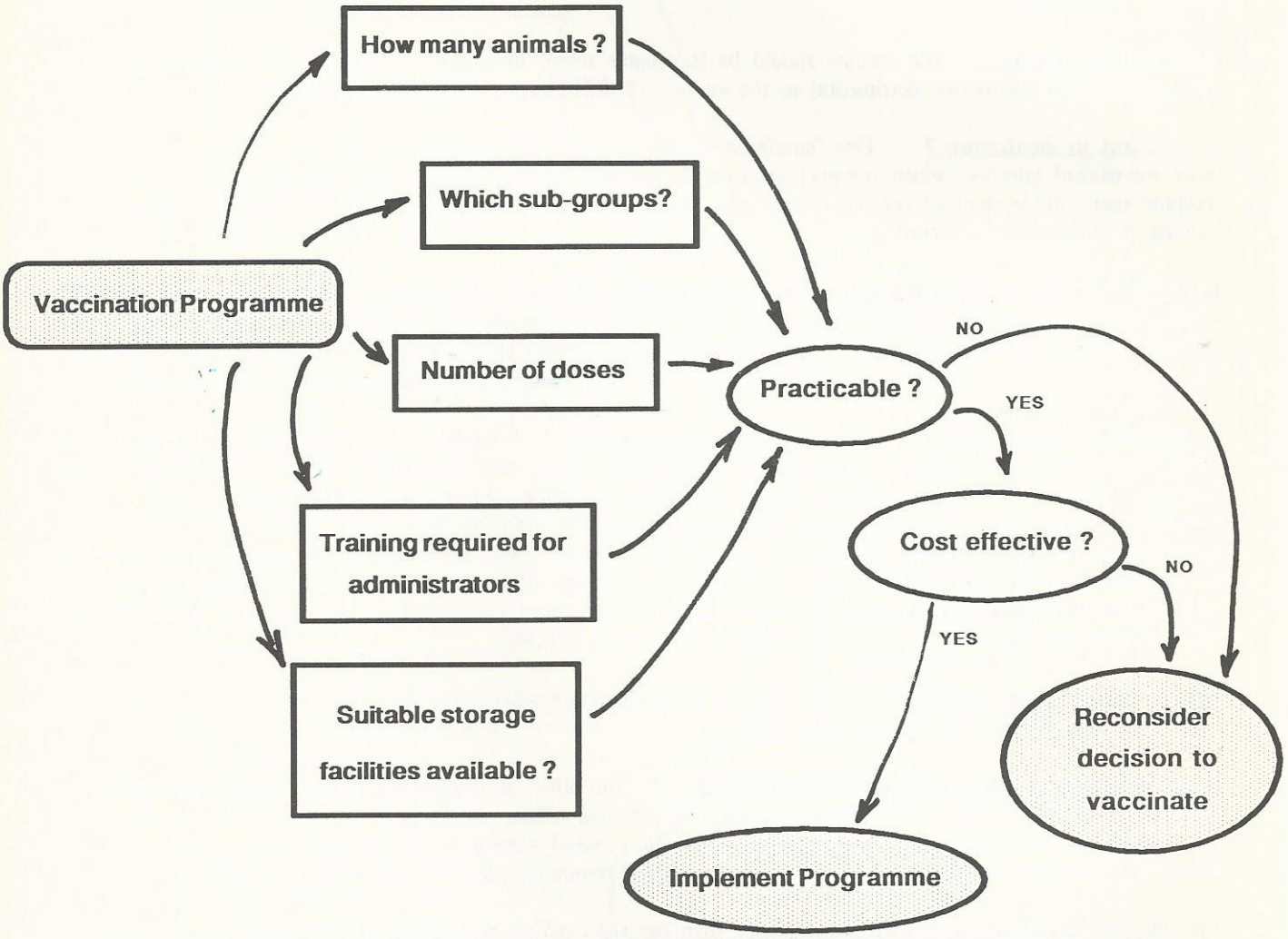
Is the type of vaccine safe ? How safe is the type of vaccine ? A variety is now available, depending to some extent on the causative organism, for example live attenuated and inactivated virus vaccines, recombinant DNA vaccines and toxoids for certain bacterial infections. Some are more inherently safe than others. Most prominent are the live attenuated vaccines which use an avirulent form of the virus. These are not recommended for use in wildlife, since even if it has been demonstrated in trials that the vaccine is effective for the particular species, transmission might occur with the resultant effects on other species being impossible to assess. The possibility that the process used to render the organism non-pathogenic has not been successful in one particular vaccine batch may be too dangerous for use in wildlife.

Does it have a short shelf life ? This may be a consideration where conditions for administering the vaccine within the time of the shelf life are unrealistic.

Is the ecological or administrative effect detrimental ? The effect of the vaccine on the environment and ecosystem is obviously important. Where possible the potential effects should be addressed in the vaccine trials and subsequent risk assessment. For example, what effect would aerosol or bait vaccines have on other animals? What are the inherent dangers of capture when compared with the disease in question?

Are the risks associated with vaccination higher than the risks or effects of disease ? If the adverse effects from vaccination do not outweigh those associated with the disease, vaccination could still be a viable option.

DESIGN OF A VACCINATION PROGRAMME AND SCHEDULE



DESIGN OF A VACCINATION PROGRAMME AND SCHEDULE

Vaccination programme Once it has been decided that vaccinating a wildlife population is a viable and prudent method for controlling a disease, a schedule should be drawn up. However, the programme may have to be abandoned due to practical difficulties.

Drawing up the vaccination programme How many animals and which sub-groups should be targeted? The number will depend on the size and accessibility of the population and the overall aim of vaccination at the outset. Relief of suffering might be more arbitrary than where herd immunity and population resistance are sought. Numbers will also depend on resources available. Vaccinating sub-groups such as the young or females again will depend on the disease attack rate and pattern. The number of doses, dictated by the vaccine type, might be a constraining factor. The most viable type would be in a single dose which affords lifelong protection: however, an assessment will again be required if booster doses at given intervals are necessary.

Training will be required for administrators, where qualified technicians are unavailable. This will probably be a major cost implication again depending on the number of animals to be vaccinated and the method of vaccination.

Storage facilities would need to be adequate. Many vaccines have to be stored below room temperature. Some field conditions may make this requirement very difficult to fulfill. If some or all of these steps are either impracticable or too costly vaccination might not be a viable measure.

III Some Examples

Phocine Distemper in Common Seals

The impetus for producing this document came from the phocine distemper epizootic which occurred around the coasts of northwest Europe in 1988. Although there were repeated public calls for vaccination this is a case where such action would probably have damaged the seal populations even further.

In early April, 1988 large numbers of prematurely born common seal pups, and later adult seals, were found on the Danish island of Anholt in the Kattegat. May and June saw very large numbers of dead seals being washed up along the Dutch and German Wadden Sea coast (Harwood and Reijnders, 1988) coast and in August, after the epidemic had spread to the east coast of England, Dutch scientists isolated the virus responsible. It was a previously unrecognised distemper-like virus of the morbilli group.

The potential effect of the disease was easily definable after the causative organism had been isolated. It was obviously highly infective and the risk of exposure via inhalation was high, particularly when animals were hauled out together in dense concentrations. The outcome of such exposure in common seals was usually fatal and mortality rates of more than 60% were recorded in some areas. It was clear then that vaccination was a control measure that could be considered further.

The aim of a vaccination programme against phocine distemper would have been two-fold. Firstly, with so much media attention and public pressure to "save our seals" it was seen as a way of reducing the amount of death and sickness among the population and perhaps of containing the outbreak. Certainly for uninfected seals taken into sanctuaries and rescue centres it would ensure protection against subsequent infection. As for mass vaccination, by September, when trials of a potential vaccine began, the epizootic was passing its peak and a high proportion of the surviving animals had probably developed natural immunity.

However, the question of population accessibility was most important in this example. Seals inhabit remote areas and islands and spend much time at sea. Capturing susceptible animals to administer a vaccine would have been an expensive, dangerous and, not least, an inexact undertaking. The only time seals can be caught in large numbers is during the pupping season and the moult. They are very sensitive to disturbance, particularly at pupping, and attempts to catch them at this time could have caused increased mortality. A vaccine, based on a canine distemper vaccine for dogs was successfully tested on captive seals in Holland and the UK. As an inactivated form however, it required two or three doses at intervals of 7-14 days (Osterhaus *et al*, 1988; Visser *et al.*, 1989) to initiate a response. This would have been impracticable in the field.

The epizootic was restricted to a defined geographical area but there were fears that the virus might spread to the Mediterranean monk seals (*Monachus monachus*) which inhabit Madeira and the north Atlantic coast of Africa and whose total population is less than 1000 individuals. What effect the disease would have had on monk seals was totally unknown but in the UK grey seals were much less susceptible than common seals. However, there was no guarantee that mass immunisation of the UK seal population in 1988 or 1989 would have prevented the disease from spreading to other populations

Using the decision trees in retrospect, it is clear that mass prophylactic immunisation of the UK seal population was not a practical or necessary control measure to prevent the spread of the epizootic.

Canine Distemper in Black-footed Ferrets

The black-footed ferret was declared an endangered species in the US in 1964. Six were taken into captivity for conservation breeding in the 1970's when a canine distemper (CDV) epizootic threatened the survival of the species. CDV causes 100% mortality in many ferret species. Four females and two males were injected with live attenuated virus distemper vaccine. Twenty-one days later the four females had clinical signs resembling CDV and later died, the cause of death was confirmed as canine distemper. It was later determined that these vaccine-induced fatalities were due to insufficient attenuation of the vaccine (Carpenter *et al,* 1976). The males were thought to have been immune before capture.

Using the first diagram to assess the potential effect of the disease, the risk of exposure causing severe mortality was obviously high. In a conservation breeding programme designed to prevent a population from becoming extinct through disease, it was therefore prudent to consider vaccination on capture.

The aim of the programme was clearly defined at the outset. Quiescent CDV infection might have become acute due to the stress of capture or because the animals were already infected and incubating the disease. This further illustrates the necessity to ensure the vaccine is administered well before exposure to infection, something which is almost impossible in a wildlife population.

The 'availability and trial status of a potential vaccine' section in this example is of particular importance. An attenuated CDV vaccine was available and controlled laboratory trials had been conducted using 150 European ferrets (*Mustela putorius*) as a model. They had suffered no ill-effects post-vaccination. The risks associated with vaccination did not, therefore, seem to outweigh the risks of disease and vaccination was carried out. There was no reason to believe the black-footed ferret would react differently to its European relative. However, further research may have alerted those involved to the risks involved in extrapolation between species. A full risk assessment at this stage may have prevented the programme from continuing.

In 1985 another outbreak of canine distemper was reported in Park County, Wyoming. In September/October of 1985, six Black-footed ferrets were captured for a captive breeding programme. The last two taken in were seriously ill with canine distemper, which had been contracted in the wild. It was probable that all captive ferrets had been exposed and would die. All did indeed perish, and capture records indicated the individuals had come from widely disperse locations. Emergency trapping was instigated to remove unexposed ferrets as founder animals for conservation breeding and six, placed in isolation, did not develop CDV. It was clear however, that insufficient animals had escaped the epizootic to maintain a viable population in the wild and all remaining Black-footed ferrets were captured for breeding and later reintroduction (May 1986; Thorne and Williams, 1988).

This example highlights the need for both care in interpreting findings from trials on related animals and the risks associated with using an attenuated virus vaccine rather than an inactivated one. Attempting to protect wildlife species with a vaccine which was not intended for such use may result in accidental death and a precautionary approach should always be adopted. Extra care should be taken when dealing with endangered species. Even though inactivated vaccines afford less protection and require several innoculations, their use may be preferable.

Measles in the Mountain Gorilla

One of the last surviving populations of mountain gorilla (*Gorilla gorilla beringei*) is found in the Parc des Volcans on the border between Rwanda and Zaire in central Africa. These animals have become habituated to humans and organized visits to them are Rwanda's greatest source of foreign currency. During 1988 unusually high numbers of gorillas were found dead. One of the dead animals had an elevation in measles antibody titre and pathological signs of the disease.

Wildlife species which live in close proximity to man be at risk from human contagious diseases. The risk to man and his animals from zoonotic infection is well recognised, but the converse threat is perhaps less obvious. The source of measles infection in the gorilla population was clearly anthropogenic.

Vaccination was considered at an early stage, with the aim of preventing further spread of disease within the population. The population was habituated and therefore accessible so that a significant proportion of the individuals could be darted with an injectable vaccine.

An attenuated measles vaccine which is used on humans and known to provide good protection to a wide range of primates, including the closely related lowland gorilla (*Gorilla gorilla gorilla*), was chosen. Early trials on a small group of animals within the Parc were a success and the gorillas showed no adverse reactions. This

subspecies-specific trial indicated the safety and efficacy of the vaccine under semi-controlled conditions (Hastings, pers comm).

Each potential risk associated with the vaccine or vaccination method was evaluated at the time of the trial and the overall assessment indicated that the debilitating effects of the disease would outweigh any unapparent risks through vaccination.

The decisions taken in this programme closely match those that would have been highlighted had a risk assessment been conducted using the decision trees in these guidelines. A notable difference when comparing it with the previous example was the use of the target species during the trial stage, eliminating the need for extrapolation.

A vaccination programme was drawn up which targeted a high proportion of the susceptible animals. It was not possible to conduct post-vaccination serology to determine immune status but no further signs of measles have been reported among the population. It will never be clear if there was a real danger of a measles epidemic among the Rwandaise gorillas, or if the virus was actually brought into the park by tourists. But no harm has been done and a major tragedy may have been averted.

References

Baer, G (1988): Oral rabies vaccination: An overview. *Rev. Inf. Dis.* **10,** 644-648.

Blancou, J; Kieny, M P; Lathe, R; Lecocq, J-P; Pastoret, P P; Soulebot, J P; Desmettre, P (1986): Oral vaccination of the fox against rabies using a live recombinant vaccinia virus. *Nature (Lond)* **322**, 373-375.

Carpenter, J W; Appel, M J G; Ericson, R C; Novilla, M N (1976): Fatal vaccine-induced canine distemper virus infection in black-footed ferrets. *J. Am. Vet. Med. Assoc.* **69,** 691.

Harwood, J; Reijnders, P J H (1988): Seals, sense and sensibility. *New. Scientist* 15 October, 28-29.

May, R M (1986): The cautionary tale of the black-footed ferret. *Nature (Lond)* **320**, 13-14.

Osterhaus, A D M E; Uytdehaage, F G C M; Visser, I K G; Vedder, E J; Reijnders, P J H; Kuiper, J; Brugge, H N (1988): Seal vaccination success. *Nature (Lond)* **337,** 21.

Rupprecht, C E; Dietzschold, B; Cox, J H; Schneider, L G (1989): Oral vaccination of racoons (*Pracyon lotor*) with an attenuated (SAD-B19) rabies virus vaccine. *J. Wild. Dis.* **25(4)**, 548-554.

Thorne, E M; Williams, E S (1988): Disease and endangered species: The black footed ferret as a recent example. *Cons. Biol.* **2,** 66-64.

Visser, I K G; Van de Bildt, M W G; Brugge, H M; Reijnders, P J H; Vedder, E J; Kuiper, J; De Vries, P; Walvoort, H C; UytdeHaag, F G C M; Osterhaus,A D M E (1989): Vaccination of harbour seals (*Phoca vitulina*) against phocid distemper with two different inactivated canine distemper virus (CDV) vaccines. *Vaccine* **7,** 521-526.