The European Agency for the Evaluation of Medicinal Products

EMEA/CVMP/682/99 - FINAL

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

NOTE FOR GUIDANCE:

DURATION OF PROTECTION ACHIEVED BY VETERINARY VACCINES

RELEASED BY CVMP FOR CONSULTATION	OCTOBER 1999
END OF CONSULTATION	30 APRIL 2000
DISCUSSED IN IMMUNOLOGICALS WORKING PARTY	SEPTEMBER 2000
ADOPTION AS FINAL BY CVMP	OCTOBER 2000
DATE FOR COMING INTO EFFECT	1 MAY 2001

Public

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Switchboard (44-20-7) 418 8400 Fax (44-20-7) 418 8447
E-mail: mail@emea.eudra.org http://www.eudra.org/emea.html

DURATION OF PROTECTION ACHIEVED BY VETERINARY VACCINES

1. Introduction.

Directive 81/852/EEC states that all claims on the efficacy of the vaccines, including the duration of protection, and the regimens of administration contained in the application for a marketing authorisation shall be fully supported by the data from specific laboratory trials and field studies.

The European Pharmacopoeia states that any claim regarding the duration of protection achieved by vaccines shall be supported by the data from trials, without specifying the methods and requirements concerned.

The formulation of claims shall take into account the guidance contained in the Position paper on Indications and Specific Claims for immunological veterinary medicinal products.

In the case of vaccines, efficacy means induction of immunity to provide protection. The nature, degree, onset and duration are the main parameters of the protection.

The duration of protection achieved by vaccines is influenced by a number of factors such as the characteristics of the causal agent(s) of the disease, the epizootiology of the infection, the immunogenicity of the active substances of the vaccines and the nature of the immune-response of the target animals.

The duration of protection may be different for each category of vaccines and for the products within a category of vaccines, as a consequence of the quality and properties of the products concerned.

In addition, it has to be realised that the duration of protection achieved under field conditions can vary from time to time and can also vary from that achievable under laboratory conditions because of the influence of a number of factors, such as the field conditions of use, e.g. exposure to the infectious agent(s) and the health, condition and immunological status of the animals to be vaccinated.

The guidance in this paper is specifically aimed at vaccines against infectious diseases, although the same principles may be applicable to products which through immunological mechanisms affect the physiological functions of an animal.

In order to avoid frequent vacccinations, it is recommended to study the vaccines in a manner which demonstrate the actual duration of protection provided and to develop products that provide as long a duration of protection as possible.

2. Scope of the guidance.

The scope of this guidance is to define what data shall be generated from trials and how such data can then be used to support claims for the duration of protection achieved by veterinary vaccines.

3. Definitions.

For the purpose of this guidance the following definitions apply:

Basic vaccination scheme:
One or more administrations of a vaccine with the second and any recommended subsequent doses given a short time after the first dose. This is the vaccination scheme which is necessary to obtain and maintain the level of protection claimed by the applicant.

Re-vaccination scheme:
One or more administrations of a vaccine used to maintain its initial protective effects, induced by the basic vaccination scheme. The first (or only) dose of the re-vaccination is given a relatively long time (e.g. 3 months or more, depending on the species and the disease) after the basic vaccination scheme.

Regimen of vaccination:
The basic vaccination scheme and re-vaccination scheme altogether.

4. Duration of Protection

For most infectious animal diseases, one administration of a vaccine does not provide protection which will last for the natural or economical life of the animals. Therefore, regimens of vaccination are in most cases necessary.

Where there are more administrations of vaccine recommended in the basic vaccination scheme and/or the re-vaccination scheme, the protection during the interval(s) between the administrations has to be also addressed.

Where there is no recommendation for more than one administration of a vaccine or for only a basic vaccination, this implies in principle a life-long protection thereafter. As the natural or economical duration of the life of animals differs for species and categories within a species and regionally, the claimed duration of protection shall then be specified and supported by sufficient data.

In cases of seasonal diseases, it will be sufficient to demonstrate the duration of protection in the year after vaccination until the end of the natural occurrence of the disease. The protection in the seasonal period(s) in the next year(s), with or without re-vaccination, will have also to be addressed.

It is not possible to generalise about the minimum period for which a vaccine shall be expected to provide protection. However, in all cases, the duration of protection demonstrated shall be justified in relation to the length of time for which an animal is likely to be at risk.

5. Data Requirements

The duration of protection that can be claimed is the longest interval between the administration of a vaccine to target animals and the observed protection against the required challenge.

The studies required to generate this data shall be conducted under well-controlled conditions. If the necessary studies are very difficult to conduct in laboratory conditions, field trials only may be carried out. Since the duration of protection from vaccination is being measured in the studies, it shall be ensured that the vaccinated target animals are not exposed to intercurrent field infection which could boost the immunity. It is usually necessary, therefore, to maintain unvaccinated target animals in contact to act as sentinels in laboratory or field studies to provide the necessary assurances on this point.

The results from vaccination-challenge trials conducted under laboratory conditions shall be, unless justified, supplemented with sufficient data from well-controlled field studies. In these field studies, target animals are vaccinated in the field and undergo thereafter a natural challenge in the field or an experimental challenge under laboratory conditions.

A. Duration of protection from the basic vaccination scheme.

a. For active immunity.
The duration of protection provided by the basic vaccination scheme shall usually be demonstrated by a challenge of vaccinated animals just before the recommended time for the start of the re-vaccination scheme.

b. For passive immunity.
The duration of protection of the progeny from passively acquired antibodies shall usually be demonstrated by a challenge at the time of natural susceptibility of the offspring of females which have been vaccinated at the maximum interval recommended between the basic vaccination scheme and parturition or lay.

In addition, data shall be presented to support the duration that is claimed for the protection of the offspring.

The nature of the disease concerned, including the age of the animals at which the onset of the disease usually occurs, as well as the onset of age resistance needs to be taken into account.

B. Duration of protection from the re-vaccination scheme.

The re-vaccination shall result in a protection that is quantitatively and qualitatively at least equivalent to the response to the basic vaccination scheme. This is best demonstrated by challenge trials at suitable times between the end of the scheme and the end of the claimed period of protection thereafter.

Vaccination-challenge trials, in particular those to study the duration of protection, are expensive and time-consuming as well as having animal welfare issues involved. In order to limit the need for frequent challenges in studies on the duration of protection, it may be considered:

- to challenge of a more limited number of immunised animals
- to measure the protection using a suitable indicator other than challenge.

Antibodies against the causal agent(s) of the infectious disease may be an example of such indicators.

For such an indicator to be acceptable, evidence shall be provided to show that the indicator plays a substantial role in the protection of the target species and that there is a sufficient qualitative and quantitative relationship between the indicator and the protection of the target species against the disease concerned.

It must be demonstrated (via serological studies or other markers of protection) that the level of response before revaccination or at the end of the protection period can be considered as equal to the one observed at the time of challenge used to demonstrate the efficacy.

The data generated by a combined vaccine can be used to support the protection to be induced by a vaccine containing fewer active ingredients provided these products are manufactured according to the same process, have the same composition (with the exception of the additional antigens) and there is no evidence of a negative or positive interference from the other active ingredients present in the combined vaccine.

As the immune systems of even related, species are different, the use of data from trials in a species other than the target species will normally not be acceptable.

In view of the diversities of species and diseases, each case has to be considered on an individual basis.

In the case of fish vaccines, long term studies are often difficult to perform under laboratory conditions. Therefore, it is essential that appropriately designed field trials are carried out.