The European Medicines Agency
*Evaluation of Medicines for Human Use*

London, 23 February 2006
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**CHMP Position Paper on Thiomersal**
**Implementation of the Warning Statement Relating to Sensitisation**

**Background:**

Thiomersal, is an antimicrobial organic mercury compound that continues to be used either in the early stages of manufacturing, or as a preservative, in some vaccines. The antimicrobial action of thiomersal relates to ethylmercury, which is released after breakdown of thiomersal into ethylmercury and thiosalicylate.

The EMEA's scientific committee, the Committee for Medicinal Products for Human Use (CHMP) evaluated the benefit/risk of medicinal products containing thiomersal and agreed on recommendations in 1999, 2000 and 2004, made public in EMEA Public Statements (EMEA/20962/99, EMEA/CPMP/1578/00 and EMEA/CPMP/VEG/1194/04).

In the most recent EMEA Public Statement, the CHMP concluded that the latest epidemiologic studies show no association between the vaccination with thiomersal-containing vaccines and specific neurodevelopmental disorders. The CHMP re-emphasised that immunisation with vaccines containing thiomersal continues to offer outstanding benefits to the general population, including infants. The benefits of vaccination far outweigh the risks, if any, of exposure to thiomersal-containing vaccines.
The CHMP acknowledged that, during some manufacturing processes, the use of organic mercury compounds is necessary and in such cases, residual levels might be present in the final product. Nevertheless, the CHMP re-iterated that, in line with the global goal of reducing exposure to mercury, the development of vaccines without thiomersal or with the lowest possible levels of thiomersal and other mercury containing preservatives should continue to be promoted.

The presence of thiomersal (and other preservatives) in the composition of vaccines should be stated on the label and a warning regarding the risk of sensitisation in relation to thiomersal and other preservatives will be included in the Summary of Product Characteristics and Package Leaflet of such products.

**Updated Position on thiomersal regarding Warning Statements Relating to Sensitisation:**

In February 2006, the CHMP adopted the updated warning statement for the Summary of Product Characteristics and Package Leaflet, with regard to sensitisation for medicinal products containing thiomersal (Annex I). The wording was updated to address a category of vaccines for which thiomersal is used in the manufacture but result in undetectable or very low residual levels of thiomersal (i.e. below 40 nanogram of thiomersal) in the finished product, where there is no scientific evidence suggesting that such levels could trigger hypersensitivity reactions.

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**ANNEX I**

**SPC & PL WORDING FOR USE OF THIOMERSAL IN MEDICINAL PRODUCTS WITH REGARD TO SENSITISATION AS AGREED BY THE CHMP IN FEBRUARY 2006**

**For thiomersal used as a preservative in the medicinal product:**

SPC statement:

- in Section 4.8 Undesirable Effects:

  "This medicinal product contains thiomersal (an organomercuric compound) as a preservative and therefore, it is possible that sensitisation reactions may occur (see Section 4.3)."

- in Section 4.3 Contraindications:

  "Hypersensitivity to any component of the medicinal product."

PL statement:

- The CHMP recommends the following statement for all medicinal products containing thiomersal:

  "This medicinal product contains thiomersal as a preservative and it is possible that <you/your child> may experience an allergic reaction."

  " Tell your doctor if <you/your child> have/has any known allergies."

- The CHMP further recommends including the following general statements for vaccines:

  " Tell your doctor if you/your child have/has experienced any health problems after previous administration of a vaccine."

**For thiomersal used in the manufacturing process:**

For thiomersal used in the manufacturing process, which results in levels of thiomersal <40ng per dose, or undetectable levels, sensitisation reactions are not expected to occur and no statements are recommended for inclusion in the product information. In other cases, the statements below should be included:

SPC statement:

- in Section 4.4 Special warnings and special precautions for use:

  "Thiomersal (an organomercuric compound) has been used in the manufacturing process of this medicinal product and residues of it are present in the final product. Therefore, sensitisation reactions may occur."

PL statement:

- The CHMP recommends the following statement for all medicinal products containing thiomersal:

  "Thiomersal is present (in trace amounts) in this product, and it is possible that <you/your child> may experience an allergic reaction."

  " Tell your doctor if <you/your child> have/has any known allergies."

- The CHMP further recommends including the following general statements for vaccines:

  " Tell your doctor if you/your child have/has experienced any health problems after previous administration of a vaccine."

**These statements concerning thiomersal and sensitisation should be presented in the SPCs/PLs together with any existing information in SPC Sections 4.4. and 4.8/PL with regard to recognition and management of sensitisation reactions (hypersensitivity).**

**The CHMP also proposes that the above statements could be used as a basis for statements in the SPCs/PLs of medicinal products which contain other organomercurial preservatives, substituting the name of the relevant preservative in the place of thiomersal.**