PENTA 14 (ADAPT)
Summary

1.1 DESIGN
An open, randomised, controlled trial in HIV-1 infected children starting or switching to a new antiretroviral therapy (ART) regimen, including a protease inhibitor (PI) and/or non-nucleoside reverse transcriptase inhibitor (NNRTI).

166 children will be randomised (76 children in Part A and 90 in Part B). All children will receive extensive information on their disease and its therapy in order to optimise adherence. 76 children in Part A will be randomised into three groups: a "maximal Therapeutic Drug Monitoring (TDM)" group, a "minimal TDM" group and a "no TDM" group. The maximal TDM group will have PI and/or NNRTI dosage adjusted annually depending on the results of a complete pharmacokinetic curve after observed intake of drug. The minimal TDM group will have the PI and/or NNRTI dosage adjusted annually on the basis of the analysis of single plasma PI/NNRTI levels after reported but unobserved intake. In both the maximal and minimal groups plasma PI/NNRTI levels after reported but unobserved intake at intermediate routine clinic visits will be related to population target levels. In the no TDM group, PI/NNRTI plasma levels will not be analysed in real time.

90 children in Part B will be randomised to maximal or minimal TDM groups only.

Enrolments into Parts A and B will run concurrently. Clinical centres who currently offer some level of TDM may randomise in Part B; other centres should randomise in Part A. Clinical centres who only use TDM for a subset of children (eg infants) may randomise this subset in Part B and other children in Part A.

Enrolment will take place over 16 months and follow-up will continue until the last randomised child has completed 96 weeks of follow-up.

1.2 POPULATION
166 HIV infected children, ages one month to 17 years old, starting a new antiretroviral regimen including a PI and/or NNRTI, with plasma HIV-1 RNA $\geq$1000 copies/ml.

1.3 OUTCOMES
Primary:
- Change in HIV-1 RNA from baseline to 96 weeks.

The adherence support tools will be made available to children in all three randomised groups and evaluated descriptively. A cost-effectiveness analysis will evaluate the health service implications of TDM, if TDM is shown to be effective.

Age related population pharmacokinetic models will be generated for specific antiretroviral drugs used in sufficient numbers of children