EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 May 2017
EMA/CHMP/VWP/124350/2017
Committee for Human Medicinal Products (CHMP)

Concept paper on revision of the Guideline on clinical development of vaccines

Agreed by Vaccines Working Party	November 2016
Adopted by CHMP for release for consultation	18 May 2017
Start of public consultation	23 June 2017
End of consultation (deadline for comments)	30 September 2017

The proposed guideline will replace Guideline on clinical evaluation of vaccines EMEA/CHMP/VWP/164653/2005

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Keywords	***Vaccines, humoral immune response, cellular immune response, vaccination schedule, immunogenicity studies, protective efficacy, effectiveness, safety, summary of product characteristics (SmPC) requirements***

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1. Introduction

The *Guideline on clinical evaluation of vaccines (EMEA/CHMP/VWP/164653/2005)* was developed during 2005-2006 and came into operation in 2007. It covers the design of clinical development programmes for new vaccines that are intended to provide pre- and post-exposure prophylaxis against infectious diseases. Some of the guidance provided is also relevant to the further development of licensed vaccines (i.e. generation of clinical data to support changes to the prescribing information in the post-authorisation period). Much of what this guideline says is still fully relevant to current vaccine clinical development but a revision is proposed to address issues that have come to light since it came into operation.

2. Problem statement

Since 2007 there have been several new vaccines developed and approved that prevent clinical diseases due to pathogens for which no vaccine was previously available. In addition, some new vaccines have been developed that have advantages over existing vaccines intended to prevent the same infectious disease. Much has been learned from these clinical development programmes and some have brought to light issues that have been addressed in scientific advice procedures that merit additions to or revisions of the current guideline. Furthermore, several ongoing programmes aimed at different infectious pathogens concern vaccination during pregnancy with the main or sole intent of providing a benefit to the fetus and this issue is not adequately reflected in the current guideline.

3. Discussion (on the problem statement)

The current guidance contains few statements that would now be considered inappropriate but it does not address several matters that have been and are important for clinical development programmes initiated and/or completed since 2007. Areas of clinical development issues that have been identified as possibly requiring revision, expansion or addition include at least the following:

- revised guidance on comparative immunogenicity studies, including considerations for interpretation of the results of trials intended to demonstrate non-inferiority or superiority of immune responses;
- situations in which age de-escalation studies are not necessary;
- use of different vaccines for priming and boosting;
- issues to consider when attempting to bridge efficacy between vaccines;
- vaccination of pregnant women to protect them and/or their infants;
- selection of appropriate control groups for vaccine efficacy studies in different circumstances;
- comparison of new and licensed vaccines containing antigens from different numbers of types or subtypes of the same organism;
- methods for derivation of immune correlates of protection (ICPs) or threshold values for interpreting immune response data by various means;
- prediction of vaccine efficacy when there is no ICP and vaccine efficacy studies are not feasible;
- vaccines with modest efficacy and/or that provide a short duration of protection;
- extrapolation of data obtained in geographically/genetically diverse populations to the EU population;
- consideration of size of the pre-licensure safety database by type of vaccine and its novelty;

- consideration of the safety database by population subgroup;
- special safety considerations by vaccine construct;
- circumstances of limited pre-licensure safety data;
- approaches to vaccine effectiveness, including when there is and is not a prior estimate of vaccine efficacy.

4. Recommendation

The Working Party recommends revising the guideline on clinical development of vaccines taking into account the issues identified above. In summary, the objective of the revision is to update the guideline based on current knowledge, including further reflection on immunogenicity studies and correlates of protection, vaccination of special populations including elderly and pregnant women, comparative studies, safety consideration by vaccine type and population and vaccine effectiveness studies.

5. Proposed timetable

It is proposed to draft the new guideline text during 2017 with the aim for release for 6 months consultation by 1Q 2018 and finalisation during 4Q 2018.

6. Resource requirements for preparation

The new text will be developed by the Vaccine Working Party members. It is proposed that there will be two Rapporteurs appointed to jointly draft the text and that this will be discussed by the working Party at teleconferences. One face to face meeting would be need to be devoted almost entirely to consolidating and agreeing the final draft text.

7. Impact assessment (anticipated)

An impact is expected on CHMP scientific advice procedures for vaccines, the content of pre-approval and post-approval clinical development programmes, on the consistency of advice given and approaches to dossier assessment and on the responses that the Working Party may provide on request to the CHMP on vaccine-related issues.

Interested parties will include sponsors involved in new vaccine development, public health bodies and national vaccine advisory committees. The draft text is anticipated to be of interest to the PDCO and comments are to be invited.

8. References to literature, guidelines, etc.

Guideline on Influenza Vaccines, Non-clinical and Clinical Module (EMA/CHMP/VWP/457259/2014)

Guideline on good pharmacovigilance practices (GVP) Product- or Population-Specific Considerations I: Vaccines for prophylaxis 5 against infectious diseases. EMA/488220/2012

Guidelines on clinical evaluation of vaccines: regulatory expectations. Annex 4 of WHO Technical Report Series, No. 924, 2016