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REVISED POSITION PAPER ON

INDICATIONS FOR VETERINARY VACCINES

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1. Introduction.

The indications being made for an immunological veterinary medicinal product shall be clearly described in the Summary of Product Characteristics (SPC) and product literature in order to inform the end user of the expected degree of veterinary vaccine efficacy.

Directive 2001/82/EC requires that all indications made by the Applicant with regard to the properties, effects and use of the product shall be fully supported by results of specific trials contained in the application for marketing authorisation.

The degree of efficacy which can be achieved will vary between different categories of veterinary vaccines as efficacy is influenced by a number of factors e.g. the characteristics of infectious agents, the epizootiology of the infection, the immunogenicity of the causal agent and the nature of the immune-response. This diversity is reflected in the different requirements of the potency tests as outlined in the monographs of the European Pharmacopoeia. Efficacy may also vary within a class of veterinary vaccines. Field efficacy can vary depending on a variety of factors and can differ from the efficacy achieved under laboratory conditions.

Immunisation is mainly intended to protect against infectious disease. To allow the user to consider the benefits and risks of the product and make an informed choice, the SPC and the product literature shall contain sufficient information on protection, observed side effects and shall clearly display adequate warnings and contra-indications.

2. Definitions

For the purpose of this paper the following definitions apply:

Immune response: The cellular and humoral responses of the animal's defence system to a specific immunogen.

Immunity: The immunological status of an animal in relation to an infectious animal disease and/or its causal agent(s), resulting from an immune response.

Indications: The indications are considered as the claims for the veterinary vaccine as they appear on the SPC.

Protection: The extent to which the condition of an animal, herd or flock is able to resist a particular infectious animal disease and/or its causal agent(s). This condition is also referred to as protective immunity. Apart from the onset, degree and duration, the nature of the protection may be further defined by reference to one or more of the following aspects

a. mortality
b the primary replication of pathogen in the target animal
c. the dissemination of the field pathogen(s) through the body of the target animal
d. the persistence of the field pathogen(s) in the body of the target animal (i.e. carrier status)
e. the transmission of the field pathogen(s) from the body of the target animal to the egg(s), embryo(s) and/or foetus(es)

f. the excretion and transmission of the field pathogen(s) from the body of the target animal to contact animals
g. the development of the lesions of the disease/disease complex in the target animal
h. the development of the clinical signs of the disease/disease complex in the target animal
i. the reduction of negative effects of the disease/disease complex on the performance of the target animal
j. the prevalence of field pathogen(s) in populations of target animals.
k. in exceptional justified circumstances, the development of an immunological parameter, such as a serological response. Such an immunological parameter shall only be accepted where a relationship has been shown between that parameter and protection and where demonstration of protection by challenge is not reasonably practical.

Efficacy: The ability of a veterinary vaccine to induce protection. The nature of this protection is defined within the categories a-k above.

3. Indications

The Applicant shall propose the indications clearly. The competent authorities shall decide on their acceptability based on assessment of the data provided in the efficacy part of the application.

3.1: Standard Indication Statements:

One of the following standard texts and wording shall be used, as appropriate, for the indications in the SPC and package insert:

For active immunisation or passive immunisation of target animals to
- prevent mortality, clinical signs and/or lesions of the disease/disease complex;
- prevent infection;
- reduce mortality, clinical signs and/or lesions of the disease/disease complex;
- reduce infection;

It is anticipated that an indication for prevention may be granted on the basis of results generated from laboratory studies, even in instances where complete prevention cannot be demonstrated in field trials.

3.2: Specific Efficacy Indications

The onset and duration of the protection of the veterinary vaccine shall be specified. Further specific indications (as outlined in section 2 above) which give more detailed information on the level of protection that can be expected following use of the veterinary vaccine shall also be included. These indications shall be supported by valid trial data.

4.0: Assessment

The assessment of efficacy is based on trials using the product by the recommended routes (e.g. respiratory), regimens of administration (i.e. vaccination schemes/schedules) and methods of application (e.g. spray). Studies shall be conducted using susceptible target animals and if appropriate, target animals with maternally derived immunity of the youngest age recommended for vaccination.

4.1: Efficacy Studies

4.1.1: Study Design

All efficacy indications shall where possible be supported with data generated from valid laboratory studies. Unless justified, results from laboratory trials shall be supplemented with data from field trials.

Where efficacy cannot be demonstrated in the laboratory (consult the Note for Guidance entitled 'Field trials with veterinary vaccines') data generated from field trials can be used to support efficacy indications. Scientific justification for such an approach must be provided.

The objective of these trials is to validate the indications for the immunological product. The variables chosen shall provide a valid and reliable measure of some important clinical or zootechnical benefit in the target animal population. These variables shall be specified in the protocol, along with the rationale for their selection.

4.1.2: Data Analysis

The role of statistics in laboratory and field trial design, conduct and analysis is important for the demonstration of efficacy. In all situations other than when judging efficacy by means of reference to the relevant monograph, a statistical analysis shall generally be performed for each trial unless a valid justification is provided. For further guidance on the role of statistics in laboratory and field trial design consult the Guidance document entitled 'Guideline on statistical principles for veterinary clinical trials'.

4.2: Examples

Where data demonstrate a decrease in clinical signs and/or lesions of the disease/disease complex in the treated animals after challenge, the indication shall be "reduction of clinical signs and/or lesions of the disease/disease complex". Specifications on the onset and duration of this protection shall be given and further specific efficacy indications may consist of references to the incidence and/or gravity of the clinical signs and/or lesions of the disease/disease complex, all of which are supported by data in the dossier. In this case, reference to an effect on infection rates with the causal agent(s) of the disease/disease complex is not acceptable.

When the dossier for a veterinary vaccine contains sufficient data regarding decreased infection rates but there is no information or noticeable effect on mortality, clinical signs and/or lesions of the disease/disease complex, the indication shall be "reduction of infection with the causal agent(s) of the disease/disease complex". In this case, reference to an effect on mortality, clinical signs and/or lesions of the disease/disease complex is not acceptable.

