Title of the Project

A phase IV multi-site observational epidemiology study to assess potential risk for adverse events following immunization that may be associated with misuse of a two-dose vial of 10-valent Pneumococcal Conjugate Vaccine (Synflorix) in Ethiopia.

Short Title: The Ethiopian Vaccine Adverse Events Study [EVAES].

Investigators and Institutional Affiliations

Status: completed

Investigators

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Abstract

The Government of Ethiopia is about to introduce a new 10-valent Pneumococcal Conjugate Vaccine (PCV10) for infants in Ethiopia. The vaccine is highly efficacious against diseases caused by *Streptococcus pneumoniae*. The selected vaccine, Synflorix™, is presented as a 2-dose vial without preservative. The two-dose vial will have significant advantages in limiting new cold-chain requirements. Multi-dose vaccines used in resource-limited settings have traditionally contained a preservative to minimize risk of microbial contamination. This allows one vial of the vaccine to be used for up to 28 days after the vial is opened provided stringent safety criteria, outlined in the multi-dose vial policy, are met. Given general public concerns about the use of preservatives, two-dose presentations of some new vaccines have been developed as preservative-free vials. Such vials should be discarded if not used within 6 hours of opening.

In Ethiopia, although specific training will be conducted to familiarize immunization staff with the necessary procedures of how to use Synflorix as a two-dose preservative-free vaccine, there remains a risk that in routine clinical settings, improper immunization practice (i.e. not discarding vials within 6 hours of opening) could result in microbial contamination, non-sterile injections, and adverse events following immunization (AEFI) such as injection -site abscesses, shock or death.

The Ethiopian society is well organized in geographic units and provides a suitable platform for conducting population based evaluation of potential AEFIs. In addition, Health and demographic surveillance systems (HDSS) routinely collect records of births, deaths, and other health related events that provide a feasible venue for a longitudinal, population-based evaluation of potential AEFIs as they can provide retrospective mortality information. Clinic- and household-based surveillance can identify and analyze suspected injection-site abscesses, the primary endpoint. In addition, secondary endpoints of shock and all-cause mortality can be investigated through hospital-based and demographic surveillance, respectively. Because surveillance is already established, data can be collated after introduction of Synflorix ™ to compare with existing data in the admission registers from the pre-vaccine era. Although the HDSS sites can provide adequate sample size for the mortality component of the study they cannot provide the necessary sample size for monitoring abscess formation; thus all kebeles in the selected woredas will be included in the study to obtain the required sample size for the latter study objective. Pharmacovigilance is important for evaluating new vaccines globally, and extended health and demographic surveillance systems in the selected woredas provide an important opportunity to evaluate the safety of current and new EPI vaccines.

Assuming that this study shows no evidence of significant adverse event outcomes, these rigorous safety assessments following Synflorix ™ introduction will add confidence in the use of a formulation that could enhance the