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MEMO

This PSUR report on measles, mumps, rubella vaccine, manufactured by Merck & Co, Inc, is in the format proposed by International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceutical for Human Use, Topic E2C. It summarizes the safety data received by Merck & Co., Inc., from worldwide sources, from 01-Jan-2001 to 31-Dec-2005.

The Measles, Mumps, and Rubella live virus vaccine manufactured by Merck & Co (internationally called M-M-R™II and registered under different tradenames in Europe) has been registered and marketed in European Union countries through national procedure for many years. This vaccine is currently used worldwide for the prevention of measles, mumps and rubella.
M-M-R™II is currently manufactured using pooled serum-derived human serum albumin [redacted] as a component of the viral growth media in the bulk manufacturing process and as a component of the bulk diluents at formulation of the final product.

Merck is planning to substitute [redacted] for [redacted] in the bulk manufacturing process of M-M-R™II. [redacted] and [redacted] which are essentially similar, are considered functionally comparable for the production of viral bulks.
A new Marketing Authorisation Application (MAA) for M-M-RVAXPRO™ (MMR-rHA) was submitted to EMEA in accordance with article 8.3(i) of Directive 2001/83/EC as a complete application, in June 2004. The positive Opinion was granted on February 23rd, 2006.
Although M-M-R™II has been licensed through National Procedure in all of the European countries for many years, the planned rHA manufacturing change obligates the CP filing of a complete, stand alone Marketing Authorisation Application, due to the use of [redacted], a product of recombinant DNA technology.

It is important to note that the composition and manufacturing process of M-M-RVAXPRO™ remain entirely identical to M-M-R™II
The modifications introduced in the new application are the following:

- To use [redacted] in the bulk manufacturing culture medium instead of [redacted] and remove [redacted] from bulk diluents .
- To harmonize the expiry titer for the mumps component of this combination vaccine to [redacted]
  The current mumps end-expiry specification currently registered in the EU countries is either [redacted]
- To harmonize the prescribing information of M-M-RVAXPRO™ across the EU. This application does not propose any fundamental changes in the indications or dosing schedule of this product.

As stated in the PSUR to ICH E2C (Clinical safety data management periodic safety update reports for marketed drugs) , the CCDS (Company Core Data Sheet) enclosed in Appendix 1 of this PSUR report corresponds to the latest version approved by the manufacturer, Merck & Co., Inc. This CCDS, internally approved in June 2004, was updated to include changes related to the rHA formulation in addition to other revisions.

The switch from M-M-R™II to M-M-RVAXPRO™ will be implemented on a worldwide scale. For this reason, the same changes were submitted for assessment to relevant Health Authorities in the US as well as in few countries of the International Area.

For the current PSUR reporting period (01-Jan-2001 to 31-Dec-2005), 100% of the product distributed was M-M-R™II, manufactured with HSA. Consequently, 100% of adverse drug reactions (ADRs) reports listed and described in this PSUR are related to the worldwide market use of M-M-R™II.

In conclusion, there is no consequence on the overall safety evaluation of the vaccine.