

## **STATEMENT FROM THE COMMITTEE ON SAFETY OF MEDICINES**

### **FURTHER DATA SUPPORT SAFETY OF THIOMERSAL IN VACCINES**

On 12 February 2003, the Committee on Safety of Medicines (CSM) considered further evidence which supports the safety of thiomersal (which contains ethylmercury) in vaccines.

Two independently-conducted UK epidemiological studies that investigated the safety of thiomersal-containing vaccines for infants have been recently completed. These studies showed no evidence of adverse developmental effects from exposure to levels of thiomersal at the amounts used in existing UK vaccines. A further study in infants has shown that ethylmercury is rapidly excreted from the body following administration of thiomersal-containing vaccines.

The CSM Chairman, Professor Alasdair Breckenridge, said 'These new studies reinforce CSM advice from 2001 that there is no evidence of neurological adverse effects caused by thiomersal in vaccines according to the routine UK immunisation schedule. The balance of benefits and risks of thiomersal-containing vaccines therefore remains overwhelmingly positive'.

#### **Key points**

- The only vaccines used in the UK routine immunisation programme that contain thiomersal are the diphtheria, tetanus and wholecell pertussis (DTwP) and diphtheria and tetanus vaccines. Thiomersal is also present in some influenza and hepatitis B vaccines. There is no thiomersal in MMR, Hib, oral polio, meningitis C or BCG vaccine
- No harmful effects are known to be associated with thiomersal at amounts used in vaccines, except for minor allergic reactions such as redness and swelling at the injection site
- Two new UK epidemiological studies, involving more than 100,000 children, further support the CSM position. Another new study has shown that ethylmercury from vaccines does not build up in the body and is rapidly excreted.
- The World Health Organisation has also recently concluded that there is no evidence of toxicity in infants, children or adults exposed to thiomersal in vaccines
- There is a worldwide goal to reduce environmental mercury exposure from avoidable sources in general. Use of thiomersal in vaccines has not been banned but US and European regulators recommended in 1999 that reducing the use of thiomersal in vaccines will contribute to this goal. CSM endorsed this recommendation in 1999 and continues to do so. Several UK licensed vaccines have had thiomersal removed or levels of thiomersal reduced since 1999.

### **What is thiomersal and why is it used in vaccines?**

Thiomersal is an ethylmercury-containing compound that has played an important role either as a preservative or in the initial stages of the manufacture of some vaccines for over 60 years.

### **What have the concerns been about?**

The mercury content of thiomersal has led to concerns that it may affect brain development when given in vaccines. However, no harm to brain development has been demonstrated as a result of the very small amounts of thiomersal present in some vaccines.

### **What is the view of the Committee on Safety of Medicines (CSM)?**

The CSM has kept the issue of thiomersal in vaccines under review. In September 2001, the CSM reviewed the available data relating to the safety of thiomersal in vaccines and advised that there is no evidence of neurological adverse effects caused by levels of thiomersal in vaccines. The only evidence of harm due to thiomersal was a small risk of hypersensitivity reactions (that typically include skin rashes or local swelling at the site of injection). The CSM concluded that the balance of risks and benefits of thiomersal-containing vaccines remains overwhelmingly positive.

### **What is the latest evidence considered by CSM?**

The two new epidemiological studies specifically set out to assess the safety of thiomersal in vaccines used according to the UK childhood immunisation schedule. One study, funded jointly by the World Health Organisation and the Public Health Laboratory Service, was conducted using the UK's General Practice Research Database (GPRD) which holds data on health care for 3 million patients (~5% of the UK population). The second study was funded by the Department of Health and used the Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC).

These studies investigated whether there is any link between early thiomersal exposure through immunisation and developmental and behavioural disorders, including autism, in more than 100,000 children in total. Both studies produced very reassuring results in that neither supports an association between thiomersal exposure through the UK immunisation programme and neurodevelopmental disorders in children.

A further study, published in *The Lancet* in November 2002, looked at how a small child's body breaks down ethylmercury from vaccines. This study found that ethylmercury from vaccines does not build up in the body and is rapidly excreted.

### **What does the new evidence tell us?**

On 12 February 2003, the CSM carefully reviewed these 3 studies and considered that they provide very reassuring evidence on the safety of the thiomersal in vaccines and further support its advice of 2001.

### **What is the view of the World Health Organisation (WHO)?**

The World Health Organisation's Global Advisory Committee on Vaccine Safety (GACVS) has also kept this issue under review and concluded in November 2002 that there is no evidence of toxicity in infants, children or adults exposed to thiomersal in vaccines.

### **What is the position in the United States of America and Europe with regard to use of thiomersal in vaccines?**

Use of thiomersal in vaccines has not been banned in USA and Europe and there is strong evidence to show that thiomersal in vaccines does not cause neurological adverse effects. Despite this, as part of a global goal to reduce exposure to mercury from avoidable sources in general, European and American regulators recommended in 1999 that vaccine manufacturers phase out use of thiomersal wherever possible. CSM endorsed this recommendation in 1999 and continues to do so.

### **What is being done in the UK to remove thiomersal from vaccines?**

Several UK licensed vaccines have had thiomersal removed or levels of thiomersal reduced since 1999. Manufacturers are actively developing research programmes to eliminate, substitute or reduce thiomersal in vaccines in accordance with the European recommendations. This may take time because manufacturers are required to ensure that the replacement or elimination of thiomersal does not affect the safety or efficacy of the final vaccine and there is no set timeframe to phase out the use of thiomersal in vaccines. While these changes are underway, the current view is that there is no reason to change current immunisation practices with thiomersal-containing vaccines.