



International
Federation of
Pharmaceutical
Manufacturers &
Associations

Fédération
Internationale de
l'Industrie du
Médicament

Federación
Internacional de la
Industria del
Medicamento



Date: Oct. 20, 2009

H1N1 pandemic influenza vaccines: the role of preservatives

As the world's leading influenza vaccine manufacturers, IFPMA IVS members are committed to the rapid and safe supply of vaccines to protect populations against H1N1 pandemic influenza. As part of this supply, manufacturers utilize vaccine preservatives where necessary, to help prevent potentially life-threatening contamination with harmful microbes. Producers use thiomersal (also known as thimerosal) to provide this protection.

Thiomersal's role and clinical profile

Thiomersal has been used widely since the 1930s in a number of medicines, including many vaccines, and contains a form of mercury that kills bacteria even in low concentrations. During this period its use has helped prevent contamination, particularly during the repeated needle-puncture of multi-dose vials of vaccines.

In recent years, concerns have been raised over the potential effects of exposure to low levels of mercury. The concerns over low level exposure have led to extensive scrutiny of the use of thiomersal, particularly in vaccines for children, because the preservative contains a form of mercury. Many scientific studies and reviews by national and international expert committees have explored whether a link exists between the use of thiomersal-containing vaccines and neurodevelopmental disorders, in particular autism. As a result of this work, an overwhelming body of evidence shows no causal link between these disorders and vaccines containing thiomersal. Expert groups have also rejected a link.

- The WHO Global Advisory Committee on Vaccine Safety issued a statement in 2006 concluding *'that there is no evidence of toxicity in infants, children or adults exposed to thiomersal (containing ethyl mercury) in vaccines'*.
- The European Medicines Agency (EMA) announced in 2004 that *'the latest epidemiological studies show no association between the vaccination with thiomersal-containing vaccines and specific neurodevelopmental disorders'*.
- The United States' Institute of Medicine's 2004 report concludes *'that the body of epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism'*.

These statements mirror the findings of numerous studies involving hundreds of thousands of children that consistently have shown no association between exposure to thiomersal-containing vaccines and neurodevelopmental disorders such as autism. For example, a Danish study of 956 children diagnosed with autism between 1971 and 2000 showed that there was no increasing trend in the incidence of autism up to 1990, although thiomersal was used in vaccines in Denmark during this period. However, the incidence of autism rose from 1991 – 2000, although thiomersal-containing vaccines were discontinued in 1992. A further example is a study in the UK that analyzed data from over 14,000 children to explore a potential link between the use of thiomersal-containing vaccines and development disorders. The researchers *'could find no convincing evidence that early exposure to thimerosal had any deleterious effect on neurologic or psychological outcome'*.

Removal of thiomersal

While expert opinion agrees on the safety of thiomersal, in recent years vaccine manufacturers and regulators have worked together to discontinue its use where possible, acting on the precautionary principle. As a result, many vaccines are now available in single-dose presentations that no longer contain thiomersal, while a number contain only trace levels resulting from the use of thiomersal during manufacture. However, it is mandatory that multi-dose vials contain a preservative that meets the WHO and relevant pharmacopeia standards, to protect against potentially life-threatening contamination.

Thiomersal in H1N1 pandemic vaccines

Influenza pandemics present significant and unique public health challenges. Vaccines are required in a short timeframe to protect large populations. As a result most vaccines are likely to be supplied in multi-dose vials as they allow efficient, rapid shipping and distribution by health authorities and speed up manufacture by avoiding the need to fill each dose into a separate container. In this situation the use of thiomersal is important to protect against contamination.

Notwithstanding the scientific data showing no link between thiomersal-containing vaccines and neurodevelopment disorders, as well as expert agreement on the safety of thiomersal used in vaccines, some countries may provide single-dose preservative-free pandemic vaccines for special groups. This may for instance include pregnant women, who although recommended for immunization may be concerned about exposure to preservatives during pregnancy.

Regulators, health authorities and manufacturers have worked hard over many years to optimize pandemic vaccine manufacturing, testing and monitoring processes. The procedures now in place ensure these vaccines can be provided as quickly as possible without compromising safety, so that their benefits far outweigh potential risks.

Further information

- WHO committee statement on thiomersal:
http://www.who.int/vaccine_safety/topics/thiomersal/statement_jul2006/en/index.html
- EMEA statement: <http://www.emea.europa.eu/pdfs/human/press/pus/119404en.pdf>
- United States' Institute of Medicine report:
http://books.nap.edu/openbook.php?record_id=10997&page=R1
- Links to many of the scientific studies conducted in the area:
http://www.immunizationinfo.org/immunization_science.cfm?cat=1