

Global Advisory Committee on Vaccine Safety (GACVS) meetings					
Date	Topic discussed	Conclusions	Other issues discussed	Recommendations	Link to WER
Dec 2000, 20-21	Guinea-Bissau study on potential impact of routine infant immunization on survival. Presentation by Dr Aaby on NSE – data from GB	GACVS determined data was of good quality and accuracy	Two major concerns with studies: <ul style="list-style-type: none"> Substantial number of infants were not evaluated because of study design (6 monthly visit), therefore potential for bias Information on actual cause of death not available. Time and intervals for outcome assessment are short 	<ol style="list-style-type: none"> determination of whether the observation of an increased mortality following DTP immunisation in GB is idiosyncratic or generalisable an expert group will be formed with John Clemens as the chair. This group will solicit, advertise and review proposals to carry out this task. In GB, the findings need to be confirmed preferably by a well-designed and executed intervention study. Studies in GB could be conducted by Dr. Aaby and colleagues, but in concertation with John Clemens' group and direct collaboration with other experts so as to meet the "multi-investigators" criteria for causality assessment. WHO needs to find the necessary funding for these studies to take place in an expeditious manner. 	
June 2001, 18-91	Review of potential impact of routine vaccination on childhood survival Update on work from expert group and secretariat ongoing research. 7 new retrospective studies	Review on literature showed that selection bias makes it very difficult to compare the studies.		Workshop in October 2001 to discuss preliminary results.	
Dec 2001, 05-06	Review of potential impact of routine vaccination on childhood survival Update on the purpose (provide constructive criticism to all study	The results of the four sites (Bangladesh, PNG, BF and Indonesia) did not confirm Dr Aaby's finding on increased mortality after DTP	<p>Infant mortality rate in all studies was lower than in GB.</p> <p>Dr Aaby stated that his hypothesis is now that the last given vaccine makes the difference. If DTP is given last,</p>	<p>PIs asked to conduct additional analysis to simulate Dr Aabys' Facilitate publication of reports</p> <p>Seek independent review of studies</p> <p>Dr Aaby's proposal for a prospective study in GB was not</p>	

	sites and improve analysis) and outcome of the workshop	vaccination. On the contrary a NS decrease mortality after DTP was observed. Results did not reveal differences between sexes	then mortality increases, this is reversed if the last given vaccine is BCG or measles. The effect is most pronounced in girls. This might explain the results of high-titre measles studies (vaccine given earlier than last dose of DTP). Are the differences in findings from the various studies and Dr Aaby's studies due to selection bias or difference in methods or are they real.	endorsed	
June 2003, 11-12	Child survival following immunization. Update on status of publication of commissioned studies.			It was confirmed the previous GACVS conclusion that the evidence available does not support any increased non-specific mortality as reported in GB	http://www.who.int/wer/2003/wer7832/en/index.html
Dec 2003, 3-4	Child survival and vaccination. The secretariat confirmed that no intervention trials have been undertaken in GB on child survival and vaccination. Update on publication status of studies	An upsurge in appearance of publications from Aaby's group was noted. Vitamin A enhances negative or positive effects of vaccines.	Possibility that visibility of this issue from continuing publication will affect immunization programmes in developing countries	Conduct a systematic analysis on the published studies and describe strengths and limitations. Establish a task force with experts in epidemiology, statistics, immunology and clinical study design. Establish a second task force to address if vaccines affects the immune system and if this could be deleterious under certain conditions.	http://www.who.int/wer/2004/wer7903/en/index.html
June 2004, 10-11	Effect of DTP on child survival. Report of task force presented. 17 published and unpublished reports were considered.	Evidence provided in papers considered does not support a deleterious effect of DTP vaccination. There is substantial evidence against such an effect.	None of the studies conducted outside GB found a deleterious effect of DTP. Insufficient justification for a RT, besides placebo-controlled or delay in DTP would be unethical	The matter to be set aside unless new and persuasive evidence comes to hand. Short version of the task force report to be posted on the web site.	http://www.who.int/wer/2004/wer7929/en/index.html
Dec 2004, 2-3	Child survival. Progress with publication of the studies commissioned				http://www.who.int/wer/2005/wer8001/en/index.html

Dec 2005, 1-2	by WHO Update on NSE of routine immunization on the immune system	Proposed workshop to address: Mechanisms by which live vaccines can have an impact on innate and unrelated adaptive immune responses. Mechanism by which biologically active components of subunit vaccines may non-specifically influence the immune system. Mechanism by which adjuvants non-specifically influence the immune system – impact on pre-existing immunity, on primed T cells, on memory B cells. Approaches to be considered for the biological assessment of non-specific effects of vaccines and vaccine components in humans: in vitro studies and in vivo testing		Meeting to be organized by IVR in October 2006	http://www.who.int/wer/2006/wer8102/en/index.html
June 2006, 6-7	Update on research and information on potential NSE of specific vaccines on mortality	Update on the outcome of meetings of an advisory group, convened by the Danish National Research Foundation and the Novo Nordisk Foundation, to advise on the evaluation of vaccination research programmes in Guinea Bissau, with respect to the	Further meeting planned to discuss methodological issues. RT taking place in GB but difficult to interpret data in the future due to a measles outbreak	GACVS considered no need to revise previous conclusions	http://www.who.int/wer/2006/wer8128/en/index.html

		possibility of non-specific effects of specific vaccines on mortality			
Nov 2006, 29-30	Update on the issue of child survival following DTP vaccination	No significant new information had been published since the last meeting. However, two papers by Aaby were in press. One a methodological paper discussing potential sources of bias. The other the extent to which such biases might have been present in recent publications.		No need for GACVS to revise its previous statement.	http://www.who.int/wer/2007/wer8203/en/index.html
June 2008, 18-19	DTP vaccination and asthma Report on two studies. Report on the workshop to discuss NSE	One study indicated a decreased risk of asthma when DTP was administered in infancy at a later age than normally recommended." Another study suggested that aP induce a more atopic-like immune response than wP Workshop focused on methodological issues in the analysis of cohort studies; what data collection systems should be implemented to examine NSE; potential RC studies.	Findings judge robust. Caveat: authors discarded results of children who received fewer than four doses.	Further discuss the roles of Th1 and Th2 cytokines. GACVS to revise statement to include NSE in general, not just in relation to DTP vaccination.	http://www.who.int/wer/2008/wer8332/en/index.html