PENTA-ID network

Carlo Giaquinto
University of Padova, Italy

HISTORY and MISSION

Paediatric European Network for Treatment of AIDS (PENTA)

(www.penta-id.org)

- Established in 1991 as collaboration between paediatric HIV centres in Europe. Aim: to undertake independent clinical trials to address questions about antiretroviral therapy (ART) in HIV infected children where answers cannot be extrapolated from trials in adults

- Activities: not just clinical trials, but cohort studies collaboration, pregnancy studies and training/ educational programmes.

- Funding comes from:

- EC (10 projects coordinated by PENTA since Biomed 1, involvement in more than 20 EU funded projects)
- MRC
- INSERM/ANRS
- US-NIH (project-based), UNICEF etc
- Italian National Institute of Health (project-based)
- Pharmaceutical companies

MRC CTU, London:
Austria, Finland,
Germany, Ireland, Italy,
Netherlands, Sweden,
Poland, UK, Ukraine,(US)

Brazil, Thailand,
Bahamas, South Africa,
Uganda, Zimbabwe

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

Argentina, Cameroon,
Mexico

PENTA 25 countries

>100 partners/sites

3 CTUs

PHPT
Thailand

PENTA HIV Trials -completed

Strategic:

- when to start monotherapy - PENTA 1
- Role f resistance testing – PENTA 8
- TDM strategy evaluation – PENTA 14
- What to start with – Penpact 1
- Treatment Interruption – PENTA 11

- 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 studies included immunolog, virlogy, QOL, adherence etc substudies

PENTA HIV Trials - ongoing

- **Strategic**:
  - **PENTA 11** - Structured Treatment interruptions (LTFU)
  - PENTA 16 (Breather)– Short cycle therapy
  - PENTA 17 (SMILE) – Simplification strategy (SOCvs EVL/Dar)
  - PENTA 20 (Odyssey) – DLG first or second line

- **Pharmacokinetics:**
  - PENTA 15 - PK of twice versus once daily 3TC and Abacavir in infants
  - PENTA 18 (Koncert)– PK new Kaletra pediatric formulation

- **Research platform:**
  - EPIICAL: HIV cure

ODYSSEY

<18 years old,
Starting 1st line or switching to 2nd line
N = 700

First-line ART
N=310
Randomisation 1:1

stratified by
PI- or NNRTI (SOC),
NRTI backbone (all) and
routine VL availability

DTG ARM
DTG + 2NRTI
155 patients

SOC ARM
bPI/NNRTI+2/3NRTI
155 patients

Second-line ART
N=390
Randomise 1:1

stratified by
PI- or non-PI (SOC),
NRTI backbone (all) and
routine VL availability

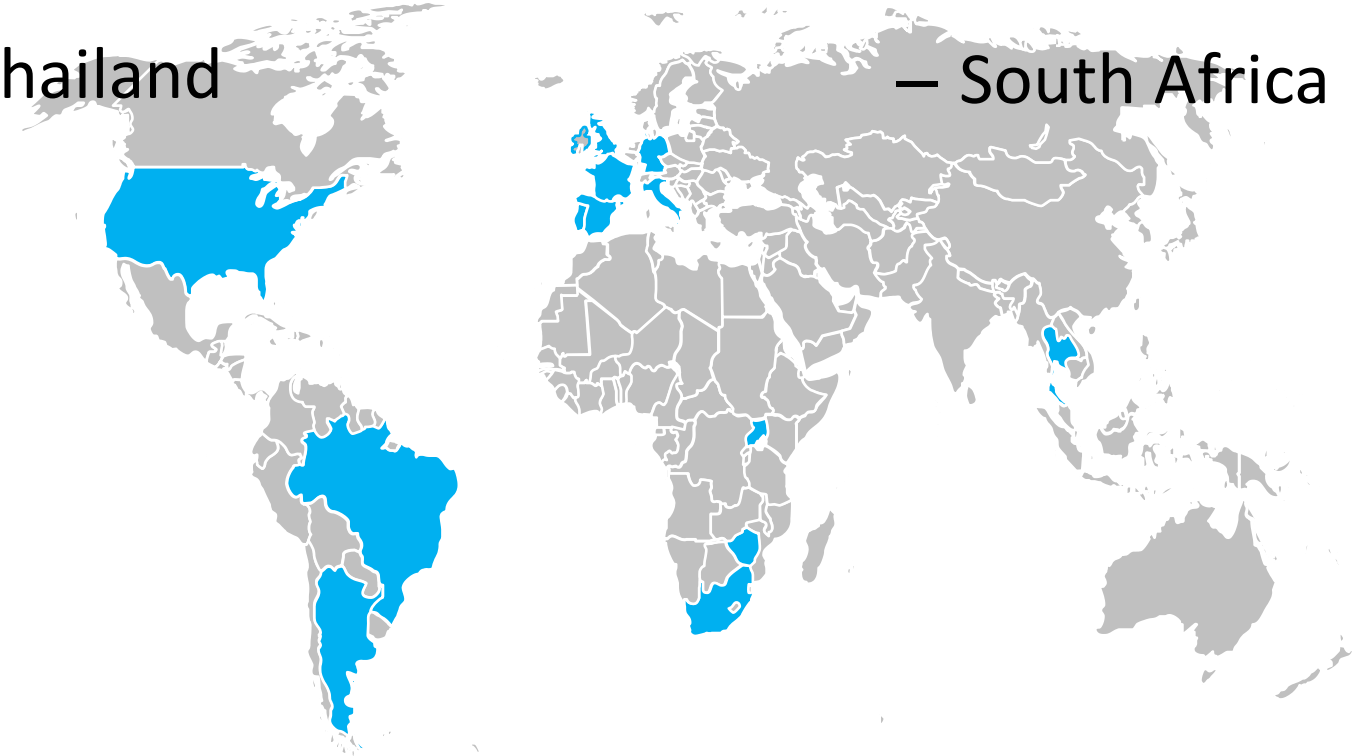
DTG ARM
DTG+2NRTI
195 patients

SOC ARM
bPI/NNRTI/RaI+2NRTI
195 patients

Follow up: until last patient reaches 96 weeks
Endpoint: virological and clinical failure

Countries

- PENTA sites
  - Europe
  - South America
  - Thailand
- USA



- Africa
  - Uganda
  - Zimbabwe
  - South Africa

From the initial focus on HIV to the broader area of Paediatric Infectious Diseases

- 2010: from PENTA to PENTA-ID

- **Focus on neglected and complex diseases**

EU funding:

- **NeoMero** (neonates)
- **NeoVanc** (neonates)
- **GRiP** ("medicine for children")
- **PREPARE** (prevention of epidemics)
- **EMIF** (creation of a European epidemiology/ICT platform)
- **COMBACTE-MAGNET** (molecules against Gram Negative infections)
- **GAPP** (clinical trials on "off-patent" drugs)
- **RESCEU (RSV)**
- **ZIKAction (ZIKA)**

- **Specific contracts and agreements with major International Paediatric Hospitals** not following up HIV positive children

- 2011: **PENTAid recognised by the EnprEMA as a level 1 Paediatric Clinical Trial Network in Europe** to conduct clinical trials in pediatric HIV, antimicrobials and vaccinology. **PENTA as PDCO member 2008 - 2014**

HISTORY and MISSION

The Foundation

- set up in 2004

- represents **the ideal legal and financially viable framework to run research and educational activities in different countries** in the field of Paediatric Infectious Diseases and Paediatrics in general

- a centre for **project development** and **project management**

- involved in 12 proposals (4 as Coordinator) to the European Commission (FP7 and IMI) in 2011 and 2012. All applications were “2 stage” and 6 out of 12 proposals went to the second stage. 4 of them have been funded in 2013. In one of them PENTA is the coordinator and in the other three is one of the main partners

- **unique expertise in running international research projects**

- **In 2015 a spin off company (PENTA-ID Innovation was set up to provide services to commercial**

PENTA-ID Activities and main projects and fundings

HIV
- Trials
- Cohorts
- EPIICAL
- Pregnancy

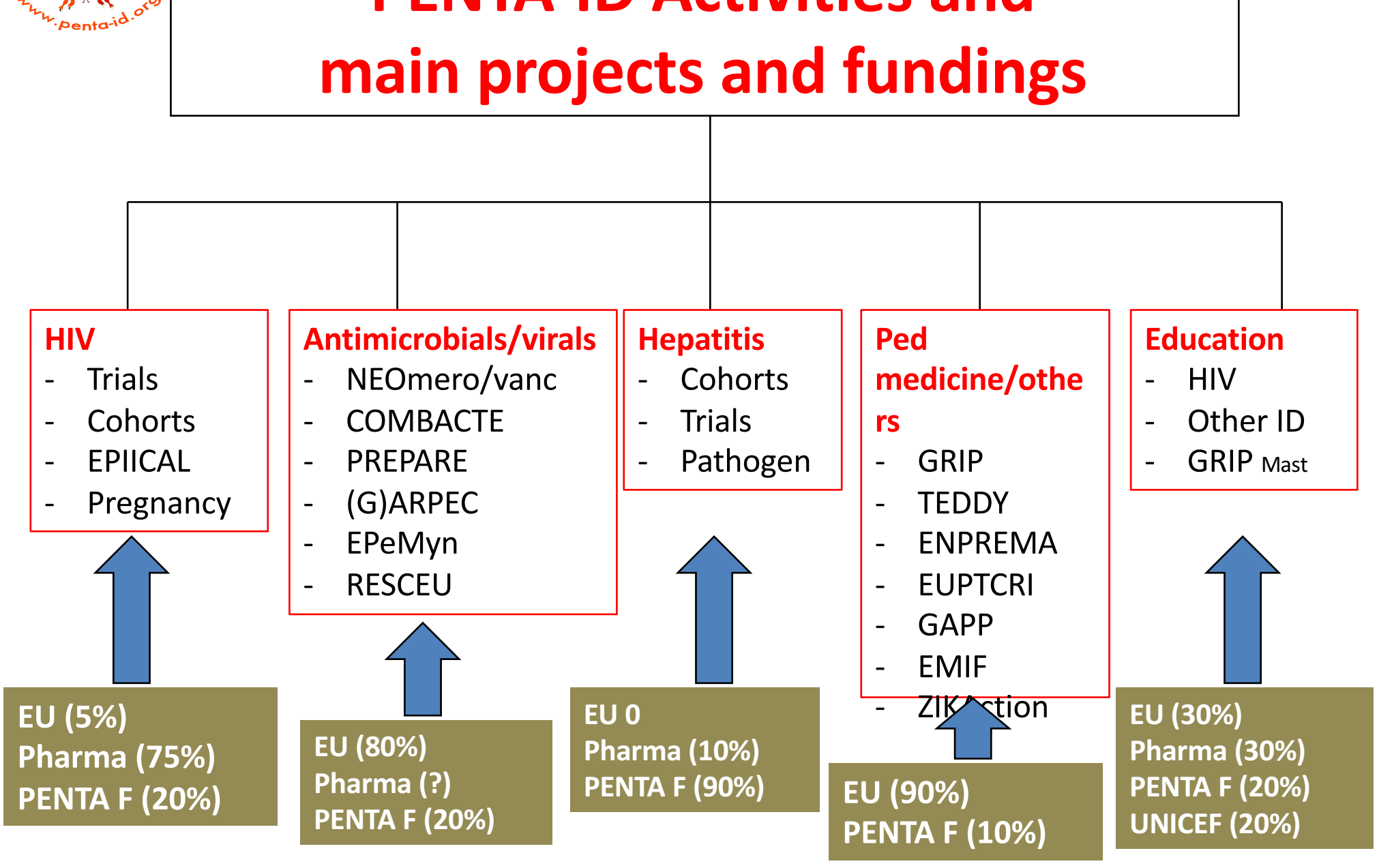
Antimicrobials
- NEOmero/vanc
- COMBACTE
- PREPARE
- (G)ARPEC
- EPeMyn
- RESCEU

Hepatitis
- Cohorts
- Trials
- Pathogen

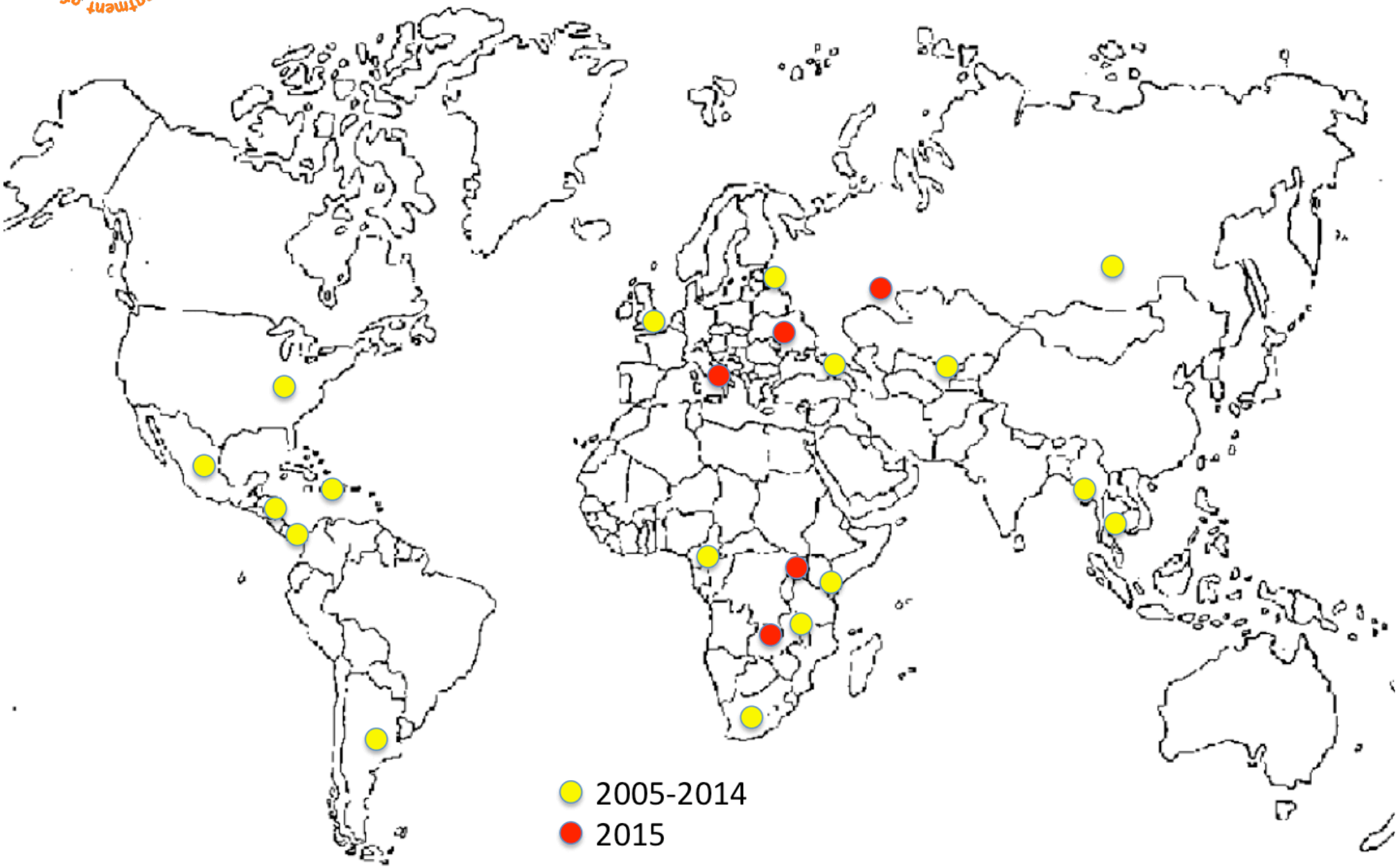
Ped medicine
- GRIP
- TEDDY
- ENPREMA
- EUPTCRI
- GAPP
- EMIF
- ZIKAction

Education
- HIV
- Other ID
- GRIP Mast

PENTA-ID Activities and main projects and fundings



Tr@inforPedHIV



NEAT
EUROPEAN AIDS TREATMENT NETWORK

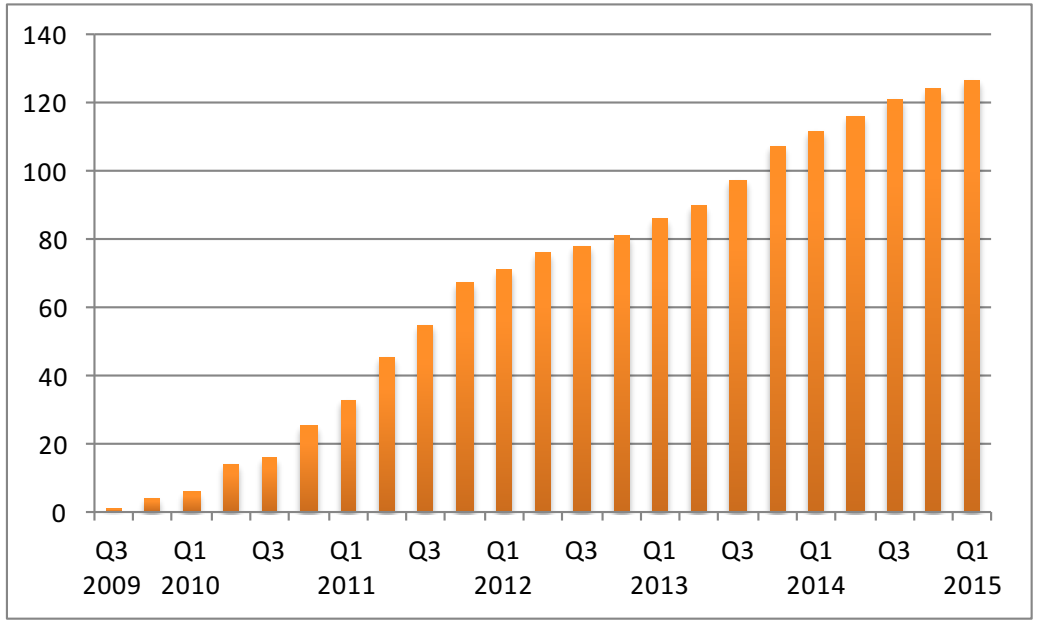
panna

EuroCoord

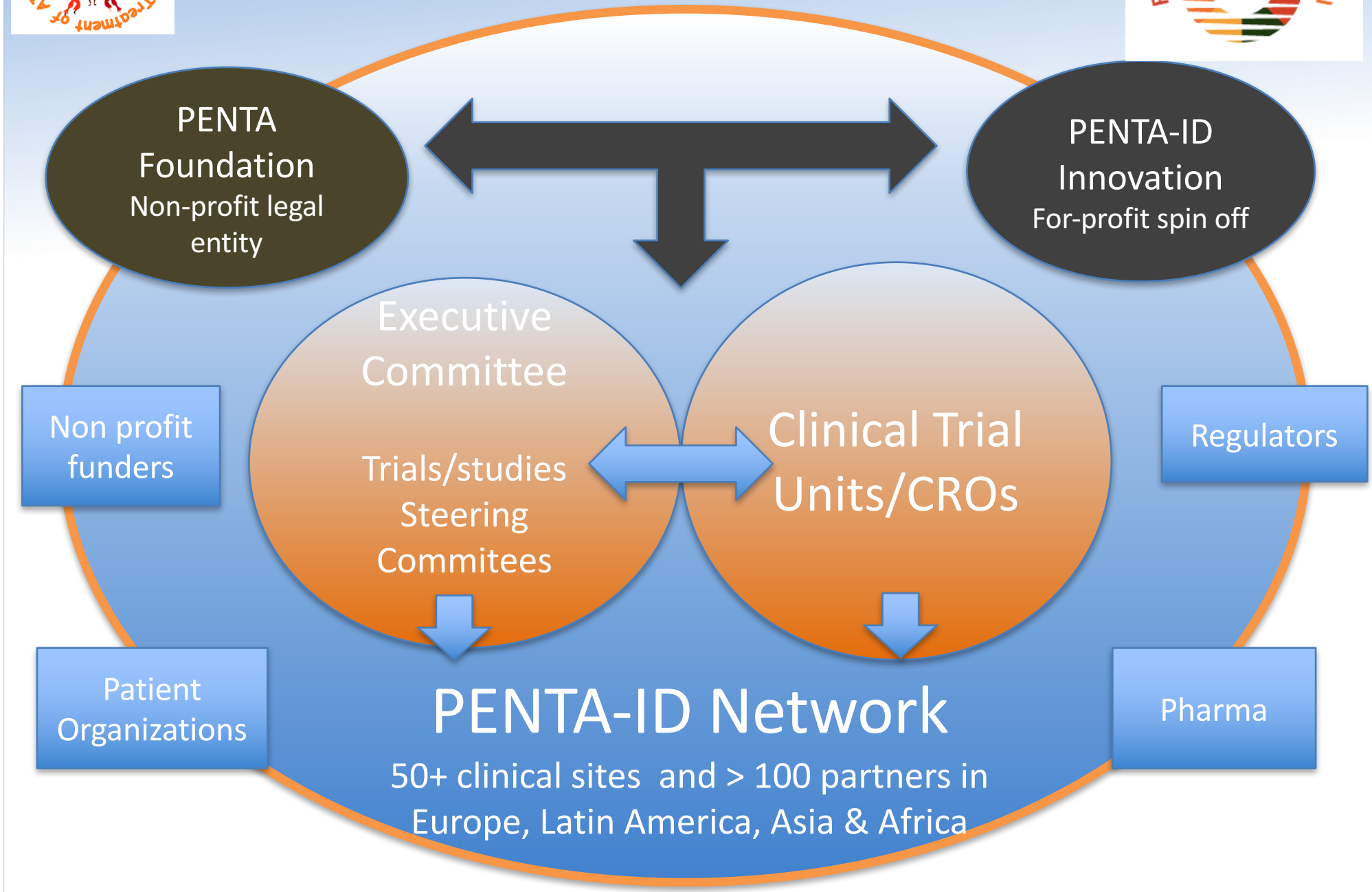
A European clinical pharmacology network to investigate the Pharmacokinetics of newly developed ANtiretroviral agents in HIV-infected pregNAnt women

Mission: Evidence-based dose recommendations for all ARVs to be used in pregnancy

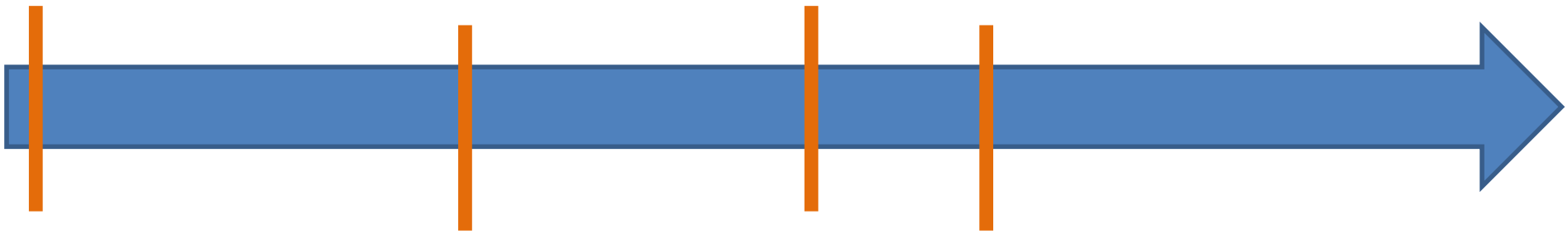
18 sites from 8 European Countries
10 agents studied



PENTA-ID Network Organization



PENTA Timeline



1991 PENTA Network

2004 Fondazione PENTA ONLUS

2012 PENTA-ID Network

2015 PENTA-ID Innovation

Unique aspects of PENTA Foundation

- Private non-profit Foundation
- SME
- International

Unique aspects of PENTA Foundation

- Experience
  - Paediatric ID
  - Wide range of funding mechanisms
  - Diverse study designs

PENTA Foundation Board

ZIKAction: Preparedness, research and action network on maternal-paediatric axis of ZIKV infection in Latin America and the Caribbean

Project Overview

Claire Thorne
Project Scientific Coordinator

Scope of H2020 Call (Deadline April 28th, 2016)

1. The **evaluation of the potentially causative relationship** between ZIKV and the severe reported complications, as well as
   - **exploration of the mechanisms involved**, or
   - alternative aetiologies if needed.

2. If such an association is confirmed, the consortium should be ready to rapidly **launch additional studies**, such as, but not limited to:
   - studies of natural history of disease,
   - **pathogen and host determinants of severity of disease**,
   - interventional trials for potential prevention (e.g. vaccines) and/or treatment strategies.

3. Evolve into **a network capable of rapidly launching a research response** to future severe infectious outbreaks caused by emerging pathogens with pandemic potential or potential to cause significant damage to health and socio-economics in the region.

   Provisions should be made so that this initial research platform may be further developed through a comprehensive **'inter-epidemic' action plan** addressing and fine-tuning the response to any obstacles identified during the ZIKV research response.

ZIKAction

European Commission

ZIKAction: Preparedness, research and action network on maternal-paediatric axis of ZIKV infection in Latin America and the Caribbean

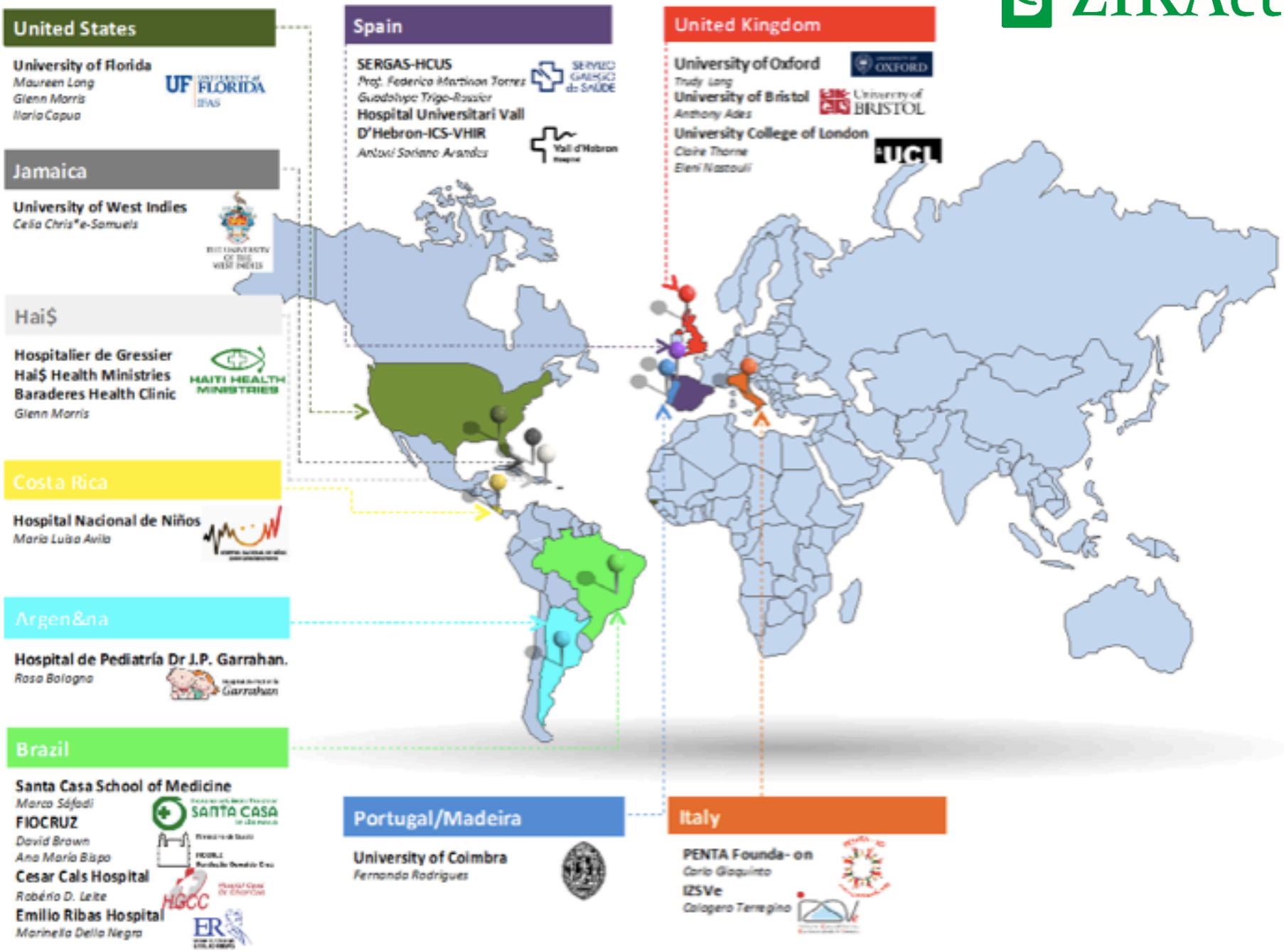
PENTA Foundation = lead

14 other partners, plus 5 third parties

5 year project

Budget: €6.9 million

Figure 1. Geographic distribution of ZIKAction Consortium



Proposal Evaluation Form

	**EUROPEAN COMMISSION** Horizon 2020 - Research and Innovation Framework Programme	**Evaluation Summary Report - Research and innovation actions/Innovation actions**

Criterion 1 - Excellence

Score: **4.50** (Threshold: 4/5.00 , Weight: -)

Criterion 2 - Impact

Score: **4.50** (Threshold: 4/5.00 , Weight: -)

Criterion 3 - Quality and efficiency of the implementation

Score: **4.00** (Threshold: 3/5.00 , Weight: -)

The work plan and resources assigned are well developed and balanced.

The work plan has a very good chance of succeeding.

The well designed proposal will provide information on all elements of the call a

The major strength of this proposal is the creation of a global paediatric network for clinical studies, diagnostics and therapeutics evaluation far beyond the Consortium which will allow collaboration with other successful consortia or initiatives.

History and Timeline

- Dec 2015: Marinella Della Negra gives a presentation about Zika in Brazil at PENTA meeting
- Feb 2016: Draft text of EU call comes out; meeting with Rohan Hazra about ZIP Study
- March & April: building consortium, writing application
- 28 April: Deadline
- 8 June: Evaluation report; on reserve list
- 9 June: Discover we are #1 on reserve list
- **13 June: Notified that ZIKAction would be fully funded**
- 16 June: First grant agreement meeting in Brussels
- July-August: sharing activities (WP) with other two projects
- **October: signing grant**

Main goals

1. Developing a multidisciplinary multinational ready-to-act **network capable of rapidly addressing any maternal and paediatric health research need** arising from the ongoing ZIKV outbreak

1. Conducting an interdisciplinary programme of research studies within this network **to address key knowledge gaps** relating to ZIKV epidemiology, natural history and pathogenesis, with a particular emphasis on maternal and child health.

Objectives

1. To conduct **prospective cohort studies in ZIKV-affected countries in South and Central America and the Caribbean in order to:**
   - Assess the **association between ZIKV in pregnancy and adverse pregnancy and fetal/infant outcomes**, including fetal demise, in utero growth restriction, microcephaly and other infant defects, and **investigate factors that may modify such outcomes**, such as previous, recent or current co-infections with dengue virus (DENV) and/or chikungunya virus (CHKV),
   - Estimate the **risk of vertical transmission** of ZIKV by gestational age and identify **risk factors** for transmission including maternal characteristics (e.g. symptomatic ZIKV infection, primary or recurrent infection), infant & viral factors, and evaluate the presence of ZIKV in breastmilk,
   - Estimate **incidence of ZIKV infection in pregnancy and in the postnatal period** in endemic and emerging/established epidemic situations and describe risk factors and clinical presentation, including the incidence of neurological disorders.

Objectives

ZIKAction

2. To develop harmonized case definitions for congenital ZIKV infection, to **define the natural history of congenital infection** and postnatally acquired, symptomatic paediatric infection, and to explore the feasibility of developing systems for longer-term follow-up of children with congenital ZIKV to allow future monitoring of late sequelae,
3. To use **animal models to investigate the timing and mechanisms** of ZIKV vertical transmission and to assess the causal role of ZIKV infection during pregnancy on fetal malformation and other adverse pregnancy outcomes,
4. To develop **ZIKV diagnostics and to establish clinical algorithms** optimised for rapid diagnosis of ZIKV in pregnant women, infants and children, supported by clinical data.

Objectives

ZIKAction

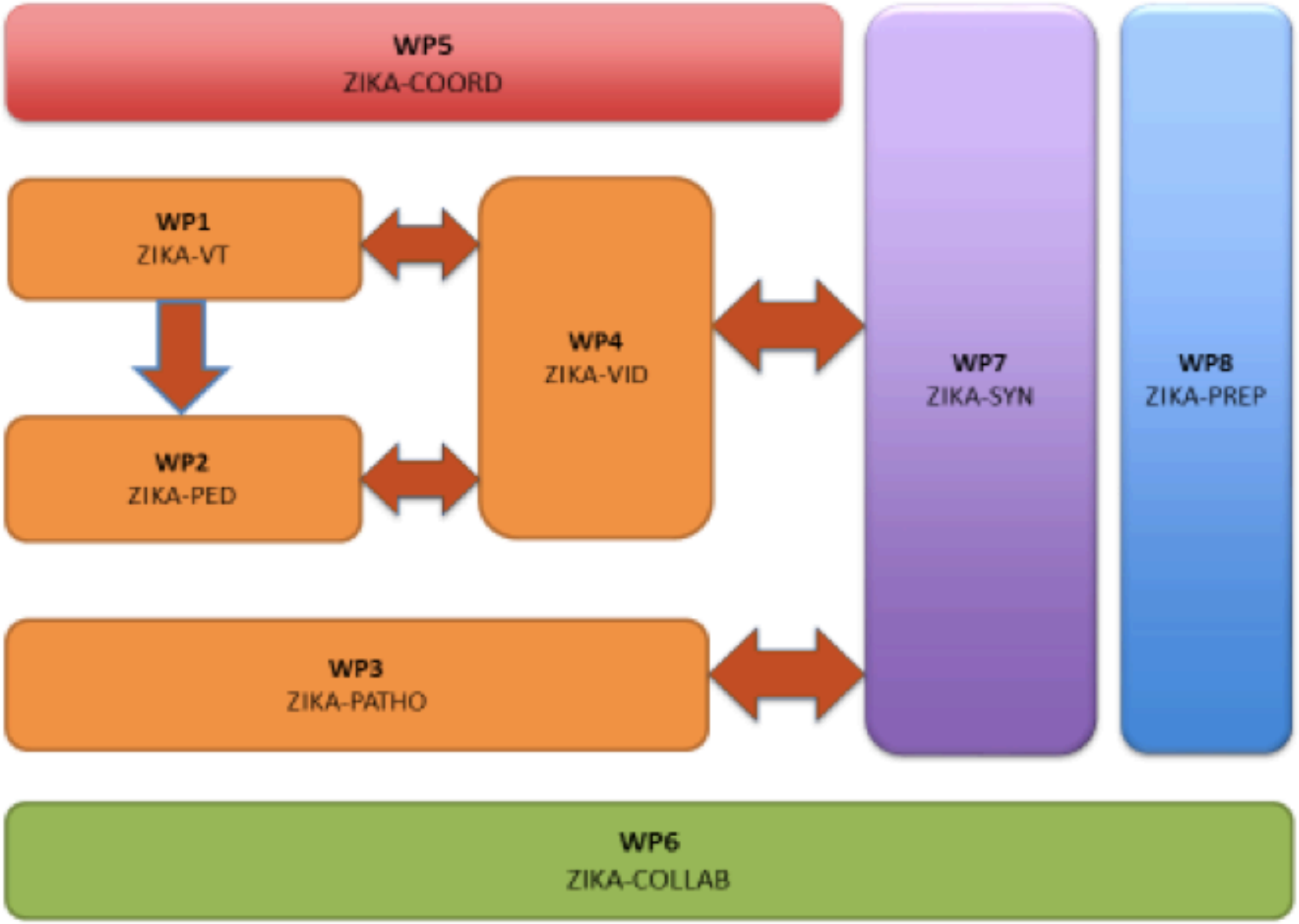
5. To develop and implement **a strategy for communication, training, data-sharing and sustainable surveillance and research in partnership with all other EU funded ZIKV consortia**, as well as other relevant national and international stakeholders, in order to facilitate the geographic and scientific expansion of activities during the course of the project, rapid dissemination and exploitation of findings, and maintenance of activities in the future

6. To develop and **implement harmonized practices for conducting laboratory and observational studies** of arboviruses and other infectious disease in Latin America in close collaboration with all other EU funded ZIKV consortia. This will include
    a. Streamlined, standardized approaches to ethics, administrative, regulatory, and logistical issues
    b. Data sharing modalities and governance structures
    c. Consolidation and updating of existing regional/global guidance on prevention, diagnosis and clinical management of arbovirus infection
    d. Creation of revision of relevant training programs to reflect clinical and epidemiological findings
    e. Maintenance of joint management structures to oversee close collaboration of all EU funded ZIKV consortia on the abovementioned tasks
    f. Creation of joint communications strategies for outcomes shared between all EU funded ZIKV consortia

Workpackage list

1. ZIKA-VT: development and implementation of pregnancy, vertical transmission and maternal natural history studies harmonized with other similar initiatives in the EU and globally
2. ZIKA-PED: development and implementation of congenital and acquired paediatric infection studies
3. ZIKA-PATHO: development and implementation of pathogenesis and animal model studies
4. ZIKA-VID: **V**irology and **I**mmunology studies, development and testing of **D**iagnostic methodologies
5. ZIKA-COORD: project management, scientific coordination, harmonization of data collection and sharing within the ZIKAction consortium
6. ZIKA-COLLAB: creating and maintaining management structures and communications activities shared with all EU funded ZIKV consortia and ensuring ethical and regulatory compliance of all activities across consortia
7. ZIKA-SYN: harmonizing data and implementing data sharing infrastructure between all EU funded ZIKV consortia, creating roadmap for more extensive data sharing
8. ZIKA-PREP: establishing a Latin American emerging infectious disease preparedness and response network common to all EU funded ZIKV consortia

Figure 5. Interaction of ZIKAction work packages



Scientific Questions

ZIKAction

- *What is the incidence of ZIKV in pregnancy and what are the risk factors?*
- *What is the seroprevalence of ZIKV in pregnant women at the start of pregnancy?*
- *What is the association between ZIKV and adverse pregnancy and fetal outcomes?*
- *What are the pregnancy outcomes (i.e. fetal demise, stillbirth, livebirth) in women with ZIKV infection?*
- *What are the potential pathological mechanisms underlying adverse outcomes?*
- *What is the rate of vertical transmission?*
- *What is the timing of vertical transmission, and what are the risk factors?*
- *What proportion of incident ZIKV infections are asymptomatic, and does this vary in women with and without prior ZIKV infection, and with or without concurrent or recent DENV or CHIKV infection?*
- *What is the clinical spectrum in maternal ZIKV infection (in pregnancy and outside pregnancy)?*
- *What is the incidence of neurological and other complications in women with ZIKV and does this differ according to pregnancy status?*
- *What is the incidence of ZIKV infection in the postnatal period?*

ZIKA-VT: development and implementation of pregnancy, vertical transmission and maternal natural history studies harmonized with other similar initiatives in the EU and globally

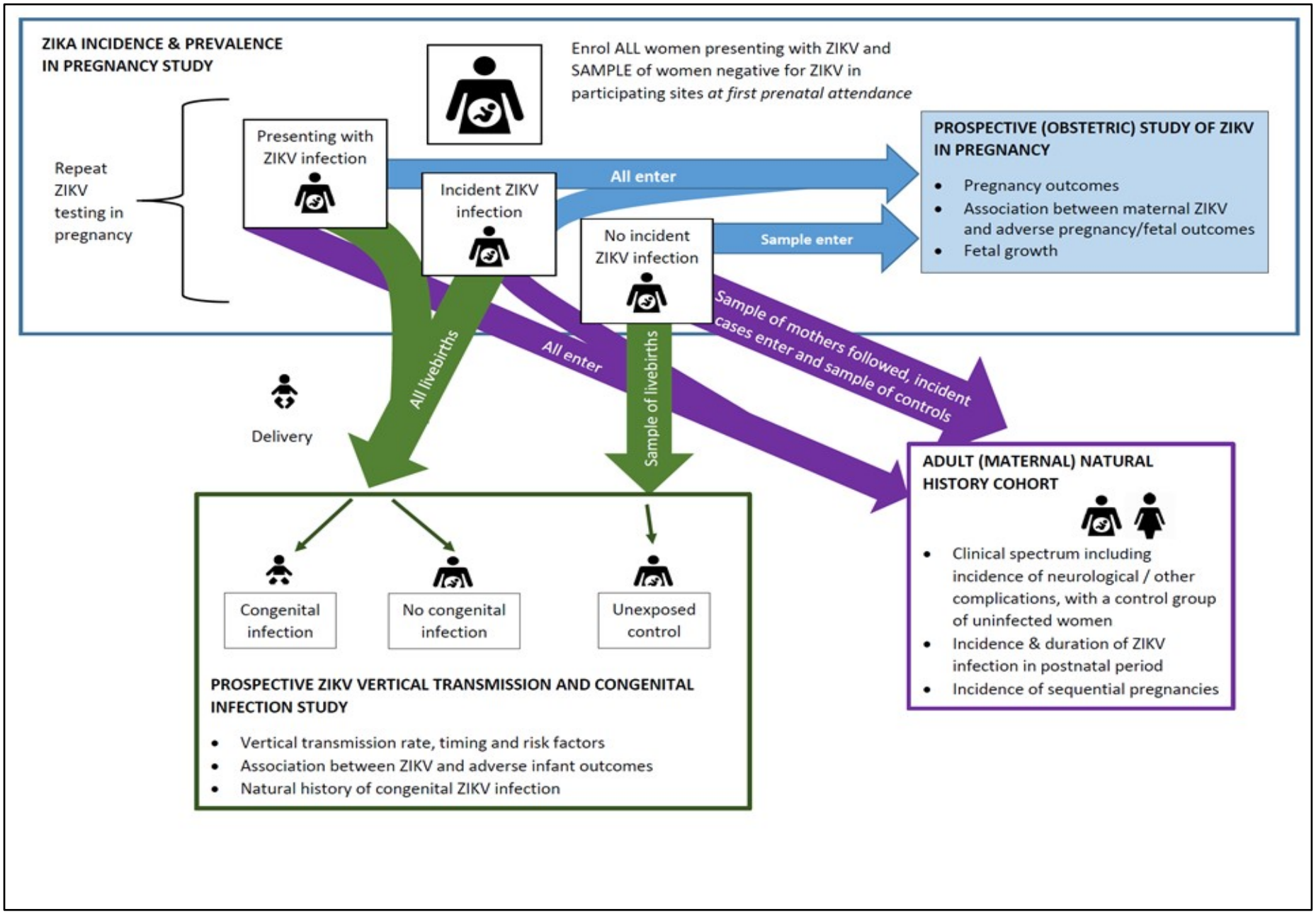
Objectives:

To conduct prospective cohort studies in South and Central America and the Caribbean in order to

1. Assess the association between ZIKV infection in pregnancy and adverse pregnancy and fetal/infant outcomes (including fetal demise, in utero growth restriction, microcephaly and other infant defects), and identify factors that may modify these outcomes such as previous, recent or current co-infections with DENV and/or CHKV
2. Estimate the risk of vertical transmission of ZIKV by gestational age at different time points in pregnancy and identify risk factors for transmission including maternal characteristics (e.g. symptomatic ZIKV infection, primary or recurrent infection), infant and viral factors, and evaluate the presence of ZIKV in breastmilk
3. Estimate incidence of ZIKV infection in pregnancy and to describe risk factors and its clinical presentation, including the incidence of neurological disorders

ZIKAction

Schematic diagram of pregnancy, vertical transmission and maternal natural history studies, with birth cohort of infants with congenital infection



ZIKA-VT: development and implementation of pregnancy, vertical transmission and maternal natural history studies harmonized with other similar initiatives in the EU and globally

- **Task 1.1 Training/education of all study personnel (M2-M54)**

  This task will be led by PENTA in collaboration with UCL, UWI and ISCMSP

- **Task 1.2 Enrollment into studies (M13-M36)**

  This task will be carried out by UWI, ISCMSP, HGCC, and other recruiting third parties

- **Task 1.3 Maternal clinical follow-up (pregnancy and postnatal) (M13-M54)**

  This task will be led by UWI, in collaboration with ISCMSP, HGCC and other recruiting third parties. This task links to Task 1 in WP7~~9~~ Harmonization of data and a roadmap towards data sharing.

- **Task 1.4 Prospective ZIKV vertical transmission study (M37-60)**

  This task will be carried out in collaboration with UWI, ISCMSP, HGCC, and other recruiting third parties.This task links to Task 7.1 in WP7.

- **Task 1.5 Laboratory testing and biobanking (M15-60)**

  This task will be led by UWI together with UCL and in collaboration with all other clinical sites involved in these studies.

- **Task 1.6 Statistical analysis (M25-M60)**

  This task will be led by UB in collaboration with UCL.

ZIKAction

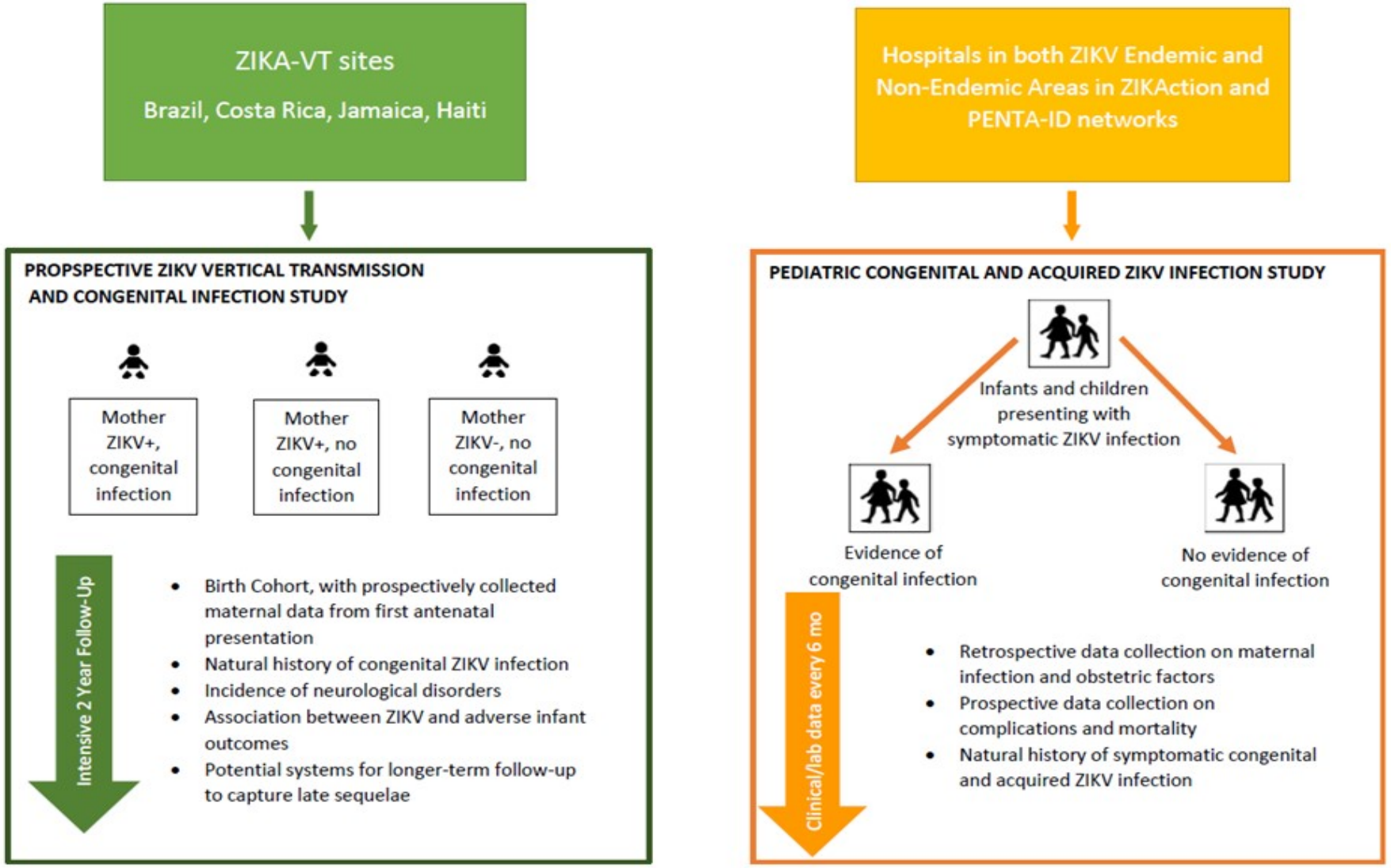
ZIKA-PED: development and implementation of congenital and acquired paediatric infection studies

Objectives

- To describe the clinical forms and the natural history of congenital ZIKV infection and postnatally acquired ZIKV infection in neonatal and paediatric populations
- To estimate the proportion of neonates born to ZIKV-infected mothers (with and without congenital ZIKV infection) presenting with neurological disorders (including developmental, ophthalmological, hearing problems), to describe these and to prospectively assess neurologic and developmental outcomes in the first two years of life
- To explore the feasibility of developing systems for longer-term follow-up of children with congenital ZIKV to allow future monitoring of late sequelae

ZIKAction

Schematic diagram of studies in ZIKA-PED



ZIKA-PED: development and implementation of congenital and acquired paediatric infection studies

Task 2.1 Development of web-based platform and data collection on paediatric ZIKV cases (M0-M6):

This task will be led by SERGAS in collaboration with ICS-HUVH.

Task 2.2 Training/education of all study personnel and quality control (M2-M54)

This task will be led by PENTA in collaboration with ICS-HUVH and SERGAS.

Task 2.3 Pediatric Clinical and Developmental Follow up: congenital infection birth cohort (M13-54)

This task will be led by ICS-HUVH in collaboration with UCL and all participating clinical centers.

Task 2.4 Pediatric Clinical and Developmental Follow up: symptomatic cohort (M13-54)

This task links to Task 1.4 in ZIKA-VT and will be led by ICS-HUVH in collaboration with UCL and all participating clinical centers.

Task 2.6 Statistical analysis (M1-M60)

This task is linked to ZIKA-SYN task Joint analysis plan, which is for the joint analysis plan for the data from all three EC-funded consortia for pooled analyses. This task will be led by UB in collaboration with UCL.

Task 2.7 Setting up systems for longer-term follow-up of children born to ZIKV-infected mothers (M54-60)

This task will be led by ICS-HUVH in collaboration with participating clinical sites.

ZIKAction

ZIKA-PATHO: development and implementation of pathogenesis and animal model studies

Objectives

- To assess and characterize the **susceptibility and receptivity of human placental explants to different strains of ZIKV.**
- To investigate the **role of ZIKV infection in the development of microcephaly and other fetal brain abnormalities, in a susceptible rodent model.**
- To understand if **severity of ZIKV infections can be caused or exacerbated by an antibody dependent enhancement (ADE) mechanism.**
- To study the **teratogenic and abort genic potential of ZIKV infections at different gestation times, in the sheep model.**

Italy: Istituto Zooprofilattico Sperimentale Delle Venezie (IZSVe)
USA: University of Florida

ZIKA-PATHO: development and implementation of pathogenesis and animal model studies

- **Task 3.1 Preparation of the documents for Ethics Committee submission (M1-M12)**

  This task will be led by IZSVeA and will link with ethics activities in ZIKA-COLLAB.

- **Task 3.2 Use of an *ex vivo* human placental culture for virus phenotyping** (M13-M24)

  This task will be led by IZSVe.

- **Task 3.3 Susceptibility and receptivity of human placental explants to different ZIKV strains (M13-M30)**

  This task will be led by IZSVe.

- **Task 3.4. Assessment of direct and indirect fetal injuries caused by the ZIKV infection in a rodent model (M13~~2~~-49)** *This task will be led by IZSVe.*

- **Task 3.5. Evaluation of an antibody dependent enhancement (ADE) of Zika infection *in vivo* model (M13~~2~~-30).** *This task will be led by IZSVe.*

- **Task 3.6 Development of a timed gestation model of Zika infection in sheep** (M01-36)

  This task will be led by UF.

ZIKAction

ZIKA-VID: Virology and Immunology studies, development and testing of diagnostic methodologies

Objectives

- To evaluate diagnostics for ZIKV infection in pregnancy and childhood.
- To determine **virological/immunological correlates of vertical transmission and protect.**
- To define the **virological/immunological characteristics of congenital ZIKV infection and how these differ in infants with and without congenital ZIKV disease.**
- To determine whether **virological/immunological characteristics of congenital ZIKV infection differ among infants presenting short-term sequelae and those who do not.**
- To describe the **natural history and virological characteristics of ZIKV infection in a cohort of male patients in relation to the potential for sexual transmission.**

ZIKAction

ZIKA-VID: Virology and Immunology studies, development and testing of diagnostic methodologies

- **Task 4.1 Evaluation of ZIKV diagnostics for pregnant women and children (M2-M54)**

  This task will be led by FIOCRUZ in collaboration with UCL and UB and contributions from all sites contributing data to either ZIKA-VT or ZIKA-PED.

- **Task 4.2 Virological/immunological correlates of vertical transmission and protection** (M13-M54)

  This task will be led by UCL in collaboration with FIOCRUZ.

- **Task 4.3 Virological/immunological profile by ZIKV infection status and presentation of symptoms** (M13-54)

  This task will be led by UCL in collaboration with FIOCRUZ.

ZIKAction

ZIKA-COORD: project management, scientific coordination, harmonization of data collection and sharing within the ZIKAction consortium

Objectives

- To provide scientific and operational oversight, coordination and monitoring in order to guarantee that the project is appropriately implemented according to the work plan and that clear, effective communications and quality principles are maintained throughout the project.
- To set up a ZIKAction specific project management structure that ensures efficient day-to-day operation of the project and full integration with shared governance structures outlined in ZIKA-COLLAB.
- To ensure accurate and timely financial, legal and contractual management.

ZIKAction

ZIKA-COORD: project management, scientific coordination, harmonization of data collection and sharing within the ZIKAction consortium

- **Task 5.1 Project Coordination** (M01-M60) **Subtask 5.1.1 Scientific and operational oversight.**

  This task will be led by PENTA in collaboration with SERGAS and contributions from CHUC, E.P.E. and ISCMSP.

- **Task 5.2 Day-to-day management** (M01-M60)

  This task will be led by PENTA in collaboration with UCL.

- **Task 5.3 Technical and financial reporting and administration** (**M01-M60)**

  This task will be led by PENTA.

- **Task 5.4 Contract and Legal Management** (M01-M60)

  This task will be led by PENTA.

- **Task 5.5 Data management** (M01-M60)(see also ZIKA-SYN)

  This task will be led by UCL and PENTA

- **Task 5.6 Quality Assurance** (M01-M60)

  This task will be led by PENTA with contribution from WP leaders.

ZIKAction

ZIKA-COLLAB: creating and maintaining management structures and communications activities shared with all EU funded ZIKV consortia and ensuring ethical and regulatory compliance

Objectives

The overall objective is to enhance the output of the respective EU funded Zika consortia through shared management structures and ethics and communications activities

- Create and maintain joint management and oversight structures
- Address ethical and information governance issues, ensuring ethical and safe care and treatment of animals and use of patient data and samples for research across and potentially outside of participating consortia
- Organizing integrated communications across consortia, including creation of Communications Oversight Board, planning of joint meetings, and organization of cross-consortia working groups to ensure clear, coherent messages that integrate all communication and dissemination activities

ZIKAction

ZIKA-COLLAB: creating and maintaining management structures and communications activities shared with all EU funded ZIKV consortia and ensuring ethical and regulatory compliance

Task 6.1: Setting-up common bodies for the global management of the scientific programmes
Joint Leadership: Xavier de Lamballerie (Inserm, ZIKAlliance), Federico Martinon Torres (SERGAS, ZIKAction), Annelies Wilder-Smith (primary lead, UmU, ZikaPlan)
Contributors ZIKAlliance: Inserm, IT
Contributors ZikaPlan: UmU, UOXF, FMER
Contributors ZikAction: PENTA, UCL, UWI, IZSVe, UF Start date: M1 End date: M60

Task 6.2: Managing ethical, regulatory and legal issues
Joint Leadership: Thomas Jaenisch (UKL-HD, ZIKAlliance), Francesca Rocchi (primary lead, PENTA, ZIKAction), Karl-Erik Renhorn (UmU, Zika PLAN)
Contributors ZIKAlliance: Inserm, EMC, UKL-HD, UKB, UOXF, CEA
Contributors ZikaPlan: UmU, LSHTM, FESP-UPE
Contributors ZikAction: PENTA, SERGAS, UWI, UF, UCL, IZSVe, ISCMSP, FIOCRUZ Start date: M1 End date: M60

Task 6.3: Organising integrated communication
Joint Leadership: Gail Carson (primary lead, UOXF, ZIKAlliance), Federico Martinon Torres (SERGAS, ZIKAction), Koren Wolman Tardy (FMER, Zika PLAN)
Contributors ZIKAlliance: Inserm, UOXF, IT
Contributors ZikaPlan: UmU, UOXF, FMER
Contributors ZikAction: PENTA, SERGAS, UCL, IZSVe, UF, ISCMSP, FIOCRUZ Start date: M1 End date: M60

Task 6.4: Organising Cross-Consortia working groups
Joint Leadership: Xavier de Lamballerie (Inserm, ZIKAlliance), Rebecca Lundin (primary lead, PENTA, ZIKAction), Annelies Wilder-Smith (UmU, ZikaPLAN)
Contributors ZIKAlliance: Inserm, UOXF, IT
Contributors ZikaPlan: UmU, UOXF, LSHTM
Contributors ZikAction: PENTA, SERGAS, UCL, IZSVe, UF, ISCMSP, FIOCRUZ Start date: M1 End date: M60

ZIKAction

ZIKA-SYN: harmonizing data and implementing data sharing infrastructure between all EU funded ZIKV consortia, creating roadmap for more extensive data sharing

7. Objectives of WP7 are:
   - 7.1. To harmonize the protocols and standardize the tools for data capture and data management
     - 7.1.1. Harmonization of protocols
     - 7.1.2. Standardization of data capture tools and data management
   - 7.2. To set up joint harmonized platforms for clinical research
     - 7.2.1. To set up a reciprocal clinical monitoring platform
     - 7.2.2. To set up a joint laboratory diagnostics EQA platform
     - 7.2.3. To set up a virtual joint biobanking platform
     - 7.2.4. Establishing principles of governance for the joint virtual biobanking platform
   - 7.3. To share data in real time in the collaborative environment of the three EC-funded consortia
     - 7.3.1. Establishing principles of data sharing
     - 7.3.2. Defining core datasets to be shared in real time, developing decentralized virtual data sharing platform
     - 7.3.3. Monitoring enrolment and accrual of patients across geography
     - 7.3.4. Joint analysis plan
   - 7.4. To prepare for sharing data with the scientific community and public health officials
     - 7.4.1. Developing the 'cahier des charges' / specifications for future data sharing
     - 7.4.2. Contribution to IPD meta-analysis based on pooled data sets
     - 7.4.3. Metadata cataloguing and publication

ZIKAction

ZIKA-SYN: harmonizing data and implementing data sharing infrastructure between all EU funded ZIKV consortia, creating roadmap for more extensive data sharing

Task 7.1: Harmonization of protocols and standardization of data capture tools

Joint Leadership: Thomas Jaenisch (UKL-HD, ZIKAlliance), Claire Thorne (primary lead, UCL, ZIKAction), Laura Rodrigues / Ricardo Ximenes (LSHTM/FESP-UPE, ZIKAplan);
Contributors ZIKAlliance: Inserm, UKL-HD, Fiocruz:, EMC-Suriname, UKB, LSHTM, FFM, FBAI, UOXF
Contributors ZikaPlan: UmU, LSHTM, UOXF, FESP-UPE
Contributors ZikAction: PENTA, UCL, UWI, SERGAS, UNIVBRIS, FIOCRUZ, UF, ISCMSP, HGCC, ICS-HUVH
Start date: M1 End date: M60

Task 7.2.: To set up joint harmonized platforms for clinical research

Joint Leadership: Thomas Jaenisch (primary lead, UKL-HD, ZIKAlliance), Claire Thorne (UCL, ZIKAction), Laura Rodrigues / Ricardo Ximenes (LSHTM/FESP-UPE, ZIKAplan);
Contributors ZIKAlliance : Inserm, UKL-HD, Fiocruz:, EMC, UKB, UOXF, FBAI, FFM
Contributors ZikaPlan: LSHTM, UOXF, FESP-UPE
Contributors ZikAction: PENTA, UCL, UWI, SERGAS, UNIVBRIS, FIOCRUZ, UF, ISCMSP, HGCC, JPG, ICS-HUVH, CHUC Start date: M1 End date: M60

ZIKAction

ZIKA-SYN: harmonizing data and implementing data sharing infrastructure between all EU funded ZIKV consortia, creating roadmap for more extensive data sharing

Task 7.3: To share data in real time within the collaborative environment of the three EU-funded consortia

Joint Leadership: Thomas Jaenisch (UKL-HD, ZIKAlliance), Claire Thorne (primary lead, UCL, ZIKAction), Laura Rodrigues / Ricardo Ximenes (LSHTM/FESP-UPE, ZIKAPlan);
Contributors ZIKAlliance: Inserm-FTA, UKL-HD, IPP, FIOCRUZ, FFM, EMC-Suriname, UOXF
Contributors ZikaPlan: UmU,LSHTM, UOXF, FESP-UPE
Contributors ZikAction: PENTA, UCL, UWI, SERGAS, JPG, UNIVBRIS, FIOCRUZ, UF, ISCMSP, HGCC, ICS-HUVH, CHUC
Start date: M1 End date: M60
¢

Task 7.4: To prepare for sharing data with the scientific community and public health officials

Joint Leadership: Thomas Jaenisch (primary lead, UKL-HD, ZIKAlliance), Claire Thorne (UCL, ZIKAction), Laura Rodrigues / Ricardo Ximenes (LSHTM/FESP-UPE, ZIKAPlan)
Contributors ZIKAlliance: UKL-HD, Inserm-FTA, LSHTM, USP, EMC-Suriname, FBAI, UOXF
Contributors ZikaPlan: UmU; LSHTM, UOXF, FESP-UPE
Contributors ZikAction: PENTA, UCL, UWI, SERGAS, JPG, UNIVBRIS, FIOCRUZ, UF, ISCMSP, HGCC, ICS-HUVH, CHUC
Start date: M1 End date: M60

ZIKAction

ZIKA-PREP: establishing a Latin American emerging infectious disease preparedness and response network common to all EU funded ZIKV consortia

Overall objective

- The overall objective is to prepare for the establishment of a Latin-American and Caribbean network for emerging infectious diseases (EID)preparedness and response equipped to support a rapid and coherent research response to the Zika outbreak in the short term, and to other vector-born and emerging infectious disease outbreaks in Latin America in the long-term**.**

Specific objectives

- To establish a regional network of excellence for research that shares knowledge, expertise and provides local support and training when and were needed in EID preparedness and response.
- To collaborate with regional and international networks to leverage synergies, share knowledge and identify and address regulatory bottlenecks in the field of EID preparedness and response.
- To leverage input and data from peer networks and research databases with the aim to speed up evidence generation and improve research efficiencies in EID preparedness and response.
- To develop a sustainability plan that will allow the network to continue beyond the funding period.

ZIKAction

Figure 6. ZIKA-PREP Member organizations and regional site locations

Coalition member organisations

- Pan American Health Organization (PAHO)
- WHO
- WHO Special Programme for Research and Training in Tropical Diseases (WHO-TDR)
- Global Research Collaboration for Infectious Disease Preparedness (GloPID-R)
- International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)
- EDCTP
- UK Public Health Rapid Response Team (RRT)
- Platform foR European Preparedness Against (Re-)emerging Epidemics (PREPARE)
- LSHTM
- MESH
- The Global Health Network

ZIKA-PREP: establishing a Latin American emerging infectious disease preparedness and response network common to all EU funded ZIKV consortia

Task 8.1: Creating core preparedness structures
Joint Leadership: Xavier de Lamballerie/Thomas Jaenisch (Inserm/UKL-HD, ZIKAlliance), Federico Martinon Torres (SERGAS, ZIKAction), Annelies Smith-Wilder (UmU, Zika PLAN), coordinated by Trudie Lang at UOXF
Contributors ZIKAlliance: Inserm, UKL-HD, FFM, Fiocruz, UOXF
Contributors ZikaPlan: UmU, LSHTM, UOXF, FUSP, Fiocruz,
Contributors ZikAction: SERGAS, UWI, HGCC, JPG, UF, CHUC, UOXF
Start date: M1 End date: M60

Task 8.2: Capacity building.
Joint Leadership: Xavier de Lamballerie/Thomas Jaenisch (Inserm/UKL-HD, ZIKAlliance), Federico Martinon Torres (SERGAS, ZIKAction), Trudie Lang (UOXF, Zika PLAN) and coordinated by Trudie Lang, UOXF
Contributors ZIKAlliance: Inserm, UKL-HD, FFM, Fiocruz, FBAI, UKB, EMC
Contributors ZikaPlan: UmU, LSHTM, UOXF, FUSP, Fiocruz,
Contributors ZikAction: SERGAS, UCL, UNIVBRIS UWI, HGCC, JPG, UF, CHUC, UOXF Start date: M1 End date: M60

Task 8.3: Set up a collaboration mechanism with other international networks (M01-60)
Joint Leadership: Xavier de Lamballerie/Thomas Jaenisch (Inserm/UKL-HD, ZIKAlliance), Federico Martinon Torres (SERGAS, ZIKAction), Koren Wolman-Tardy (FMER, ZikaPLAN) and Annelies Wilder-Smith (UmU, Zika PLAN) and coordinated by Trudie Lang, UOXF
Contributors ZIKAlliance: UKL-HD, Inserm, UOXF
Contributors ZikaPlan: FMER, UmU,, ECLAMC, Ulster
Contributors ZikAction: SERGAS, UOXF

Task 8.4: Develop and implement a sustainability strategy plan (M01-60)
Joint Leadership: Xavier de Lamballerie/Thomas Jaenisch (Inserm/UKL-HD, ZIKAlliance), Federico Martinon Torres (SERGAS, ZIKAction), Annelies Wilder-Smith (UmU, Zika PLAN) and coordinated by Annelies Wilder-Smith, UmU
Contributors ZIKAlliance: UKL-HD, Inserm, UOXF
Contributors ZikaPlan: UmU, UOXF
Contributors ZikAction: SERGAS

ZIKAction

European Commission

ZIKA-PREP: establishing a Latin American emerging infectious disease preparedness and response network common to all EU funded ZIKV consortia

REDe

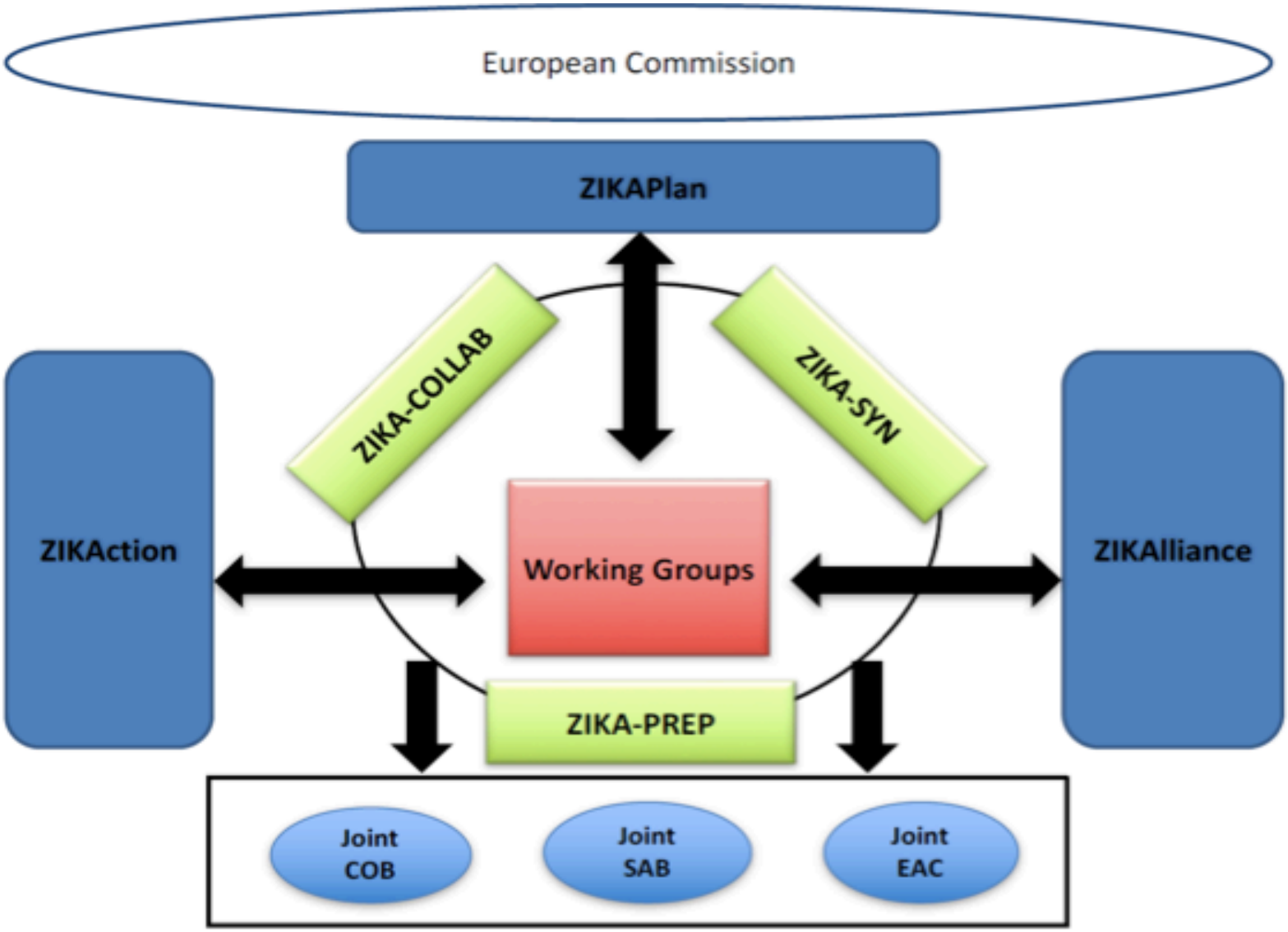
Research Capacity Network

THE PREPAREDNESS RESEARCH CAPACITY NETWORK FOR THE EU ZIKA CONSORTIA

https://rede.tghn.org/

ZIKAction

European Commission



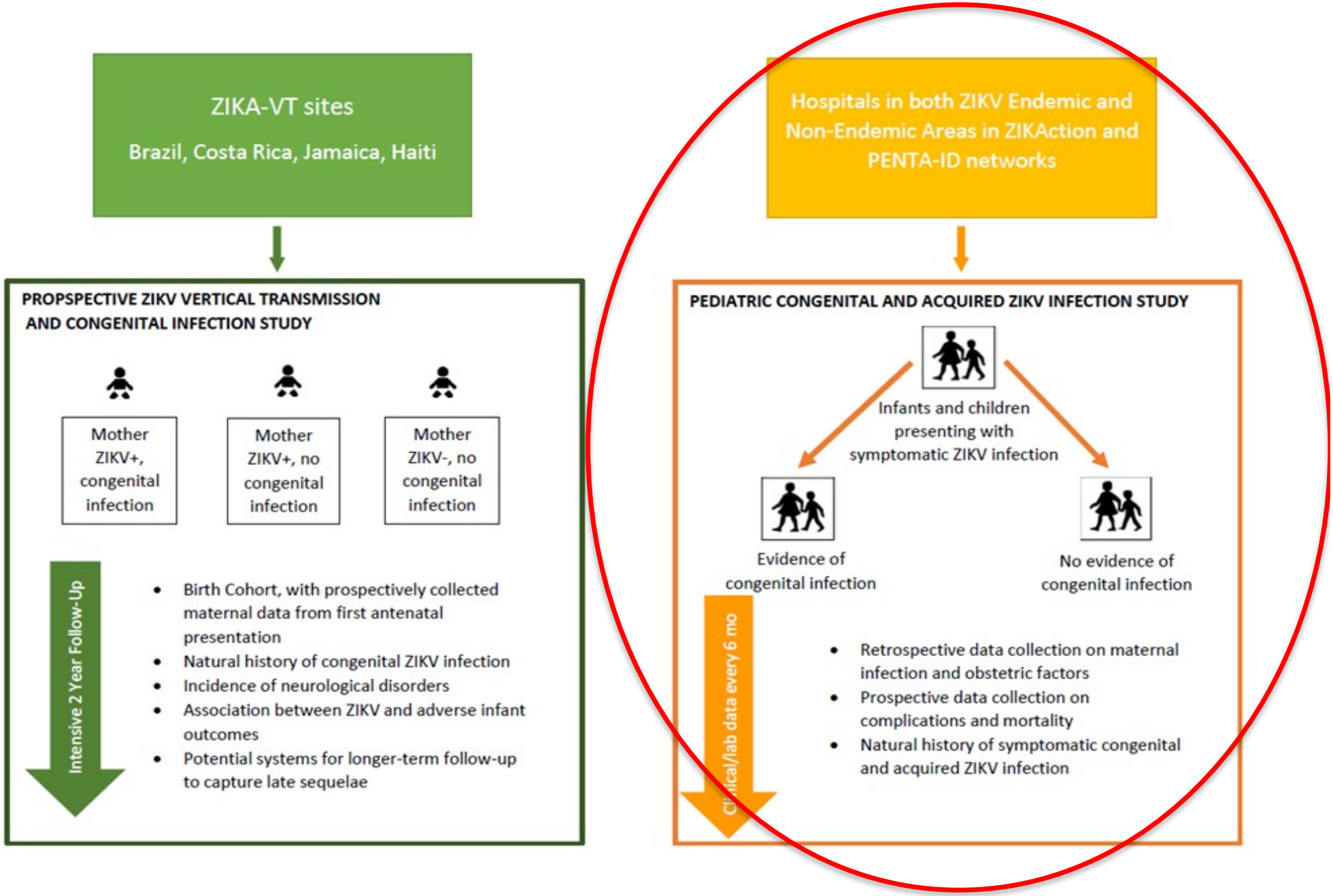
ZIKAction

Preparedness, research and action network on maternal-paediatric axis of ZIKV infection in Latin America and the Caribbean

ZIKA-PED Work Package

Antoni Soriano-Arandes
ZIKA-PED Work Package Co-Lead

Schematic diagram of studies in ZIKA-PED



ZIKA-PED Symptomatic Cohort Study

Task 2.4 Pediatric Clinical and Developmental Follow up: symptomatic cohort

- Neonates and children presenting with symptomatic ZIKV infection, either congenital or acquired, will be enrolled from ZIKAction sites… in a prospective observational cohort study to assess the natural history of infection among these children.
- **At enrolment, retrospective data** will be sought on birthdate, sex, geographic data (place of birth, residence, travel history), delivery details, mode of transmission (vectorial/congenital), date of diagnosis and test results, time of maternal ZIKV-infection if applicable, anthropometrics, clinical manifestations, and results of specific investigations (laboratory, neurological, radiological, ophthalmological, etc) to date.
- **From enrolment, data will be collected prospectively** with updated clinical and lab information sought at least every 6 months over the course of two years of follow-up, including neurological and non-neurological complications and other sequelae, and mortality.

ZIKA-PED Symptomatic Cohort Enrollment Feasibility

1. **Could we screen consecutive children at first presentation** (not referral!) **with rash and fever at your center with the aim to enroll confirmed ZIKV PCR+?** Up to what age?
2. **What is standard of care (SoC) for children presenting to hospital services with rash?**
   a. Any protocol? Not only for ZIKV, also for other arboviruses.
   b. Which serology/PCR tests (if any) are carried out, and for which infections (ZIKV/DENV/CHIKV, other?
   c. In case of neurological complications, what would the protocol be?
3. **What kind of follow up data would be available for these children?**
   – Is there a long term SoC for these particular cases? Any protocols or exams to be conducted at these visits?
4. **Are ZIKV infection or other arboviruses such as dengue notifiable conditions in your country?** If yes, **what is/are the reporting definition(s)?**
5. **Could you provide us with an update of the current epidemiology of ZIKA in your hospital (or region)?**

ZIKA-PED Feasibility Follow-up Questions

1. **ZIKV, CHIKV and DENV infection are notifiable diseases**
    1. Are all symptomatic cases reported?
    2. If so, which case definitions are used?
    3. If not, how are cases reported?
2. **Are serology and PCR for ZIKV, CHIKV and DENV carried out on all children who present with symptoms of ZIKV/DENV/CHIKV infection?**
    1. Are these analyses carried out locally, or do children need to present to your referral center?
    2. Exactly which tests are conducted?
    3. Are results sent along with notification of disease in central registry?
3. **Would telephone follow-up every 6 months (up to 24 months of follow up) with primary care physician or family be possible?**

ZIKA-PED Sites

Country	Clinic or hospital site
Argentina	Hospital de Pediatria Samic Prof. Dr. Juan P. Garrahan
Brazil	Santa Casa Hospital, São Paulo
Brazil	Cesar Cals Hospital, Fortaleza
Cape Verde	Hospital Dr. Agostinho Neto
Costa Rica	Hospital Nacional de Nino
Haiti	Haiti Health Ministries, Gressier
Haiti	Baraderes Health Clinic
Haiti	Gressier Health Clinic
Jamaica	University Hospital of the West Indies, Kingston
Jamaica	Victoria Jubilee Maternity Hospital, Kingston
Jamaica	Spanish Town Hospital, Kingston

Celia Christie-Samuels

Toni Soriano

Marco Safadi

Marinella della Negra

ZIKA-PED Symptomatic cohort: case definition

- **CDC (USA)** (June 2016): >1 of the following: acute onset of fever, maculopapular rash, arthralgia, and conjunctivitis.
- **WHO** (Feb 2016): RASH OR FEVER + >1 of the following: arthralgia or arthritis, or conjunctivitis (nonpurulent/hyperemic).
- **PAHO** (April 2016): RASH + >2 of the following: fever, conjunctivitis (nonpurulent/hyperemic), arthralgia, myalgia, or periarticular edema.
- **ECDC** (March 2016): RASH WITH OR WITHOUT FEVER + >1 of the following: arthralgia, myalgia, or conjunctivitis (nonpurulent/hyperemic).
- **MoH Singapore** (Aug 2016): FEVER + RASH + >1 of the following: headache, myalgia, arthralgia, or nonpurulent conjunctivitis.

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ZIKA-PED Symptomatic cohort: case definition

- **CDC (USA)** (June 2016): >1 of the following: acute onset of fever, maculopapular rash, arthralgia, and conjunctivitis.
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ZIKA-PED Symptomatic cohort

Table 1. Clinical characteristics of an adult cohort with suspected Zika virus disease, Singapore, August 26–September 5, 2016*

Characteristic	Zika virus positive, n = 149	Zika virus negative, n = 210
Demographic data		
Mean age, y (SD)	38.1 (14.2)	34.2 (12.1)
Sex		
M	92 (61.7)	129 (61.4)
F	57 (38.3)	81 (38.6)
Ethnicity		
Chinese	109 (73.2)	122 (58.1)
Malay	15 (10.1)	17 (8.1)
Indian	9 (6.0)	24 (11.4)
Other	16 (10.7)	47 (22.4)
Singapore residents	113 (75.8)	131 (62.4)
Signs and symptoms at presentation		
Rash	139 (93.3)	94 (44.8)
Fever	118 (79.2)	181 (86.2)
Myalgia	63 (42.3)	124 (59.1)
Headache	35 (23.5)	75 (35.7)
Conjunctivitis	35 (23.5)	32 (15.2)
Arthralgia	34 (22.8)	50 (23.8)
Pruritis	17 (11.4)	17 (8.1)
Any gastrointestinal symptom†	10 (6.7)	25 (11.9)
Fulfilled case definition		
United States‡	149 (100.0)	206 (98.1)
World Health Organization§	57 (38.3)	64 (30.5)
PAHO¶	73 (49.0)	50 (23.8)
ECDC#	83 (55.7)	55 (26.2)
Singapore Ministry of Health**	81 (54.4)	51 (24.3)

ZIKA-PED Symptomatic cohort

Table 2. Performance of case definitions for diagnosing Zika virus infection in a human cohort during an outbreak, Singapore, August 26–September 5, 2016*

Case definition	Sensitivity, %	Specificity, %	PPV, %	NPV, %	LR+ (95% CI)	LR– (95% CI)
United States	100	2	42	100	1.02 (1.00–1.04)	0
WHO	38	70	47	61	1.3 (0.9–1.7)	0.9 (0.8–1.0)
PAHO	49	76	59	68	2.1 (1.5–2.8)	0.7 (0.6–0.8)
ECDC	56	74	60	70	2.1 (1.6–2.8)	0.6 (0.5–0.7)
Singapore MOH	54	76	61	70	2.2 (1.7–3.0)	0.6 (0.5–0.7)

*ECDC, European Centre for Disease Prevention and Control; LR, likelihood ratio; MOH, Ministry of Health; NPV, negative predictive value; PAHO, Pan American Health Organization; PPV, positive predictive value; WHO, World Health Organization; +, positive; –, negative.

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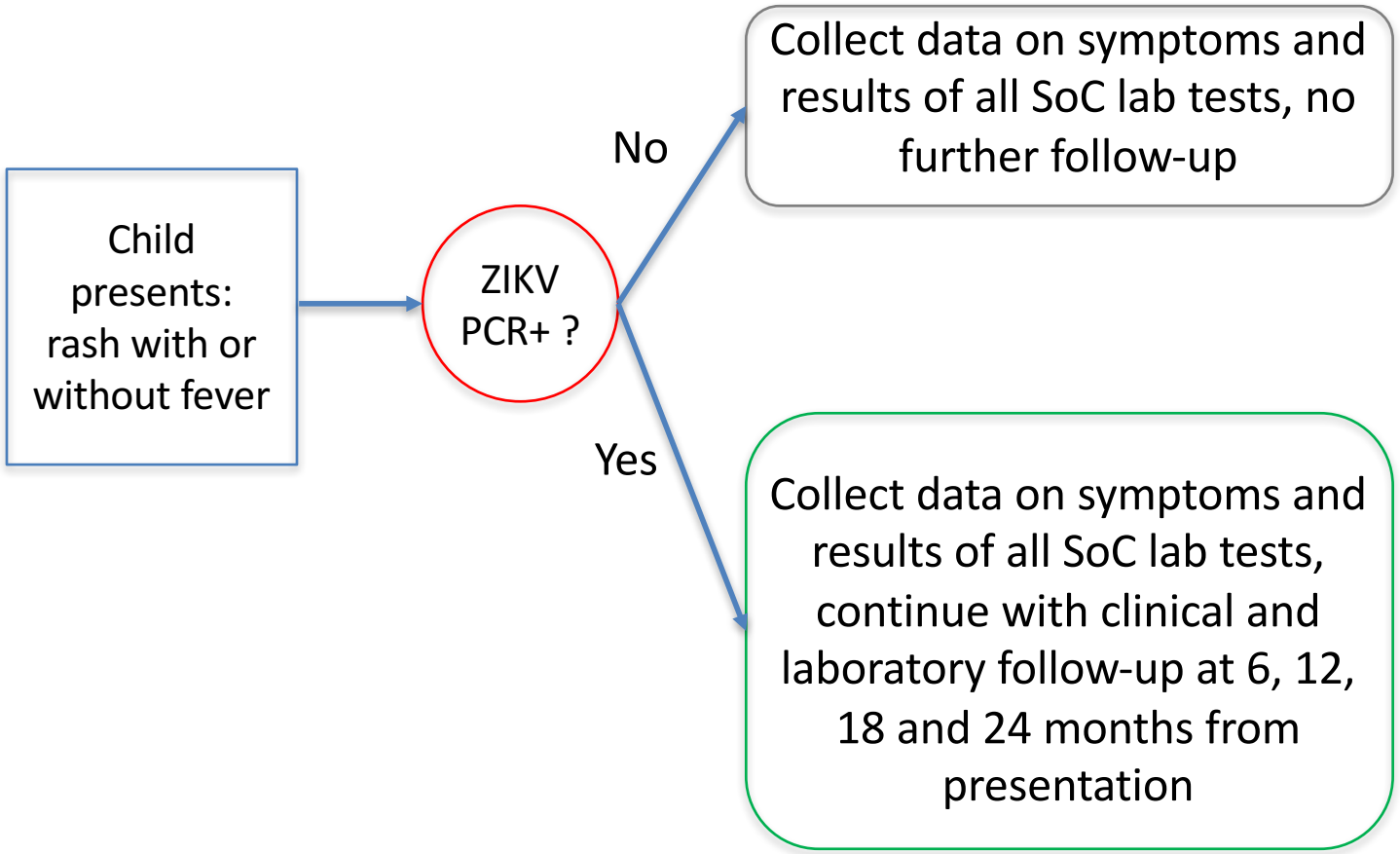
ZIKA-PED Symptomatic cohort



ZIKAction: Preparedness, research and action network on maternal-paediatric axis of ZIKV infection in Latin America and the Caribbean

Project Management

Tiziana Grossele,
ZIKAction Project Manager

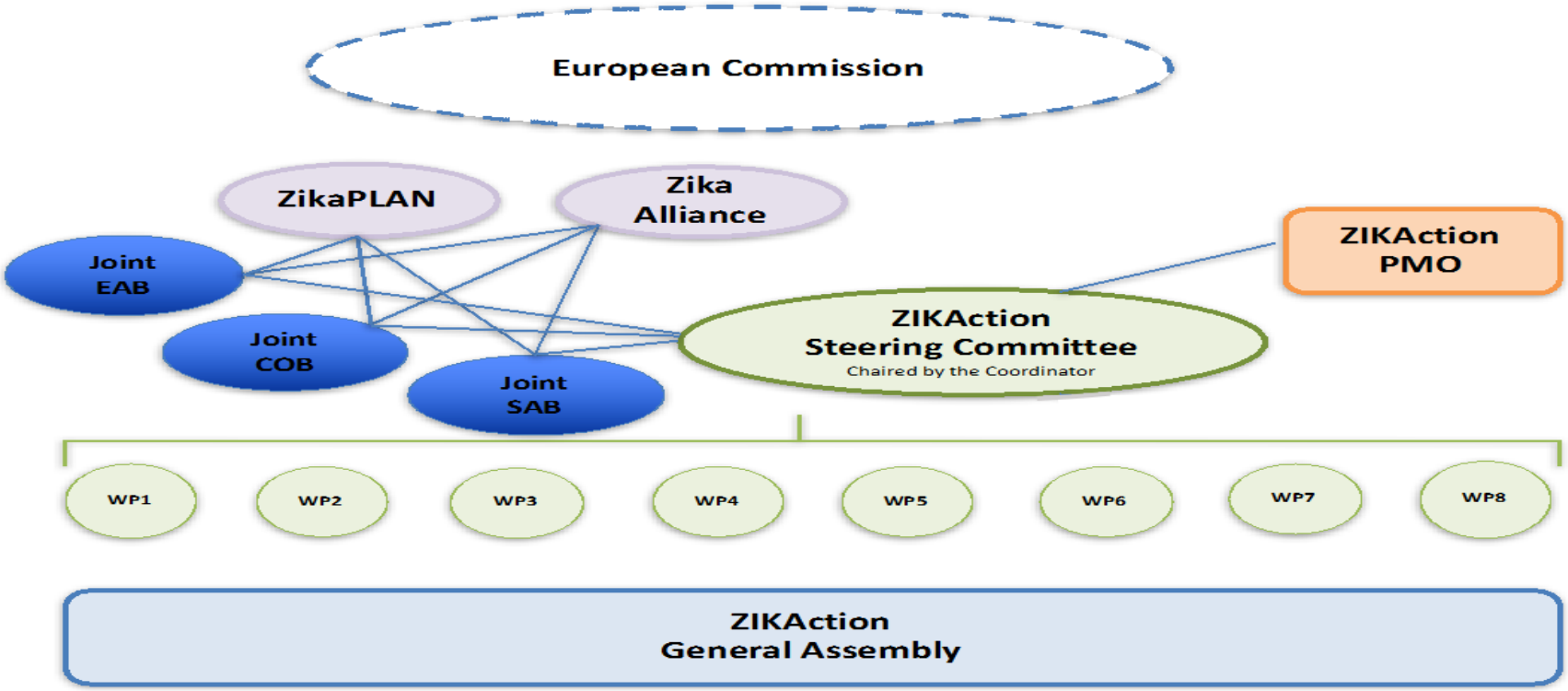
Project beneficiaries

PARTICIPANT NUMBER	BENEFICIARY NAME	BENEFICIARY SHORT NAME	COUNTRY
1	Fondazione PENTA ONLUS	PENTA	Italy
2	University College London	UCL	UK
3	Servizo Galego de Saude - Hospital Clínico Universitario de Santiago de Compostela	SERGAS	Spain
4	The University of the West Indies	UWI	Jamaica
5	Istituto Zooprofilattico Sperimentale delle Venezie	IZSVe	Italy
6	Hospital de Pediatría Samic Prof. Dr. Juan P. Garrahan	JPG	Argentina
7	University of Bristol	UB	UK
8	Fundaçao Osvaldo Cruz	FIOCRUZ	Brazil
9	Emerging Pathogens Institute (EPI), Department of Infectious Diseases and Pathology, College of Veterinary Medicine, University of Florida	UF	US
10	Irmandade da Santa Casa de Misericórdia de São Paulo	ISCMSP	Brazil
11	Secretaria de Saude (Hospital Geral Dr. César Cals)	SDS(HGCC)	Brazil
12	Institut Català de la Salut – Hospital Universitari Vall d'Hebron	ICS-HUVH	Spain
13	Centro Hospitalar e Universitario de Coimbra E.P.E.	CHUC, E.P.E.	Portugal
14	University of Oxford	UOXF	UK

Project key elements

- ✓ **Funding:** European Union H2020 RIA
- ✓ **Project number:** 734857
- ✓ **Coordinator:** PENTA Foundation
- ✓ **Partners:** 14 including PENTA, plus 5 third parties
- ✓ **Duration:** 5 years (October 1st 2016 - September 30th 2021)
- ✓ **Budget:** € 6,916,081.25 million
- ✓ **Collaborating consortia**: ZiKAction+ZikAlliance+ZikaPlan

Governance structure



Work Packages and beneficiaries involvement

		WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	Person months
		ZIKA-VT	ZIKA-PED	ZIKA-PATHO	ZIKA-VID	ZIKA-COORD	ZIKA-COLLAB	ZIKA-SYN	ZIKA-PREP	Ethics - PENTA	
1	PENTA	8,0	18,2	0,0	0,0	43,8	15,0	6,0	0,0	0,0	91,0
2	UCL	25,0	10,0	0,0	19,0	6,0	9,5	11,0	3,0	0,0	83,5
3	SERGAS	0,0	9,5	0,0	0,0	21,9	36,1	3,0	8,0	0,0	78,5
4	UWI	36,5	0,0	0,0	1,0	4,0	8,5	6,0	10,0	0,0	66,0
5	IZSVe	0,0	0,0	45,0	0,0	0,0	5,5	0,0	0,0	0,0	50,5
6	JPG	0,0	13,0	0,0	1,0	0,0	0,0	2,0	3,0	0,0	19,0
7	UB	23,1	22,4	0,0	3,0	0,0	0,0	2,0	2,0	0,0	52,5
8	FIOCRUZ	0,0	0,0	0,0	29,0	0,0	7,5	12,0	0,0	0,0	48,5
9	UF	45,5	0,0	51,2	1,0	0,0	6,5	10,0	3,0	0,0	117,2
10	ISCMSP	15,0	18,0	0,0	1,0	11,0	8,0	9,2	0,0	0,0	62,2
11	SDS (HGCC)	21,5	0,0	0,0	1,0	0,0	0,0	4,0	3,0	0,0	29,5
12	ICS-HUCH	0,0	26,0	0,0	1,0	11,7	0,0	4,0	0,0	0,0	42,7
13	CHUC	0,0	26,0	0,0	0,0	0,0	0,0	7,0	7,5	0,0	40,5
14	UOXF	0,0	0,0	0,0	0,0	0,0	0,0	0,0	20,0	0,0	20,0
	Total	174,64	142,07	96,20	58,00	101,39	96,60	75,20	57,50	0,00	801,6

Involvement of Coimbra in the ZikAction Tasks

- **WP 2 – ZIKA-PED, Coimbra with with 25 person months**
- Task 2.3 Pediatric Cohort and Developmental Follow Up: congenital infection birth cohort(M13-M54)
- Task 2.4 Pediatric Clinical and Development Follow-up: symptomatic cohort (M13-M54)

- **WP7 – ZIKA-SYN, Coimbra with 7 person months**
- Task 7.4: To prepare for sharing data with the scientific community and public health officials (M1-M60)

- **WP8 – ZIKA-PREP, Coimbra with 7,5 p erson months**
- Task 8.2: Capacity building (M1-M60)
- Task 8.3: Set up a collaboration mechanism with other international networks (M1-M60)
- Task 8.4: Develop and implement a sustainability strategy (M1-M60)

Deliverables ZIKA-PED WP until March 2018

- D2.1: ZikAction unique ZIKA-PED Stat Analysis Plan
  Due 30/06/2017

- D2.2: ZikA-PED First Study subject approval package
  Due 30/09/2017

- D2.3: ZIKA-PED All Approvals Package Due 31/03/2018

Deliverables ZIKA-SYN WP until March 2018

- D7.1: Harmonized protocol on pregnant women Submitted 31/01/2017
- D7.2: Joint data sharing and virtual biobanking agreement Due 30/06/2017
- D7.3: Final Joint Analysis Plan Due 31/03/2018

Deliverables ZIKA-PREP WP until March 2018

- D8.1: Strategic Plan and governance structure for single preparedness network Submitted 29/03/2017
- D8.2: Open Access Zika Community platform Due 30/09/2017
- D8.3: Regional centres and capacity development Due 31/03/2018

Budget

Cost category	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	Total
Direct personnel costs	780.430	480.835	405.917	354.283	513.443	400.894	315.267	306.081	**3.557.150**
Other direct costs	982.819	280.000	148.140	120.000	439.500	48.000	0	0	**2.018.459**
Total Direct budgeted costs	1.763.249	760.835	554.057	474.283	952.943	448.894	315.267	306.081	**5.575.609**
Total Indirect costs	398.196	154.398	138.514	118.571	238.236	112.223	78.817	76.520	**1.315.475**
Subcontracting	0	0	0	0	10.000	0	0	15.000	**25.000**
Third party costs	170.465	143.243	0	0	0	0	0	0	**313.708**
Total budgeted costs	2.161.444	915.233	692.572	592.853	1.201.179	561.117	394.084	397.601	**6.916.084**
Total EC contribution	**2.161.444 €**	**915.233 €**	**692.572 €**	**592.853 €**	**1.201.179 €**	**561.117 €**	**394.084 €**	**397.601 €**	**6.916.084 €**

Coimbra overall budget

Cost category	WP2	WP7	WP8	Total
Direct personnel costs	60.390	49.060	50.645	160.095
Other direct costs	77.500	0	0	77.500
Total Direct budgeted costs	137.890	49.060	50.645	371.196
Total Indirect costs	19.472,50	12.265	12.661,25	44.399
Subcontracting	0	0	0	0
Third party costs	60.000*	0	0	0
Total budgeted costs	157.363	61.325	63.306	281.994
Total EC contribution	€ 157.363	€ 61.325	€ 63.306	€ 281.994

Coimbra other direct costs in the project

Other costs	**Cost**	**Justification**
Travel	12.500	Travel costs(1 travel/year, 1 person)
Other goods and services	30.000	Lab materials (PCR reagents)
	30.000	Test analysis (PCR real time for 150 tests)
	5.000	Publication fees
Total	77.500	

Direct and indirect costs

- **Direct costs** = all eligible costs
- Cost categories
  - Personnel costs (PIs, researchers, lab tecnicians, etc)
  - Other costs (travel, subsistance, lab materials, sequencers, DNA sequencing, serology, CFS, publication fees, Ethics fees)
  - Subcontracting costs (externalized activities)

- **Indirect costs** = covered by a uniform 25% flat-rate of each beneficiary eligible direct costs.

Timesheets

- **Written recording** of personnel time working in the project;
- Hours claimed must be verifiable;
- Time must be recorded on **daily basis** since the first day
- A reference to task, WP and type of activity must be mentioned
- Timesheets must be **reconciliable** with absence for holydays, illness, travel, etc

Reports to the European Commission

- Reporting periods both scientific and administrative
  M1-M18 M19-M36 M37-M48 M49-M60
- Only **eligible costs** can be claimed to the European Commission
- Costs must be claimed in **euros**
- **Personnel costs** are eligible, if they are related to personnel working for the beneficiary under an employment contract (or equivalent appointing act) and assigned to the action ('**costs for employees (or equivalent**)'). They must be limited to salaries (including during parental leave), social security contributions, taxes and other costs included in the **remuneration**, if they arise from national law or the employment contract (or equivalent appointing act).
- Only the **depreciation cost of equipment** can be claimed per every reporting period.
- All the costs statements will be evaluated and **approved by the coordinator** before the bebeficiaries submit them to the European Commission.
- All the costs statements are submitted through the Participant Portal.

European Commission funding instalments

- **Pre-financing payment** up to 100 % of the average EU funding per period MINUS **5 %** of the maximum grant amount *(see Article 5.1)* for **Guarantee Fund**. 30 days after signing the GA

- **Interim payments** calculated by the Commission/Agency (on the basis of the costs declared in the financial statement) up to 90% of the maximum grant amount. After approving the periodic report.

- **Final payment** at the end of the project

Reference documents

- Grant Agreement plus its annexes
- Consortium Agreement
- Project Handbook
- ZikAction Website www.zikaction.org
- Twitter account @ZikAction

ZIKAction

European Commission

Thank you

Obrigado