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COMMITTEE ON HUMAN MEDICINAL PRODUCTS (CHMP)

CONCEPT PAPER ON THE REVISION OF THE GUIDELINE ON DOSSIER STRUCTURE AND CONTENT FOR PANDEMIC INFLUENZA MARKETING AUTHORISATION APPLICATION (CPMP/VEG/4717/03)

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AGREED BY THE BIOLOGICS WORKING PARTY	16 May 2007
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1. INTRODUCTION

In 2004, CHMP adopted two guidelines on scientific aspects and the procedure for the fast-track authorisation of pandemic influenza vaccines: the *Guideline on dossier structure and content for pandemic influenza vaccine marketing authorisation application* (EMEA/CPMP/VEG/4717/03) and the *Guideline on submission of marketing authorisation applications for pandemic influenza vaccines through the centralised procedure* (EMEA/CPMP/VEG/4986/03). The procedure involves the submission of a core pandemic dossier (resulting in the approval of a mock-up pandemic vaccine) during the interpandemic period, followed by a fast-track approval of the pandemic vaccine, based on the submission of the pandemic variation.

2. PROBLEM STATEMENT

Since the development and publication of the *Guideline on dossier structure and content for pandemic influenza vaccine marketing authorisation application*, several core pandemic dossiers have been submitted and reviewed. Two mock-up pandemic vaccines have received a marketing authorisation in 2007. The experience gained from the assessment of the submitted core dossiers indicates that some sections of the guideline need to be clarified or reviewed.

Additionally, the *Guideline on influenza vaccines prepared from viruses with the potential to cause a pandemic and intended to be used outside of the core dossier context* (EMEA/CHMP/VWP/263499/ 2006) was recently published. It is important to include references to this guideline in the revised guideline on dossier structure and content for pandemic influenza vaccine marketing authorisation application and clarify the difference between pandemic vaccines and vaccines prepared from viruses with a pandemic potential.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The core dossier concept has been accepted and used by influenza vaccine manufacturers as a tool to allow the fast track approval of the pandemic vaccine. The experience gained so far in the evaluation of core pandemic dossiers indicated that some sections of the guideline need to be clarified or reviewed in order to provide clearer guidance to the vaccine manufacturers for the development of mock-up pandemic vaccines and the preparation of core dossiers.

4. RECOMMENDATION

The Biologics Working Party (BWP) and Vaccine Working Party (VWP) recommend to revise the guideline on dossier requirements and content for pandemic influenza vaccine marketing authorisation application. All parts of the guideline will be updated if required, but in particular, following sections have been identified for revision:

1. Introduction / scope

The differences between pandemic vaccines (for which the core dossier concept applies) and 'pre-pandemic' vaccine (vaccines prepared from viruses with pandemic potential) and the difference uses of these vaccines will be described.

2. Quality

- Section 3.1.1. Vaccine reference virus

This section will be revised to clarify what information is required to document the genetic stability and the potential contamination of the reference virus prepared using reverse genetics technology.

3. Non-clinical safety and immunological requirements

- Section 4.2.will be updated and brought in line with the guidance included in the *Guideline on influenza vaccines prepared from viruses with the potential to cause a pandemic and intended to be*

used outside of the core dossier context. The section on challenge experiments will be updated to reflect current regulatory thinking.

4. Clinical requirements

- Section 5.2.1. Target population
This section will be updated with respect to studies in special populations (children, elderly).

- Section 5.2.3 Immunological criteria
Further reflection is needed on what information would be required in case a vaccine does not meet all 3 serological criteria (as described in CPWP/BWP/214/96). The principle to supplement the clinical data with the results from non-clinical challenge studies (e.g. in ferret or non-human primates) will be elaborated.

Further guidance on the study of neutralising antibodies and cell-mediated immunity will be included. Some reflections might be included on the study of neuramidase inhibitor antibodies.

- Section 5.2.6 Post-approval commitments
This section will be revised to reflect the work by the Pharmacovigilance working party on the core pharmacovigilance plan for pandemic influenza vaccines. The need to revise sections 5.3.2 to 5.3.5 on the post-approval clinical investigations, immunogenicity, effectiveness and safety of the final pandemic vaccine will be considered.

The need for cross antigenicity and cross protection studies with the mock-up vaccine will be addressed.

5. PROPOSED TIMETABLE

After adoption of the concept paper, it is anticipated that the draft revised guideline will be adopted and released for 3 months consultation in the last quarter of 2007.

6. RESOURCE REQUIREMENTS FOR PREPARATION

BWP will be responsible for the revision of the quality section of the guideline; VWP will develop the revised non-clinical and clinical requirements. The need for a drafting groups in the margins of the BWP and VWP will be considered.

7. IMPACT ASSESSMENT (ANTICIPATED)

The principle of core pandemic dossiers as a tool to facilitate the fast-track approval of pandemic influenza vaccines is well accepted by industry. The provision of updated guidance in the revised guideline is expected to impact positively on the development of mock-up pandemic vaccines and the preparation of core dossiers. It will also facilitate the evaluation of pandemic core dossier by the assessors from the Competent Authorities.

8. INTERESTED PARTIES

Pharmaceutical industry and Competent Authorities and assessors.

9. REFERENCES TO LITERATURE, GUIDELINES

- Guideline on dossier structure and content for pandemic influenza vaccine marketing authorisation application (EMEA/CPMP/VEG/4717/03)

- Guideline on submission of marketing authorisation applications for pandemic influenza vaccines through the centralised procedure (EMEA/CPMP/VEG/4986/03)
- Guideline on influenza vaccines prepared from viruses with the potential to cause a pandemic and intended to be used outside of the core dossier context (EMEA/CHMP/VWP/263499/ 2006)
- Note for guidance on harmonisation of requirements for influenza vaccines (CPMP/BWP/214/96)