## The European Agency for the Evaluation of Medicinal Products Evaluation of Medicines for Human Use

London, 29 June 2000 EMEA/CPMP/1578/00

## **EMEA POSITION STATEMENT Recent developments concerning thiomersal in vaccines**

Thiomersal is an organo-mercurial compound with an antimicrobial action related to the release of ethylmercury. It has been used for many years in medicinal products: it is used in vaccines mainly as a preservative in the finished product. Cumulative exposure to mercury from a range of sources (food, medicinal products) could lead to a concern because of its potential accumulation in various organs.

Epidemiological studies designed to assess whether there is any association between the vaccination with thiomersal containing vaccines and specific neurological disorders in children like speech disorders and tics have been recently evaluated by the Centre for Disease Control and Prevention (CDC) in the USA. It was considered that the inconclusive observations generated from the studies so far do not provide sound scientific information and, because of the potential implications of some screening-phase findings, further studies are needed.

The European Medicines Evaluation Agency's scientific Committee for Proprietary Medicinal Products (CPMP) has been promoting the general use of vaccines without mercurial compounds as a preservative and has requested vaccine manufacturers to submit manufacturing plans to eliminate organo-mercurials used as preservatives in their finished products. Provided that the benefit/risk analysis remains unchanged, a stepwise approach in the removal of such a preservatives is deemed acceptable as stated in the EMEA press release dated 8 July 1999. A similar approach has been recommended by the Centre for Disease Control and Prevention (CDC) in the USA.

Eight multivalent vaccines have been centrally authorised in the European Union between July 1996 and May 1999. Seven out of these eight vaccines are indicated for infant and childhood immunisation against a number of diseases including Diphtheria (D), Tetanus (T), Hepatitis B (Hep B) and pertussis (P).

Three of the centrally authorised vaccines contain thiomersal as a preservative: Tritanrix Hep B, containing DTPw (whole cell pertussis) and Hep B antigens, Triacelluvax, containing DTPa (acellular pertussis) and Primavax containing DT Hep B. Development work for the replacement of thiomersal as a preservative is ongoing and requires changes in several steps of the manufacturing procedure. The overall development work is scheduled for completion by 2<sup>nd</sup> quarter 2001 for Tritanrix Hep B and by 4<sup>th</sup> quarter 2001 for Triacelluvax. Primavax is not currently marketed because of changes in vaccination schedules, and its marketing authorisation should be withdrawn by July 2000.

No new marketing authorisation applications for vaccines containing thiomersal as a preservative have been submitted to the EMEA since the recommendation issued in the EMEA/CPMP press release of 8 July 1999. New vaccines for childhood immunisation that do not contain thiomersal as a preservative are in the pipeline for centralised EU authorisation and should be available by the end of 2000. Thiomersal-free monovalent Hep B vaccines will be available in EU as of August 2000.

Taking into account all of the above the CPMP recommends the following:

- Vaccination with existing vaccines, including those containing thiomersal, continues to offer benefits to the general population and infants. The CPMP considers that the benefits of vaccination far outweigh the risks, if any, of exposure to thiomersal-containing vaccines.
- The CPMP recommendations of 8 July 1999 remain valid, that for vaccination in infants and toddlers, as a precautionary measure it would be prudent to promote the general use of vaccines without thiomersal and other mercurial-containing preservatives. Moreover, the use of the available thiomersal-free vaccines should be recommended for vaccination of new-borns.

Contacts for further information: Dr John Purves (+44-20) 74 18 84 01

Dr Marisa Papaluca Amati (+44-20) 74 18 84 36