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CHMP

GUIDELINE ON CLINICAL EVALUATION OF NEW VACCINES

ANNEX: SPC REQUIREMENTS

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INTRODUCTION (background)

The QRD "Human" Product Information template with explanatory notes (version 7.1 EMEA 06/2006) and the Convention to be followed for QRD templates (version 6.0, 04/2003) provide general guidance on format and text and should be read in conjunction with this Annex.

This Annex to the Guideline on clinical evaluation of new vaccines provides guidance on the format and content of sections 4 (Clinical particulars) and 5 (Pharmacological properties) of the SPCs that raise some issues specific for vaccines. Where appropriate, recommendations are made for standardised text.

SPC REQUIREMENTS

4.1 Therapeutic indications

The indication should routinely cover:

- The disease(s) to be prevented (including specific types of an organism if appropriate)
- The minimum age for use (e.g. infants from the age of 2 months)
- Appropriate age categories (e.g. neonates, infants, children, adolescents, adults)
- The maximum age for use if such a limit would be appropriate based on factors such as the disease epidemiology or antigen content of the vaccine

It may also be necessary to mention:

- Particular populations for which the vaccine is suitable (e.g. naïve, primed, at risk).
- Populations for which the vaccine is not suitable should usually be mentioned elsewhere.

4.2 Posology and method of administration

Posology

If appropriate, this section should clearly describe and separate doses and schedules for primary and booster vaccinations. In general, the recommendations should reflect the minimum age at the time of the first dose, minimum dose interval and minimum interval between the last dose of the primary series and first (and perhaps sequential) booster dose(s) that were evaluated in clinical studies.

For most vaccines intended for use in infancy, and for many intended to boost antigens routinely delivered in infancy, it will be necessary to include a general statement regarding the need to follow official guidance on the exact timing of these doses.

Advice on dose and schedule may need to be given separately for different age groups or other defined populations (e.g. the immunosuppressed).

It may be appropriate to state whether interchangeability of vaccines within a schedule can be recommended.

Method of administration

The route of administration should be specified (e.g. oral, i.m.).

For injectable vaccines, the route of injection should be specified, preferably with the place of first choice (e.g. deltoid muscle).

Important statements may include:

- For oral use only, do not inject
- Do not inject intravascularly
- Exceptional administration subcutaneously to patients with thrombocytopenia or bleeding disorders. Any data on safety or immune responses under these circumstances should usually appear in 4.4.

4.3 Contra-indications

The contra-indications should usually be limited to absolute contra-indications that should apply at the time of administration.

The following should usually appear as a minimum:

- TRADENAME should not be administered to subjects with known hypersensitivity to any component of the vaccine.
- As with other vaccines, TRADENAME should be postponed in subjects suffering from an acute severe febrile illness.

4.4 Special Warnings and precautions for use

Appropriate common statements might include:

- As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.
- (Tradename) should under no circumstances be administered intravascularly.
- Thiomersal has been used in the manufacturing process of this medicinal product and residues of it are present in the final product. Therefore, sensitisation reactions may occur.
- As with any vaccine, a protective immune response may not be elicited in all vaccinees.

This section may also describe:

- Lack of protection or limits of any cross protection there may be against strains or serotypes not in the vaccine.
- Situations (e.g. administration to persons already in the incubation phase) or populations (e.g. elderly) in which the efficacy of the vaccine has not been investigated or could not be anticipated.
- Factors that might be associated with an impaired immune response.

For live attenuated vaccines, the potential for transmission of vaccine strains should be described, as well as the possibility of reversion to virulence or of re-assortment with wild-type strains.

4.5 Interaction with other medicinal products and other forms of interaction

The section should clearly differentiate endorsements for concomitant administration that are based on clinical data as opposed to statements based on general principles. In general, satisfactory data obtained on concomitant administration with a representative vaccine of a certain type (e.g. giving a combination vaccine against diphtheria, tetanus, pertussis and other antigens vaccine with one of the MMRs on the market) should serve to support a general statement for co-administration.

Clinically important or potentially clinically important immune interference should be mentioned.

If there are no data regarding co-administration with a type of vaccine that is very likely to have to be co-administered, this should be stated.

Appropriate common statements may include:

- It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited.
- Immunoglobulin is not to be given with TRADENAME or
- If it is necessary to provide immediate protection, TRADENAME may be given at the same

time as (normal/x-specific) immunoglobulin. Injections of TRADENAME and immunoglobulin should be made into separate limbs.

4.6 Pregnancy and lactation

For vaccines that will be administered only in the pre-pubertal years, it is sufficient to state:

- TRADENAME is not intended for use in adults. Human data on use in pregnancy or lactation and animal reproduction studies are not available.

For vaccines to be used in individuals of childbearing age, the section should describe the available nonclinical and clinical experience.

For inactivated vaccines, it is usual to advise the following:

- As with other inactivated vaccines, harm to the fetus is not anticipated. However, TRADENAME should only be used during pregnancy when there is a clear risk of infection.

For live attenuated vaccines it is usual for use to be contra-indicated in pregnancy. However, if the vaccine is a well known product for which there is reported experience, it may be sufficient to discourage vaccination during pregnancy unless clearly necessary.

Regarding lactation, in the absence of data, it is usual to state for inactivated vaccines:

- The effect on breastfed infants of administration of TRADENAME to their mothers has not been studied.

Recommendations for live attenuated vaccines must be considered on a case-by-case basis.

4.7 Effects on ability to drive and use machines

For vaccines that will be administered only in the pre-pubertal years, it may be sufficient to state:

- TRADENAME is not intended for use in adults.

The usual considerations apply regarding statements to be made when the vaccine is intended for adults.

4.8 Undesirable effects

Some considerations specific to vaccines may include:

- Details of local and systemic reactions
- Special notes on certain ADRs such as fevers, febrile convulsions
- ADRs and ADR rates separated according to age group, number of doses, previous vaccination history, occurring in studies or reported from post-marketing surveillance
- Special notes on any increased rate of ADR(s) observed on concomitant administration with other vaccines.

4.9 Overdose

Any experience with overdose should be mentioned. It may be appropriate to mention that overdose is unlikely due to the mode of presentation (e.g. single dose pre-filled syringe).

5.1 Pharmacodynamic properties

This section should briefly summarise (tabulation may be appropriate) the most pertinent immunological data (using the most relevant parameters) and any estimates of efficacy or effectiveness considered to be valid (with caveats regarding the population in which these were measured). As necessary, the data should be broken down by primary series and boosting, by age group or by other factors, such as immunosuppression.

The section may include details of the established or putative immunological correlate of protection.