The safety and immunogenicity of plasmid pTHr DNA, modified vaccinia virus Ankara (MVA) human immunodeficiency virus type 1 (HIV-1) vaccine candidates were evaluated in four Phase I clinical trials in Kenya and Uganda. Both vaccines, expressing HIV-1 subtype A gag p24/p17 and a string of CD8 T-cell epitopes (HIVA), were generally safe and well-tolerated. At the dosage levels and intervals tested, the percentage of vaccine recipients with HIV-1-specific cell-mediated immune responses, assessed by a validated ex vivo interferon gamma (IFN-gamma) ELISPOT assay and Cytokine Flow Cytometry (CFC), did not significantly differ from placebo recipients. These trials demonstrated the feasibility of conducting high-quality Phase 1 trials in Africa.