# Vaccines against tick-borne encephalitis (TBE)
# WHO position paper 10 June, 2011

## Grading of scientific evidence in support of key recommendations

| Table II. Are the currently available TBE vaccines responsible for serious adverse vaccine reactions? | | | | |
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| | | | Rating | Adjustment to score |
| **Quality Assessment** | No of Studies/Starting Score | | 5 RCTs[1] | 4 |
| | Factors decreasing confidence | Limitation in study design | None serious[2] | 0 |
| | | Inconsistency | None serious | 0 |
| | | Indirectness | None serious | 0 |
| | | Imprecision | Serious[3] | -1 |
| | | Publication bias | None serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final Score** | | | **3** |
| **Summary of Findings** | **Quality** | | | We are moderately confident in the estimate of effect on health outcome: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different |
| | **Conclusion** | | | Currently available TBE vaccines are not causally associated with serious adverse vaccine reactions. |

[1]All RCTs on safety concern western vaccines; for Russian vaccines, only two observational studies are available. The latter studies are referenced below, but not included in the table. Our conclusions on the safety of TBE vaccines are based mainly on information on Western vaccines. In clinical studies (RCTs as well as observational) current vaccines (also Russian) have been consistently described as moderately reactogenic, but without being causally associated with severe adverse reactions. However, some lots of EnceVir have recently caused safety concerns (see below).

[2]The RCTs suffer from inappropriate randomization and/or lack of concealment. Yet no serious adverse event were detected in either groups and hence this is not seen a critical limitation with respect to serious events. [3]Trials are of limited size, so that very rare adverse events could have been missed.

A recent Cochrane review *(Demicheli et al, 2009*) summarized seroconversion data obtained from 11 vaccine trials including 4 RCTs of currently licensed Western vaccines (Encepur children, Encepur Adults, and FSME-IMMUN® "new"). *(Ehrlich 2003; Loew-Baselli 2006; Schoendorf 2007a; Schöndorf 2007b)*. In these 4 trials a total of 5063 children and adults were included. Although adverse events were commonly reported (transient redness and pain at the site of injection in up to 45% of the cases and fever in up to 5-6%), none of these events were considered as serious.An RCT recently conducted by *Pöllabauer EM et al (2010)* compared safety between Encepur Children® and FSME-IMMUN Junior®. Systemic reaction rates were low and similar between the vaccines.

With TBE-Moscow and EnceVir® small-scale observational studies on systemic and local adverse events have suggested a moderate reactogenicity profile with no significant differences between the two vaccines. The reactogenicity of these Russian vaccines were assessed in a trial that included 325 children and 400 adults *(Pavlova LI et al 2003).* No severe adverse events were recorded. Similar conclusions on the safety of TBE-Moscow were reached in other studies *(Pavlova et al 1999, Krasilnikov et al, 2002).* Furthermore, until in 2010, passive post-marketing surveillance of EnceVir® did not reveal any serious adverse events *(Il'ichenko TE at al 2009).* However, in 2010 and first part of 2011 some lots of EnceVir have been associated with frequent occurrence of high fever and allergic reactions, in particular in children and adolescents. Pending the outcome of ongoing investigations, EnceVir is currently not recommended by Russian authorities for use in children aged 3 - 17 years.

During the period 2001-2009 about 42 million doses of FSME-IMMUN® and 30 million doses of Encepur® have been produced. Since 1982, approximately 25 million people have been immunized with TBE-Moscow (current version of the vaccine used since 1999); the corresponding figure for EnceVir (in use since 2001) is not available.

# References


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