

Date 6 February 2018

Dear Mr Bigtree

Many thanks for your message expressing interest in learning more regarding the safety and effectiveness of the DTP vaccine. I was asked by our outgoing Executive Director, Anthony Lake to prioritize the response to your letter, as he was preparing to leave office, and he asked me to convey his apologies for not responding himself.

I would like to assure you that we take the issue of vaccine safety very seriously. Vaccine safety, along with the safety of all health interventions, are closely followed and monitored by ourselves, in close association with technical agencies like the World Health Organization (WHO). The wellbeing of children, as you are aware, is central to the mandate of UNICEF and we do not compromise in any way in fulfilling this mandate.

There are various independent and multidisciplinary expert bodies at global and national level, which regularly review the evidence on the impact of vaccines and on its safety profile and provide advice to WHO and UNICEF. Notably, the Strategic Advisory Group of Experts (SAGE) is the principal advisory group to WHO for vaccines and immunization (established in 1999). It is charged with advising on overall global policies and strategies, ranging from vaccines (impact and safety) and technology, research and development, to delivery of immunization and its linkages with other health interventions. The Global Advisory Committee on Vaccine Safety (GACVS) responds to vaccine safety issues of potential global importance (established in 1999). The GACVS provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern with the potential to affect in the short or long term national immunization programmes. The Immunization and Vaccines Related Implementation Research Advisory Committee (IVIR-AC) provides independent advice on matters related to implementation research and their relevance to immunization policies and practices, and reviews best practices relating to methods for conducting and reporting on quantitative immunization and vaccines-related research (including vaccine impact and safety evaluations).

Some authors have suggested that some of the vaccines routinely administered to infants and children also affect the risk of illness and death from conditions other than the specific infectious diseases they are designed to prevent. The hypotheses concerning these "non-specific effects" of vaccines include that, under some circumstances, some vaccines (for example, measles and Bacillus Calmette-Guérin (BCG)) lower subsequent risk, whereas others (such as DTP) increase subsequent risk of illness and death from other causes. It is further postulated that the magnitude of these effects depends on other factors, including gender and vitamin A supplementation status. The potential for non-specific vaccine effects has led some authors to question whether the vaccination schedules currently recommended by WHO should be adjusted.

WHO with the support of several independent experts has been reviewing and discussing evidence around the non-specific effects of vaccines and immunization programmes since 2001. In 2012, SAGE requested that WHO review the evidence concerning the possible non-specific effects of routine infant vaccines on mortality. A working group was established in March 2013 to review data on non-specific mortality effects and assess whether current evidence is sufficient to inform adjustments in policy recommendations, or if further scientific

investigation is required. A systematic review was conducted to evaluate the non-specific effects on all-cause mortality, in children under 5, of Bacillus Calmette-Guérin (BCG), diphtheria-tetanus-pertussis (DTP), and standard titre measles containing vaccines (MCV); to examine internal validity of the studies; and to examine any modifying effects of gender, age, vaccine sequence, and co-administration of vitamin A.

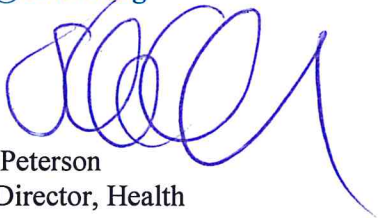
In 2014 SAGE reviewed the outcomes of this review and concluded that, regarding the possible non-specific effect of DTP on all-cause mortality, the available data neither exclude nor confirm the possibility of beneficial or deleterious non-specific effects of DTP vaccines on all-cause mortality. Randomized controlled trials did not contribute any evidence on non-specific effects of DTP. Evidence was largely from observational studies considered at a high risk of bias. Further, SAGE stated that further observational studies are unlikely to contribute to policy decisions. SAGE considered that the non-specific effects on all-cause mortality warranted further research. SAGE recommended that the IVIR- AC be tasked with providing advice on which priority research questions need to be addressed to inform policy decisions, and what kinds of studies and study designs would provide answers to these questions. SAGE concluded that the evidence does not support a change in policy for DTP, and emphasized the benefit of DTP in preventing disease and the importance of the current recommendation.

In conclusion, I would like to reiterate that UNICEF (and WHO) takes the issue of vaccine safety very seriously and for several decades has reviewed the evidence to guide policy decisions. While available evidence does not support a change in DTP vaccination policy, there is substantial evidence on the benefits of DTP (and pentavalent) vaccines in preventing disease and on the substantial risk for unvaccinated population DTP vaccines as evidenced by diphtheria, pertussis and tetanus cases and deaths that we are seeing today. In a number of locations globally, we are experiencing diphtheria outbreaks with high case fatality, which is a direct result of these children not receiving the recommended doses of vaccines in their childhood. Diphtheria, Tetanus and Pertussis were among the leading causes of childhood death in the pre-vaccine era causing several hundred thousand cases each year.

I hope my message provides you with the information that you were seeking. I am copying representatives of our member states who are included in your original message.

Please do not hesitate to contact us if you have further queries or require clarifications. The appropriate point of contact in our office is Dr. Robin Nandy, Principal Advisor and Chief of Immunizations and he can be contacted at rnandy@unicef.org

Sincerely,



Dr. Stefan Peterson
Associate Director, Health
UNICEF Headquarters