The European Agency for the Evaluation of Medicinal Products
Human Medicines Evaluation Unit

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CONCEPT PAPER ON THE DEVELOPMENT OF A COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP) POINTS TO CONSIDER ON CELL-DERIVED INFLUENZA VACCINES

1. INTRODUCTION

At the CPMP meeting in May 1999, the need for an annex to the current *CPMP Note for guidance on the harmonisation of influenza vaccines* was highlighted following the discussion at the BWP, of the specific issues arising from the evaluation of cell-derived influenza vaccines.

The current *CPMP Note for guidance on the harmonisation of influenza vaccine* covers quality as well as safety and efficacy issues that are mainly related to the yearly change of vaccine strains in influenza vaccines produced on eggs, and does not include guidance on the more recent, innovative influenza vaccines. The scope of this concept paper is to address the quality and related safety and efficacy issues which are pertinent to cell-derived influenza vaccines including, where relevant, the issue of yearly strain adaptation.

2. PROBLEM STATEMENT

Current guidelines and requirements for influenza vaccines[i,ii] have been drafted for vaccines that are produced on eggs. Previously unlicensed mammalian cell substrates are now being proposed for influenza vaccine manufacture and influenza-specific aspects, i.e. the yearly strain change and consequent time constraints, have to be taken into account. This has an impact on the applicability of existing guidance and in particular on the feasibility of testing of the virus seeds for extraneous agents.

Production and control of cell-derived influenza vaccine may be compared to classical inactivated vaccines such as Inactivated Poliomyelitis, Hepatitis A and Rabies. A number of available guidelines and requirements would be applicable to the cell substrates used for a cell-derived influenza vaccine:

- Ph. Eur. Monographs on extraneous agents and cell substrates[iii,iv]
- ICH and WHO guidelines on cell substrates[v,vi]
- Veterinary guidelines on viral contamination (which take into account species-specificity)[vii]

However, the need for additional specific guidance for this type of vaccine is foreseen, with particular consideration being given to the following quality issues:

- Testing for extraneous agents in the cell substrate
- Testing for extraneous agents in the seed viruses
- Production issues related to extraneous agents
- Issues related to biological standardisation
- Other issues such as tests for the effectiveness of viral vaccine inactivation, endotoxin levels, validated tests for residual host cell protein, information on antigenic characterisation and testing for cross-reactivity of specific antisera raised against egg-produced and cell-produced vaccine viruses.

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3. RECOMMENDATION

It is proposed that a Points to consider be prepared for CPMP giving EU scientific guidance on these issues to supplement the *Note for guidance on the harmonisation of influenza vaccines*. This might be adopted as an annex to the above mentioned Note for guidance.

4. TIMETABLE

A Points to consider on cell-derived influenza vaccines should be available for submission to the CPMP in November 1999, for release for external consultation for 3 months. During the annual meeting of the Ad hoc Influenza Working Party in spring 2000, the comments received will be consolidated and an Annex to the *Note for guidance on the harmonisation of influenza vaccines* will be finalised for transmission to the CPMP for adoption.

[i] CPMP guidelines
[ii] European Pharmacopoiea Commission
[iii] European Pharmacopoiea Commission, extraneous agents
[iv] European Pharmacopoiea Commission, cell substrates
[v] ICH guideline on cell substrates
[vi] WHO guideline on cell substrates
[vii] CVMP guidelines