

# **Summary of the systematic literature review and meta-analyses of the immunogenicity, duration of protection, effectiveness/efficacy and safety of rubella vaccination**

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The full report can be found on the SAGE website (background documents for SAGE October 2019)

## **Summary**

### *Background*

This report summarises the results of a systematic review of the literature and meta-analyses of the immunogenicity, duration of protection, effectiveness/efficacy and safety of rubella-containing vaccine (RCV) in order to update the WHO rubella vaccine position paper.

### *Methods*

We performed a systematic literature review for studies published since 2010 in which one or more doses of RCV were given at any age. We extracted data on the following outcomes: immunogenicity, duration of protection, vaccine efficacy or effectiveness and safety. Where appropriate, meta-analyses were performed. Quality of all included studies was assessed using the GRADE methodology.

### *Results of the search and selection*

We included 36 papers (32 randomized controlled trials (RCTs) and 4 observational studies) for analysis of the immunogenicity of one or two doses of RCV (RA27/3 strain) in children and adolescent girls, and 14 papers (5 RCTs and 9 observational studies) to assess the duration of protection of RCV. One paper on vaccine effectiveness (VE) (BRDII strain) was included, and 74 studies on safety, including three on safety in pregnancy.

### *Results of the review of included studies*

Seroconversion after a single dose of RCV (RA 27/3 strain) was 99% (95% CI: 98%-99%) in children (GRADE evidence rating, high) and 100% (100%-100%) in adolescent girls (GRADE evidence rating, moderate), independent of co-administration with other vaccines. Seropositivity after a second dose of RCV (RA 27/3 strain) was 100% (99%-100%) (GRADE evidence rating, high). For duration of protection, the studies showed a seropositivity of 88%-100% measured 1-20 years after one or two RCV doses (GRADE evidence rating, moderate). We did not find any additional studies on vaccine efficacy of RCV published since 2010. The single new study on VE of RCV reported 100% VE after one and two doses (BRDII strain) (GRADE evidence rating, low). Among 34,332 individuals participating in the RCTs, after exclusion of severe adverse events (SAE) not associated with RCV according to the authors, 140 SAE were reported as possibly related to RCV. Among the case reports on SAEs, the association with RCV was confirmed in one report, where a previously healthy man died of encephalitis. At post-mortem examination, rubella virus (vaccine strain) was detected in brain tissue. For outcomes on safety in general the GRADE evidence rating was moderate. No cases of CRS or other SAEs were reported in studies following almost 3,000 women who were inadvertently vaccinated against rubella during pregnancy (GRADE evidence rating, low).

### *Conclusions*

Our literature review confirms the evidence that is presented in the current WHO rubella vaccine position paper, dating from 2011. Single and two doses of RCV are highly immunogenic for a long period of time, they are effective in preventing rubella and CRS, and they are safe to be administered to immunocompetent individuals.