trial, the vaccine remained efficacious as there was a significant difference in the prevalence of infection. This is in sharp contrast from previous trials in malaria naïve volunteers or Gambian adults which suggested that vaccine efficacy was short lived [6,23].

Therefore the present ~~invention~~disclosure provides the use of a *Plasmodium* antigen which is expressed at the pre-erythrocytic stage, preferably a sporozoite antigen, in the manufacture of a medicament for vaccinating against severe malaria disease, in combination with a pharmaceutically acceptable adjuvant or carrier.

In one aspect, there is provided a use of RTS,S in the manufacture of a medicament for vaccination against severe malarial disease, in combination with a pharmaceutically acceptable adjuvant, wherein the target population is children of between 1 and 5 years of age and wherein the adjuvant is a preferential stimulator of a Th1 cell response and comprises 3D-MPL and QS21.

The invention is particularly concerned with reducing the incidence of severe *P. falciparum* disease.

The preferred target population for such a vaccine is children, in particular children under 5 years of age and especially children 1-4 years of age.

Preferably the *Plasmodium* antigen is a *P. falciparum* antigen.

The antigen may be selected from any antigen which is expressed on the sporozoite or other pre-erythrocytic stage of the parasite such as the liver stage. Preferably the antigen is selected from circumsporozoite (CS) protein, liver stage antigen-1 (LSA-1), liver stage antigen-3 (LSA-3), thrombospondin related anonymous protein (TRAP) and apical merezoite antigen-1 (AMA-1) which has recently been show to be present at the liver stage (in addition to the erythrocytic stage). All of these antigens are well known in the field. The antigen may be the entire protein or an immunogenic fragment thereof. Immunogenic fragments of malaria antigens are well know, for example the ectodomain from AMA-1.

Preferably the *Plasmodium* antigen is fused to the surface antigen from hepatitis B (HBsAg).