



**Paediatric European Network for
Treatment of AIDS (PENTA)
*since 1993***

Since 2004 Penta Foundation

PENTA - AIMS



- To build a network of paediatric centres to undertake multicentre trials in a timely manner
- To address therapeutic questions specific to HIV infection in children which cannot be assumed/answered by trials in adults
- By collaboration and contact between paediatricians, often in small centres, to improve the levels of diagnosis and clinical care available to HIV infected children in Europe
- To expand the network to countries where ART therapy is being used in children
- To complement US and adult trials

Why the PENTA Network?



- PENTA aims to address questions:
 - which would otherwise not be addressed by the pharmaceutical industry (strategic questions)
 - Which require separate evaluation in children
 - Which require relatively large numbers of children
 - Includes collaboration with other networks and countries outside Europe
- Trials and Cohort studies are complimentary:
 - Involve the same groups of paediatricians

PENTA Trials -completed

Most have evaluated antiretroviral therapies, and have been randomised and blinded. LTFU is continuing

- Strategic:
 - when to start monotherapy - PENTA 1
 - Role of resistance testing – PENTA 8
 - TDM strategy evaluation – PENTA 14
- PK, Toxicity and tolerability
 - PENTA 3 - ZDV+ddC vs ZDV alone
 - PENTA 4 - 3TC vs placebo added to mono or dual NRTI ART
 - PENTA 13 - PK of twice versus once daily 3TC and Abacavir in children
- Activity & Toxicity of new combinations
 - PENTA 5 - ZDV+3TC vs ZDV+ABC vs 3TC+ABC
 - NFV vs NFV placebo
- PENTA 7 - PK and activity of early ART in infants

Most trials have included immunology, virology, adherence, substudies

PENTA Trials - ongoing and Planned in Europe

- **Strategic:**

- PENTA 9 (PENPACT1) - What to start with; when to switch
- PENTA 11 - Structured Treatment interruptions (LTFU)
- PENTA 16 – Short cycle therapy
- PENTA 17 – Simplification strategy (kaletra OD)
- PENTA 20 – NRTI sparing strategies in PI naive children

- **Pharmacokinetics:**

- PENTA 15 - PK of twice versus once daily 3TC and Abacavir in infants (completed)
- PENTA 18 – PK new Kaletra paediatric formulation



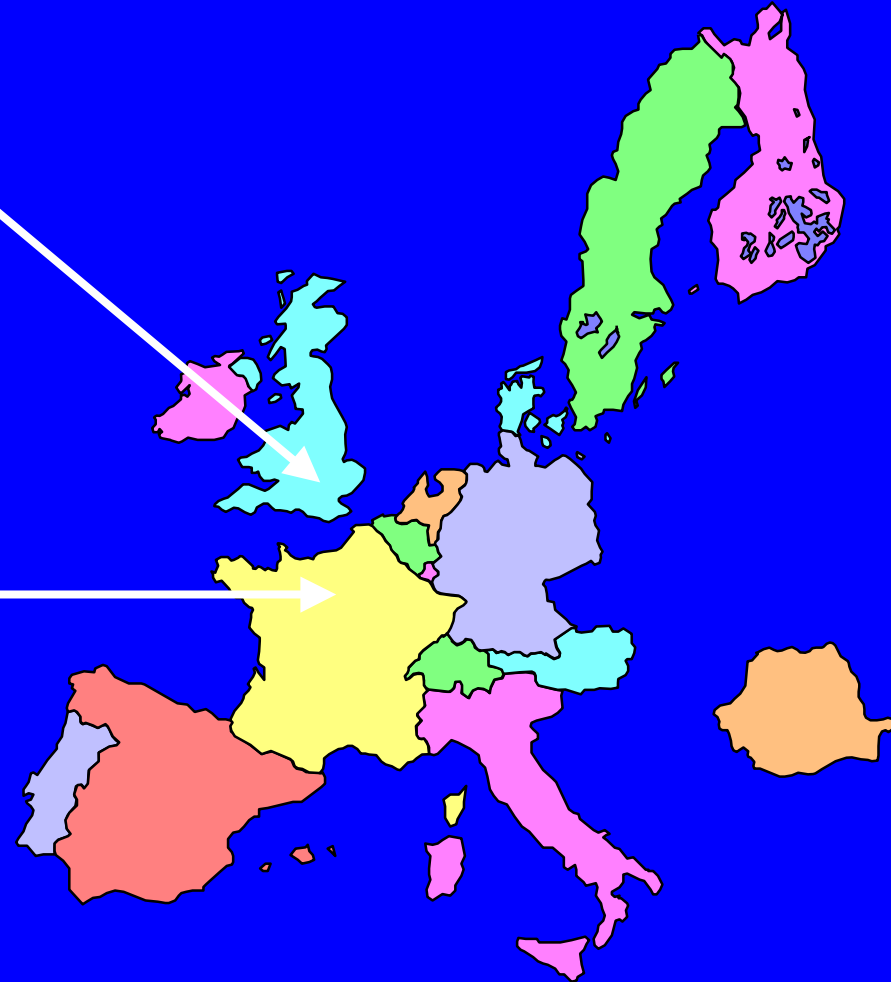
PENTA countries

MRC CTU, London:
Austria, Finland,
Germany, Ireland,
Italy, Netherlands,
Sweden, UK

Brazil, Thailand

INSERM SC10,
Paris: Belgium,
Denmark, France,
Portugal, Poland,
Romania, Spain,
Switzerland

Argentina



Penta: participating centres/sites

	Clinical	Lab	Trial centres	NGO/DSMC
France	10	4	1	2
Switzerland	3			
Belgium	1			1
Portugal	2			
Spain	6	2		
UK	15	5	1	2
Eire	1			
Italy	10	3		1
Holland	2	2		
Germany	5	1		
Sweden	1			
Denmark	1			
Poland	1			
Romania	3		1 (coord)	
Thailand	2		1 (coord)	
Brazil	3			
Argentina	2			
Total	68	17	4	6



PENPACT 1

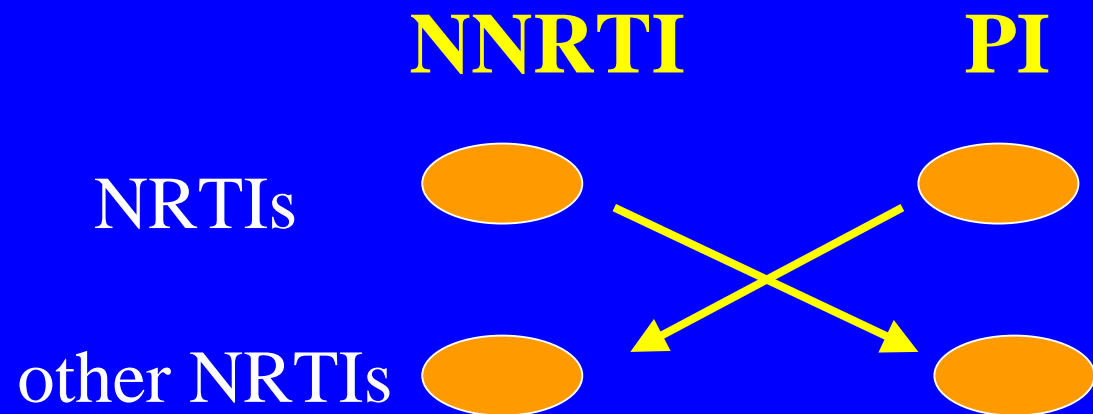
1st collaborative PENTA & PACTG trial
(PENTA 9 / PACTG 390)

A randomised clinical trial to compare different strategies of starting and changing antiretroviral therapy in previously untreated children in terms of long term virological suppression.



PENPACT 1

- What to start with
- Second randomisation - switch at VL >1,000 vs. >30,000 copies/ml





PENTA 18 Trial

(in collaboration with ABBOTT)

A study of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1 infected children.



PENTA/ECS network

Clinical Trial Network

- PENTA trials
- NEAT

Cohorts:

- ECS
- HPPMCS
- Cohere
- Cohort coll.
- Postmark surv
- 3C4kids.

ECS: background

- An epidemiological study of HIV-infected pregnant women and MTCT, incorporating a birth cohort of infected and uninfected children, established in 1985
- Currently including around 9,500 mother-child pairs
- ECS network includes clinical sites in 10 countries in **Western Europe** (Belgium, Denmark, Germany, Italy, the Netherlands, Spain, Sweden, UK), **Central Europe** (Poland) and **Eastern Europe** (Ukraine [since 2000]; Kazakhstan commencing enrolment in 2009)
- Overall coordination is based at UCL Institute of Child Health, with the Eastern European coordination led by the Perinatal Prevention of AIDS Initiative)
- Core epidemiological study, plus nested and supplementary studies, including European Paediatric HIV and Lipodystrophy Study and Ukraine Cohort of HIV-infected childbearing women

Epidemiology Studies and Cohort Collaborations

Complement trials by:

- Addressing questions at a population level
 - Effect of HAART
 - Long-term side-effects including lipodystrophy
- Assist with long-term follow-up of trials
- Provide data to:
 - explore questions to be addressed by trials
 - inform trial design
- Pharmacovigilance studies

PENTA / ECS achievements

PENTA

- Unique paediatric clinical trial network
- More than 1500 children enrolled in trials to date
- Major contribution to ART registration for children (e.g. 3TC, ABC, Kaletra etc)
- Paediatric HIV guidelines
- 32 major papers in peer-reviewed journals

ECS

- Findings have contributed to development of evidence-based guidelines and of clinical trials
- 84 publications in peer-reviewed academic journals overall; 36 papers and conference presentations since start of 2006
- Provides the only epidemiological investigation of MTCT, HIV in pregnancy and paediatric HIV in Eastern Europe to date



PENTA/ECS network

Clinical Trial Network

- PENTA trials
- NEAT

Cohorts:

- ECS
- HPPMCS
- Cohere
- Eurocord
- Cohort coll.
- Postmark surv.
- 3Cs4kids

Pregnancy studies

- ECS
- PK (PANNA)
- Toxicity
- etc

Training:

- tr@inforPedHIV
- African training
- ACTIVATE



**A European clinical
pharmacology network to
investigate the
PhArmacokiNetics of
aNtiretroviral Agents in HIV-
infected pregnant women
(PANNA)**

HIV[e]DUCATION



Tr@inforpedHIV - Zimbabwe

Tr@inforPedHIV 2009 - Zimbabwe

Distance learning

9 modules on paediatric HIV topics

Residential Course

Kampala 20th - 22nd January 2009

Basic epidemiology, virology and immunology

Mother to child transmission and prevention programmes

Antiretrovirals: Principle of ART treatment and strategies, guidelines, toxicity and resistance

Opportunistic infections, management and prevention (including Hepatitis coinfection, TB coinfection)

HIV and nutrition

Psychosocial aspects: including family issues, learning about HIV, adolescents with HIV

An additional module covering issues specific to an African setting

Registration fees: distance learning + Residential Course: ?

(Registration includes: memory stick with course modules, participation in the 3 day symposium, final CME certificate, and accommodation per diem support. Please note - transport not included)

To register contact: ?

For further information : Sabrina sac@ctu.mrc.ac.uk or www.anecca.org www.pentatrials.org www.espid.org



Delegates at the 2007 Tr@inforPedHIV course In Kampala found it a very useful update and a practical approach to managing HIV in children.

The course is appropriate for trained paediatricians looking after HIV positive children, trainee paediatricians, specialist nurses, pharmacists and dieticians.

PENTA Training activities



Europe:

- ESPID/PENTA integrated distance and residential learning courses since 2005 (more than 500 participants from 28 countries)
- ACTIVATE (Hungary, Belarus, Scotland)

Africa:

- Cameron March 2007
- Uganda December 2007
- Zimbabwe January 2009
- *Ghana/Togo December 2009*

Latina:

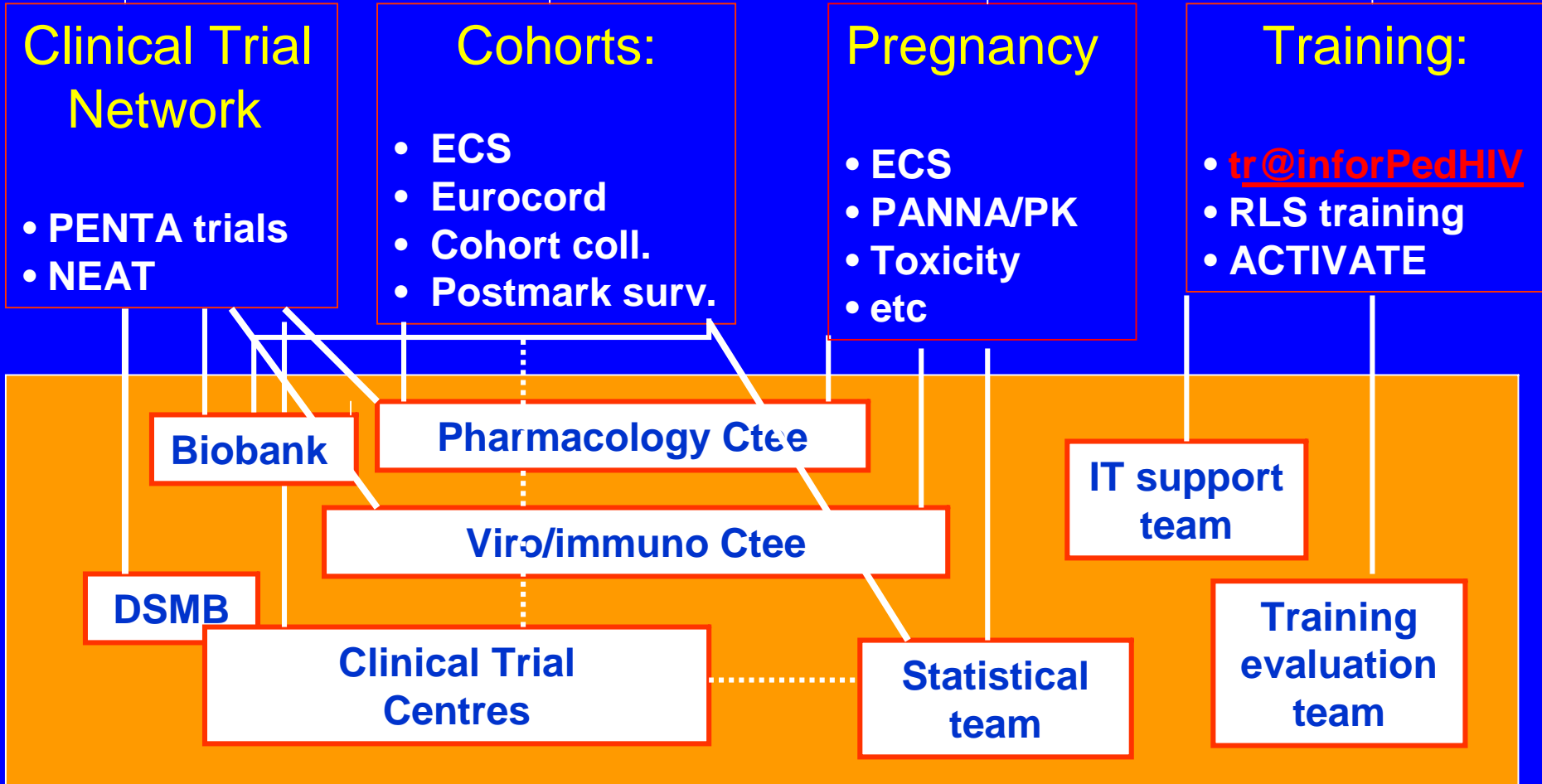
- Salvador Spring 2008
- *Argentina August 2009*

Asia:

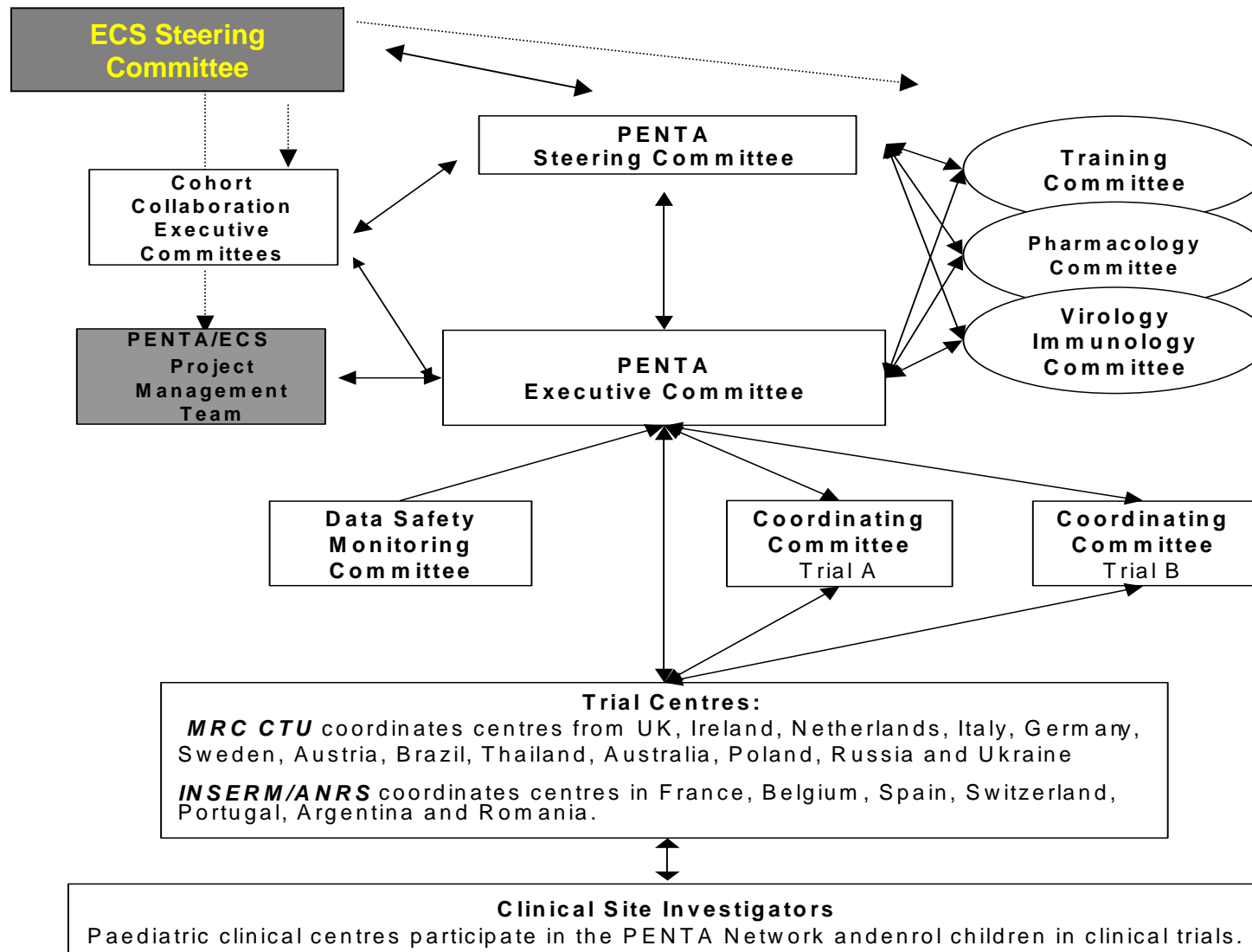
- Thailand November 2008



PENTA/ECS network



PENTA/ECS Network Management structure



PENTA Foundation 2006 – 2010 funding

European Commission:

PENTA/ECS (FP6) - coordination

PENTA LABNET (FP7) - coordination

ACTIVATE (DG SANCO) – coordination

NEAT – Partner

CHAIN – Partner

MRC, INSERM/ANRS, Italian Institute of Health, national AIDS program

Pharmaceutical companies for specific projects

NICHD (PENPACT 1)

Training activities

New European Scenario for PENTA

- Less children born with HIV infection in Western Europe
- Growing epidemic in Eastern Europe (women and children)
- Vertically infected children are becoming young adults (..and transition to care is not always easy ..)

EU paediatric regulation

WHO ARV paediatric formulation “document”

PENTA network beyond “just” running clinical trials

Penta: strategic plans for the future

- Collaboration with adults HIV networks (Eurocoord, Neat, Chain)
- Collaboration with other PID networks in Europe (*“incubator”* for PENTi) and the US
- Extend collaboration to mid developed and developing countries (EDCTP)
- Collaboration with the EMEA (PENTA is represented within the PDCO)
- Participation to the European Network for “Medicine for Children” - TEDDY
- Implementing training/education programs for developed and developing countries on clinical research