

Minority Opinion in the MMRV Working Group

**Withdraw the ACIP recommendation for MMRV vaccine for age 1 to 2 years.
Always use separate MMR and Varicella vaccines.**

Risks and Benefits to Individual Children: MMRV and MMR+V are considered equally effective in preventing disease, so for the individual child it is a trade-off between one additional vaccine injection and 3.0 (95% CI, 0.5-5.5) additional mild injection site adverse event per 100 children¹ (MMR+V) versus 4.3 (95% CI, 2.6-5.6) additional febrile seizures per 10,000 children², 7.5 (95% CI, 5.4-9.4) additional mostly mild fever episodes per 100 children¹ and 1.1 (95% CI, 0.2-1.8) additional measles-like rash per 100 children¹ (MMRV). The additional systemic adverse events after MMRV are, in my view, worse than the extra injection and injection site adverse events after MMR+V.

There is also the established medical principle of *'first, do no harm'*, and it is better to provide patients with an expected small inconvenience than a small risk of an unexpected health problem. The fact that there is already an excess risk of febrile seizures after MMR and MMR+V vaccinations, acceptable due to the importance of MMR vaccination, should make us think twice before increasing this risk further unless there are substantial additional benefits to the patients.

The added risk of both fever and febrile seizures may be triggered by the higher varicella-zoster virus component in MMRV versus in the stand alone Varicella vaccine. The fact that MMRV increases the risk for three types of systemic adverse events means that there could also be an increased risk of other adverse events that have not been investigated, caused by the same trigger.

Health Care Costs and Benefits: Separate MMR+V vaccination may require an additional physician office visit for some children. The combined MMRV vaccination will require additional office and/or emergency room visits due to febrile seizures, fever and measles-like rash. A formal cost-benefit analysis is not available.

Public Trust in Vaccines: Among many parents there is significant distrust and/or caution towards vaccines in general and MMR type vaccines in particular. To maintain and increase trust it is important for the medical community both to vigorously dispel any false claims about vaccine adverse events (e.g. MMR and autism) and to take decisive action when a true adverse event is found. In a worst case scenario, vaccine skeptics could use MMRV as an example where the government recommends a vaccine which is scientifically proven to cause excess febrile seizures, when a safer and equally effective alternative exists, arguing that one should hence not believe the government when it comes to other recommended vaccines.

Vaccine Coverage: The administration of separate MMR and Varicella vaccines could result in lower vaccine coverage compared to the single MMRV, especially for Varicella, but potentially also for MMR and other vaccines. Parent knowledge about MMRV causing excess febrile seizures and a general lack of trust in vaccines may also result in lower vaccine coverage.

Summary: The most important criterion is the risks and benefits to the individual child, which favors MMR+V over MMRV, while the other criteria favor MMRV and MMR+V about equally. In the important task of comparing the effectiveness of different medical treatments, only the best alternative should be recommended when there is a clear difference. It is hence my view that the recommendation for MMRV should be withdrawn for 1 to 2 year old children.

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¹ FDA CBER Clinical Review, 2005, ²Unpublished VSD and Merck Studies.