Statement on Rotarix and Rotateq vaccines and intussusception

In December 2009, WHO recommended routine immunization of infants for prevention of rotavirus disease, the most common cause of serious gastroenteritis among infants worldwide. Currently two rotavirus vaccines – Rotarix (manufactured by GSK Biologicals) and RotaTeq (manufactured by Merck & Co., Inc.) – are available. Because a previous rotavirus vaccine (Rotashield, manufactured by Wyeth) was associated with intussusception, an uncommon form of bowel obstruction, the risk of this adverse event was specifically evaluated in pre-licensure trials of the current licensed rotavirus vaccines. In trials, each involving >70 000 participants, conducted mainly in Finland and the United States of America for RotaTeq, and in 11 countries in Latin America for Rotarix, no increased risk for intussusception was observed. Nonetheless, WHO has recommended ongoing post-marketing intussusception monitoring when these vaccines are introduced into different populations. On 6 and 13 August 2010, the Global Advisory Committee on Vaccine Safety (GACVS) reviewed by teleconference preliminary data from post-marketing studies. On 22 September 2010, the United States Food and Drug Administration approved a label change for Rotarix to advise practitioners of new data regarding intussusception.

Since 2007, the Pan American Health Organization has collaborated with Ministries of Health, the United States Centers for Disease Control and Prevention (CDC), and PATH, to evaluate, in Brazil and Mexico, the potential risk of intussusception after Rotarix immunization during routine use. Preliminary analyses of the surveillance data collected have identified a clustering of 18 hospitalizations following intussusception (none of which were associated with fatality) in the period 1 to 7 days after the first dose in Mexico, corresponding to a rate of intussusception that was about 4-5 times higher than in later periods after vaccination, after adjusting for age. No clustering was observed after the first dose in Brazil. If these findings in Mexico are confirmed, they would translate to a risk of about one to two additional intussusception hospitalizations per 100 000 vaccinees or about 20-40 additional cases per year nationwide at current vaccination rates (the Mexican birth cohort is approximately 2 million).

A similar study sponsored by GSK Biologicals in a different population in Mexico also found a possible increased risk of intussusception of about 1.7-fold in the 30-day period following the first dose, with a clustering of cases in the first week after vaccination. In Australia, post-marketing surveillance studies found no increased risk of intussusception up to 9 months of age with either Rotarix or RotaTeq vaccines, but there was the possibility of a temporal increase in intussusception in the first week after vaccination with both vaccines, although these findings are based on relatively few cases. In the United States, data from both the CDC and from an evaluation sponsored by Merck & Co., Inc. do not show evidence of an increased risk of intussusception with RotaTeq; however, the population of children under active surveillance in the United States who have received RotaTeq is not yet large enough to rule out the level of risk in the first week after vaccination suggested by preliminary analyses of studies of Rotarix in Mexico.

Post-marketing surveillance indicates the possibility of an increased risk of intussusception shortly after the first dose of rotavirus vaccination in some populations. If confirmed, the level of risk observed in these post-marketing studies is substantially lower than the risk of one case of intussusception in 5 000-10 000 vaccinees identified after Rotashield vaccination. The documented benefits of rotavirus vaccination against rotavirus-related disease are substantial. For example, in Mexico, nationwide use of Rotarix vaccine would prevent approximately 12 000 hospitalizations and 700 deaths from diarrhoea each year, a benefit that greatly outweighs the risk of vaccine-associated intussusception found in this preliminary analysis of possibly 20-40 cases. Furthermore, some studies have suggested that rotavirus vaccines may have an overall long-term protective effect against intussusception, an effect that might outweigh any short-term increased risk in the period shortly after the first dose of vaccine. Further data collection and analyses of information from Latin America and other surveillance systems are ongoing, and GACVS will continue to review these data as they become available.