



Penta

Child Health Research



Annual Report **2019**



Letter from the President



What happened in 2019? This was a **key year** for us as we further developed the Penta strategic plan, the strategic plans for each scientific content area and platform and held our bi-annual Penta Investigator's Meeting. As we move forward, we are keen to support the Penta network in developing opportunities for collaboration and allowing a greater role for younger mid-career professionals.

We haven't just made strides forward in terms of our strategic direction; we have also made great progress in our strategic clinical trials. We have exceeded our recruitment target in the SMILE study by recruiting 318 patients, closed recruitment in the NeoVanc project with 240 patients enrolled for the study as well as achieved our recruitment target of 150 patients for the EARTH study.

We have also completed the PED-MERMAIDS study, part of the PREPARE EU funded project, whereby we reached a total 847 patients. This study has **been pivotal in contributing to the standardized data on clinical characteristics, management and outcome of children hospitalized for acute respiratory infections and Antibiotic Resistant Infections and sepsis** in Europe. These data are the basis to draft standardized protocols for the management of these infections in the paediatric field and will form an incredibly informative pre COVID-19 baseline comparison.

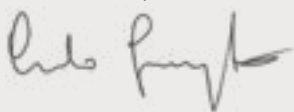
As this annual report goes to press, **we are in the midst of a global pandemic of COVID-19** – caused by a previously unknown coronavirus SARS-CoV-2. We will soon be in a position to share our portfolio of research studies and we invite you all to contribute, collaborate and work with us to transform the prevention and treatment of infection in children.

We would like to acknowledge the **dedicated work of our network of collaborators**, the trust of our strategic partners, the commitment from our staff and the financial and operational resources made available by those who believe in our mission.

Our **true strength lies within the Penta family** – the invaluable commitment and enthusiasm of the youngest investigators and the Foundation staff.

Finally, **a special thanks to all the children and families** who have contributed to our activities and studies. We are working for them, but without them nothing is possible!

Carlo Giaquinto

A handwritten signature in dark ink, appearing to read 'Carlo Giaquinto', with a stylized, flowing script.

1. ABOUT US





We are a **global
independent
scientific network**
dedicated to
paediatric
research

Our vision

**A world where all children
with infection get the
treatment they need**




Our mission

**To be a leading global
research partnership
working to transform the
prevention and treatment
of infection in children**



What makes us unique


One network
One vision
One voice



Our network of collaborators and investigators share our vision. We are all convinced of the power of our partnership and are serious about changing prevention and treatment options for children with infection everywhere – for good.

Our values


Sharing,
understanding
and belonging



We encourage and support the sharing and exchange of ideas, innovations, data and proposals within the network, and we value every contribution.

Our guiding principles

Inclusion, team
spirit, responsibility,
transparency



As an international collaborative platform coordinating and undertaking research designed to improve child health and combat infections – we include and respect investigators throughout our network. Making space for all those passionate about our mission is something we pride ourselves on - we seek to create a genuine platform for teams to build a body of research that counts for children's wellbeing.

Penta's history

Penta is an alliance of
people united by
a common vision



1. ABOUT US

The Paediatric European Network for Treatment of AIDS (PENTA) was **established in 1991** as a collaboration between paediatric HIV centres in Europe. The primary aim of the Network was to undertake independent clinical trials to address specific questions about antiretroviral therapies in HIV infected children.

Funding from the European Union, international organizations such as UNICEF and the World Health Organization, the pharmaceutical industry, the UK's Medical Research Council (MRC), France's INSERM and Italy's Istituto Superiore di Sanità (the research branch of the Ministry of Health) helped Penta investigators answer critical issues in HIV care.

Over time, as the network started to grow beyond just HIV, clinical trials and observational studies, Penta became an ideal platform to **generate, develop and support research and training activities** – thus the Penta Foundation was born.

Recognising that other infections in children were similarly neglected, in 2011 **Penta evolved into Penta ID (Infectious Diseases)**, extending its research (both clinical and basic) to other paediatric infectious diseases. With the growing threat of antimicrobial resistance – Penta has since built an **ambitious and unique agenda** to tackle this, developing prevention and treatment strategies for children and newborns.

1991

Penta
Paediatric
European
Network for
Treatment of
AIDS

2004

**Penta
Foundation**

2011

Penta ID
Extension of
network
to address
other
Infectious
Diseases

2016

**Penta ID
Innovation**
A for profit
spin-off

2019

Penta UK
Our UK
based
charity

Our key partners

Penta's diverse range of activities is only made possible through our long-standing collaboration with 3 leading Clinical trials centres MRC CTU at UCL (UK), INSERM (France) and PHPT (Thailand)



We have entered into a number of framework collaboration agreements with other organizations that help us deliver our vision. In Italy our key partners are **Padua Hospital (Azienda Ospedaliera di Padova)**, **Ospedale Pediatrico Bambino Gesù (OPBG)** in Rome and the not-for-profit research organization **Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF)**.

In Africa, we have a growing group of investigators and signed a Memorandum of Understanding with our longstanding collaborator,

Joint Clinical Research Centre (JCRC) in Uganda. We are working with **Doctors with Africa CUAMM**, a Non-Governmental Organization, to collaborate on projects to protect and improve the wellbeing and health of vulnerable communities in Sub-Saharan Africa. This includes the training of local researchers and doctors, the development of policies, information systems and organizational models concerned with child healthcare, infectious diseases (HIV/TB/Malaria), nutrition and chronic non-transmissible diseases.

We intend to continue to grow and develop new collaborations to further our research and educational programmes.

We have also set up a partnership with the **Global Accelerator of Paediatric Formulation (GAP-f)**, an innovative collaborative model that will accelerate availability of optimized treatment options for infectious diseases, such as HIV, tuberculosis and viral hepatitis, affecting children in low – and middle – income countries. Another key partner for us is **Global Antibiotic Research & Development Partnership (GARDP)**, who Penta is working with to tackle serious and drug-resistant infections in children by accelerating development of antibiotic treatments including: clinical trials designed to meet regulatory requirements, and trials with a focus on public health interventions to inform treatment guidelines.

We continue to be involved at the regulatory level as a member of the **European Network of Paediatric Research at the European Medical Agency (Enpr-EMA)**. Penta is also part of the **WHO's Paediatric Antiretroval Working Group (PAWG)** and **Paediatric Antiretroviral Drug Optimization (PADO)**.

Finally, we have teamed up with **Virology Education**, an established educational

platform that works with us in the implementation of targeted training programmes.

Penta and the **Centre for Clinical Epidemiology and Outcome Research (CLEO)**, opened a shared working space in Athens, Greece in 2018. This collaboration has led to the joint working on RANIN-KIDS (Reducing Antimicrobial use and Nosocomial Infections in KIDS: A European Network), which CLEO is coordinating and Penta is providing scientific and management support. This is expected to lead to many more exciting collaborations in the future.

A **real marker of Penta's success in the developing collaborations has been its work on EPPICC**, an international network of cohort studies. EPPICC began as part of EuroCoord, and grew into an international network coordinated by Penta, carrying out epidemiological research on HIV-infected pregnant women, children and children exposed to HIV in utero.

We intend to **continue to grow and develop new collaborations** to further our research and educational programmes.

Future collaboration

MUJHU Makerere University John Hopkins University Research Collaboration

Established in 1922, Makerere University is one of the oldest and most prestigious English Universities in Africa. It currently acts as an enrolling site for clinical trials focused on HIV and paediatric pneumonia. The upcoming collaboration between Penta and MUJHU aims not only to ensure the delivery of the best care to sub-Saharan African children, but also to engage a younger generation of paediatricians and scientists who could become future leaders in paediatric trials.

www.mujuhu.org

www.ctu.mrc.ac.uk

www.inserm.fr

www.phpt.org

www.aopd.veneto.it

www.ospedalebambinogesu.it

www.cvbfn.net

www.jcrg.org.ug

www.gap-f.org

www.ema.europa.eu

www.cleoresearch.org/en

www.gardp.org

www.doctorswithafrica.org

www.virology-education.com

2019 at a glance

TOTAL FUNDS MANAGED BY THE
FOUNDATION

13.4 M Euros

TR@INFORPEDHIV
COURSES

WITH OVER
8 500
HEALTHCARE
WORKERS TRAINED
IN **8** COUNTRIES

13 PENTA IS
THE COORDINATOR
5
8 PENTA IS
A PARTNER

EU FUNDED
ONGOING PROJECTS

PENTA FOUNDATION
STAFF

31

PENTA STUDY COMPLETED

1 PED-MERMAIDS
COORDINATED BY PENTA AND
PART OF THE PREPARE PROJECT,
RECRUITED A TOTAL OF
847 PATIENTS

STUDIES CONCLUDED ENROLMENT

- 3**
- **SMILE**, a clinical trial to evaluate the safety and antiviral effect of a single daily integrase inhibitor given with Darunavir/Ritonavir compared to the standard treatment among HIV-1 infected, virologically suppressed paediatric patients, exceeded its recruitment target by recruiting 318 patients.
 - **NEOVANC** recruited 240 patients. This study's aim is to develop an optimal dosing and monitoring regimen for vancomycin use in preterm neonates and infants under 3 months of age.
 - The **EARTH** study, part of the EPIICAL project, reached its goal of enrolling 150 children across 5 sites in South Africa and Mozambique. The EARTH study has the primary aim to identify potential participants in proof-of-concept trials directed towards a HIV cure, and to look at clinical, virological and immunological features of early treated children in limited-resource settings.

Since we started



OVER

1000

CLINICIANS, RESEARCHERS,
SCIENTISTS



MORE THAN

110 31

ENROLLING SITES IN COUNTRIES



OVER

120

PEER-REVIEWED
SCIENTIFIC ARTICLES



35 9 26

STUDIES

ONGOING

COMPLETED



MORE THAN

50000

WOMEN AND
CHILDREN ENROLLED
IN OUR STUDIES
(SINCE 2012)



EU FUNDED PROJECTS

24

9 PENTA IS
THE COORDINATOR
15 PENTA IS
A PARTNER



**“Doctor, thanks to your team
for taking care of my child.
We left Hoima district with no
hope, until we reached Baylor
and met the ODYSSEY team who
have taken good care of my son”**





*Dr Pauline Amuge,
Research Coordinator
Baylor College of Medicine Children's
Foundation-Uganda (Baylor-Uganda)
Trial Manager- ODYSSEY (PENTA 20)
Site PI- SMILE (PENTA 17)
Co-investigator-BREATHER Plus
Co-investigator-D3 trial*

It's a worthwhile journey, and I encourage young investigators to connect with Penta and be part of the lives of thousands of children's lives.

As soon as I completed my residency in paediatrics and child health, I received an opportunity to join Baylor-Uganda. My passion to enable children achieve their full life potential, especially those living with HIV, was nurtured while I worked as the ODYSSEY trial manager with a passionate site Principal Investigator, Dr Adeodata and Chief Investigators-Di Gibb and Pablo Rojo. Knowing that results from the ODYSSEY trial would make dolutegravir a once-daily safe drug available as a dispersible tablet for children as small as 3kg, made me walk daily into the clinic with great hope for the future of our African children living with HIV.

Penta's strength lies in giving young people opportunity. During my first Penta investigators' Meeting in Venice, I experienced the collaborative Penta family which revealed opportunities for growth of young investigators.

Sooner than I expected, I grew to site principal investigator of the SMILE trial at Baylor-Uganda; a role that I quickly stepped into having the robust support from Penta, INSERM and MRC CTU at UCL. There's continuous learning and growth while positively impacting the future of our children. Recently, Penta introduced me to a new horizon of research training and capacity building for a new research proposal which aims to make a fixed dose combination of dolutegravir based Fixed Dose Combination (FDC) and a fixed dose combination of darunavir and ritonavir FDCs readily available in WHO dosing weight bands.

It's a worthwhile journey, and I encourage young investigators to connect with Penta and be part of the lives of thousands of children's lives.



2.

HOW WE OPERATE / ORGANIZATIONAL STRUCTURE





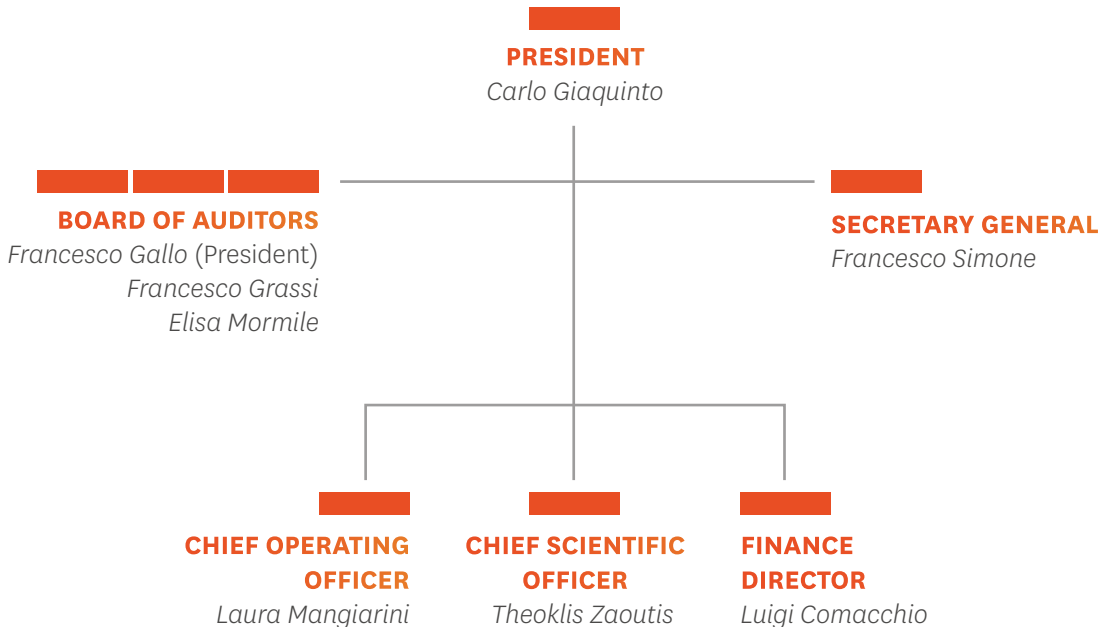
The flexible,
multidimensional,
Penta environment

Penta Foundation board

Members of the Board

The Foundation is managed by a Board of Directors consisting of no less than three and no more than eight members, who hold office for three years.

Penta Board Members:
 Carlo Giaquinto (*Chair*)
 Diana Gibb (*Vice Chair*)
 Mike Sharland (*Vice Chair*)
 Paolo Rossi
 Claire Thorne
 Franco Zacchello



Penta Foundation staff

A wide range of personnel coming from 11 different countries based in 4 cities (Padova, Rome, London and Athens) is dedicated to the activities of the Penta Foundation. We are ready to meet the needs of our future projects and challenges.

As of 2019, we have 31 core staff members, while other external consultants have been added to cover project specific activities.



Penta Foundation operational areas

Grant and project management

The Penta Foundation provides project management activities, from proposal submission to project end, as well as overall administrative and legal support to new grant applications and to project implementation throughout the project life cycle, including application and coordination of large international consortia.

From 2005 to 2019, we were involved in more than 35 major projects (approximately 50% EU funded and 50% from other donors) each of them including several partners from different regions and countries.

Data hosting, analytics and management

The Data team standardizes data management procedures for observational studies sponsored by Penta, ensures legal and regulatory compliance of all data management activities, including data archiving and secondary use of data, and build relationships to explore opportunities using 'big data'.

Regulatory and Clinical

The Regulatory & Clinical team interacts with the Project Team, providing guidance on ICH GCP guidelines and Ethical standards during project and protocol design and implementation. The team liaises with the Regulatory Agencies and Ethics Committees, and the European Medicines Agency for Paediatric Investigation Plan applications.

Communications

Our Communications Team coordinates the internal and external communications of the organization and across the network and beyond. Our communications are designed to ensure the work of the Penta Foundation and the Penta ID network translates scientific discovery and clinical research into messages that engage their intended audiences. Future efforts will be directed towards exploring new communication routes in order to reach our ever-increasing network of individuals and organizations who we can influence to achieve our vision of a world where all children with infection get the treatment they need.



Training and Education

The Training team manages and supervises the coordination of all Penta training courses held around the globe. We are committed to delivering high quality, interactive, comprehensive, tailored training courses to healthcare workers, with a particular focus on low-middle income countries. This is achieved through the innovative approach of combining face-to-face courses with digital e-learning methods.

The team collaborates with our experienced and expert teaching faculty, drawn from the extensive Penta ID Network, to ensure core teaching content is accurate and constantly updated and to identify new training opportunities.

Penta is dedicated to bringing the expertise of our network not only to healthcare professionals and scientists around the world but also to students in schools.

The Education team organizes creative socio-educational programmes for younger people on sexual health and the prevention of HIV and other sexually transmitted diseases. This is done through targeted individual and group interventions, both in the hospital environment and in schools.

Penta ID Scientific Organization



Following the reorganization of Penta's scientific work in 2018, each content area and platform developed a draft strategic plan which was then further discussed in a Scientific consultation meeting in December 2019. This enabled adjustment of the plans to the global research needs, as well as also addressing the needs of the Penta network. A number of key actions were highlighted at the consultation, including the need for the network to provide greater opportunities for collaboration and consultation in developing Penta's scientific agenda and allowing a greater role for younger mid-career professionals. These recommendations have been built into Penta's 2020 Strategic Plan – and the Penta Board will be approving the final plan and scientific priorities in early 2020.

Scientific priorities agreed for the Penta network are:

- HIV & viral infection
- Severe sepsis and antimicrobial resistance
- Infection in pregnancy
- Neglected or emerging childhood infections

The Penta network will support research that seeks to better understand both the dynamics of transmission and how to achieve optimal health outcomes for pregnant women and children.

The network's research will embrace basic, pharmacological, clinical, social and population sciences.




3. ACTIVITIES AND ACHIEVEMENTS





Not just
clinical trials,
but **cohort and
pregnancy studies**
and educational
programmes

Objectives




Penta does so much more than clinical trials: we have extensive observational and cohort studies, pregnancy studies, a basic science platform across the different content areas, training and educational programmes, and a unique and ever growing


network of investigators who are leading champions for child health in their home countries.

In 2019, we started to up our ambition, we have begun to review other serious children's infections that we can begin to tackle.


In 2019 the objectives were:



Support clinical research to address HIV, antimicrobial resistance and other infections in women and children



Develop a coordinated platform of clinical and basic science investigators for child health and infections



Build the capacity of the network to undertake high quality research and deliver optimal clinical care

Research activities

Penta seeks to deliver **high quality meaningful research** – generating evidence that matters and makes a difference to practice. In our 28 years of operation we have developed considerable expertise in developing and running independent multicentre/ multinational research projects that do just this.

Our work on HIV has contributed to new treatment strategies and new drugs and drug combinations for children with HIV. This has made HIV in children a treatable condition – death is now the exception, while it used to be a certainty in the first year of life for most babies born with the virus. Our scientific studies may well take us closer to the elusive prospects of a cure.

Results from Penta studies have been used by companies for regulatory purposes – and our efforts **have decreased the time for drugs to be accessible**

by children in Europe, Africa and Asia. We are also building data systems that are critical to pharmacovigilance – which is the monitoring of the effects of medical drugs after they have been licensed for use. This is especially important to identify and evaluate previously unreported and unrecognized side effects.

Penta has contributed vital data on what form of Dolutegravir babies and children can take. This has helped WHO update its guidance for countries.

Dolutegravir is an important HIV drug that is more effective, easier to take and has fewer side effects than alternative drugs that are currently used. It also has a high genetic barrier to developing drug resistance, which is highly desirable and necessary for children who face lifelong treatment.

Our unique collaborative platform has expanded in recent years to include **observational and cohort study collaborations** and pregnancy studies that can address the vertical transmission of infections. When Zika was recognized as an emerging threat, Penta was the network able to quickly pull together global expertise in transmission dynamics, design studies and develop a platform to answer critical questions about the nature of the infection and its impact on babies.

Penta seeks to bridge the gap between science and trials and is developing studies to look at immunological and virological responses to treatment, microbiological studies including those addressing drug resistance and cohort-based studies to compare treatment and outcomes across different European countries. There is now a basic science platform established to create and manage a network of cutting-edge laboratories dedicated to the development and implementation of the following areas: molecular and

cellular immunology, molecular microbiology, multi-omics technologies, metagenomics and bioinformatics. With this platform, we intend to pursue discovery research on disease pathogenesis that will pave the way for the development of more targeted clinical treatments and drive ‘precision medicine’.

Currently, the Penta Foundation and its network are involved in research projects in various developing countries that address several **critical neglected areas in infections in children beyond HIV**, including arboviruses and antimicrobials.

We have been involved, as coordinator or partner, in a **growing number of non HIV-related projects**. In some of them, Penta, with its very well-established network of paediatric hospitals, represents a gateway for paediatric expertise. This is especially true in projects (such as PREPARE, RESCEU, COMBACTE, VALUE-DX and ECRAID) where the main research focus is on adults. This expertise is enhanced through our participation in large national networks such as **INCiPiT**, the Italian Network for Paediatric Clinical Trials, whose mission is to foster and support the planning, conduct and completion of all types of clinical studies conducted in the paediatric population in Italy by profit or not for profit sponsors, and **PEDIANET**, an Italian primary care epidemiological network.



“Let me tell you the story of how *the Penta Experience* changed the model of HIV care in Central America.”





Dr. Luis G. Castaneda V.
Centro de Excelencia Para Niños
con Inmunodeficiencia (CENID)

“Learning to implement solutions with the available resources.”

It all started in October 2005, when three paediatric ID specialists from Panama, Ecuador and El Salvador were invited to participate in the first Tr@inforPedHIV course in Rome.

The relatively small numbers of paediatric HIV cases in Latin America, in the global context of the adult pandemic, caused children to be neglected and left paediatricians in a very isolated situation. Latin America, especially Central America, is a region where the cohorts of paediatric patients are small, and isolated in each of the different countries' health facilities, with scarce access to resources and technical advice.

It was with funding from the Italian Government and the advice of the Penta group that in 2008 the first Latin American Tr@inforPedHIV course was held in El Salvador. By bringing together the paediatricians and paediatric ID, as well as other professionals taking care of the paediatric HIV patients in the region, we were able to understand the individual efforts of each centre and the need to work together.

This inspired us to expand the experience to the rest of Latin America, and the creation of a collaborative partnership that we later called the **Pediatric Latin American Network for Treatment of Aids** or “PLANTA”.

Since 2005, a total of nine courses have been held throughout the region - expanding technical capacity throughout the Americas. “The Penta experience” not only changed the provision of care to paediatric HIV patients in El Salvador, but also improved the quality of care in Central America, by unifying the region in a group sharing experiences and knowledge.

Over the years we have grown with our Penta colleagues, implementing new concepts and techniques, becoming more efficient in managing the health of our children. The cumulative experience of teachers and local providers has been essential for generations of knowledge in our countries, and the friendship forged over the years between European and Latin-American paediatricians has had an impact not only in the area of HIV, but more generally in children's health.

For El Salvador, the experience gained over the years working with the Penta community has shaped the practice of caring for children with HIV, learning to implement solutions with the available resources.

Ongoing projects

Penta has a strong portfolio of ongoing research projects and a growing network of investigators



Projects in 2019

HIV projects and studies

KALETRA

Purpose

The aim of this EPPICC study is to assess the safety and efficacy of Kaletra (Lopinavir/ritonavir) oral solution in children aged 14 days to 2 years with HIV-1 infection in Europe

from 2019 until 2021

Total budget
€ 534,864

Funder
AbbVie

Role
SPONSOR

PENTA 17 SMILE

Strategy for Maintenance of HIV suppression with integrase inhibitor + darunavir/ritonavir in children

Purpose

To evaluate safety and antiviral effect of a once daily integrase inhibitor administered with darunavir/ritonavir compared to standard of care among HIV-1 infected, virologically suppressed paediatric participants

Key achievement

Enrollment target of 300 patients exceeded with a total of 318 patients enrolled

from 2013 until 2020

Total budget
€ 2,664,962

Funder
Janssen, Gilead,
ViiV Healthcare

Role
SPONSOR

PENTA 20 ODYSSEY

A randomised trial of dolutegravir - based antiretroviral therapy vs. standard of care (SOC) in children with HIV infection starting first-line or switching to second-line ART

Purpose

To assess the efficacy and toxicity of dolutegravir plus 2 NRTI versus standard of care among HIV positive children and adolescents

Key achievement

ODYSSEY data used by ViiV Healthcare to file submissions to the FDA and EMA for the first-ever dispersible formulation of dolutegravir (DTG) for children living with HIV

from 2014 until 2021

Total budget
£ 10,466,721

Funder
ViiV Healthcare

Role
SPONSOR

EPIICAL

Early treated Perinatally HIV Infected individuals: Improving Children's Actual Life

Purpose

To implement a predictive platform for the early identification of novel therapeutic strategies for HIV infected children

Key achievement

- EARTH (Cohort of Early Anti-Retroviral Treatment in HIV-perinatally infected Children) study enrolment target was reached with a total of 150 patients recruited.
- Six scientific publications accepted to journals and eight oral and poster presentations accepted at CROI 2020.

from 2016 until 2024

Total budget
€ 8,561,664

Funder
ViiV Healthcare

Role
COORDINATOR

DOLOMITE

Dolutegravir in pregnant women and exposed infants in Europe

Purpose

To provide a comprehensive programme of work encompassing the pharmacokinetics, usage and safety of dolutegravir in pregnancy

from 2018 until 2022

Total budget
€ 3,139,241

Funder
ViiV Healthcare

Role
COORDINATOR

EMPIRICAL

Empirical treatment against cytomegalovirus and tuberculosis in severe pneumonia in HIV-infected infants: a randomized controlled clinical trial

Purpose

To develop an empirical treatment against cytomegalovirus and tuberculosis in severe pneumonia in HIV-infected infants

from 2019 until 2024

Penta budget
€ 571,421

Total budget
€ 7,680,619

Funder
European Commission – EDCTP2

Role
PARTNER

BREATHER Plus

A randomized open-label 3-arm, 96-week trial evaluating the efficacy, safety and acceptability of weekends off dolutegravir-based antiretroviral therapy (ART) and monthly long-acting injectable ART compared to daily dolutegravir-based ART in virologically suppressed HIV-infected children and adolescents aged 12 - 19 years in sub-Saharan Africa

Purpose

To evaluate alternative strategies to treat HIV-infected adolescents in sub-Saharan Africa successfully without the requirement for daily oral therapy

from 2019 until 2024

Penta budget
€ 88,190

Total budget
€ 7,401,328

Funder
European Commission – EDCTP2

Role
PARTNER

REACH

Research on HIV, tuberculosis (TB) and/or hepatitis C (HCV) in patients with mono-, co-infections and/or comorbidities in the context of fostering collaboration with the Russian Federation

Purpose

To address key research questions in the global health response to the epidemics of HIV, HCV and TB in the priority populations of pregnant women, children and adolescents

from 2019 until 2020

Penta budget
€ 1,056,734

Total budget
€ 2,986,749

Funder
European Commission – Horizon 2020

Role
COORDINATOR

Antimicrobials

NeoVanc

Treatment of late onset bacterial sepsis caused by vancomycin susceptible bacteria in neonates and infants aged under three months

Purpose

To develop an optimal dosing and monitoring regimen for vancomycin use in preterm neonates and infants under 3 months of age

Key achievement

Recruitment period completed with a total of 240 patients enrolled.

from 2014 until 2020

Penta budget
€ 653,370

Total budget
€ 5,993,000

Funder
European Commission – The Seventh Framework Programme - FP7

Role
COORDINATOR

COMBACTE-MAGNET

Combatting Bacterial Resistance in Europe - Molecules Against Gram Negative Infections

Purpose

To determine more effective treatment strategies for intensive care unit (ICU) infections, particularly with Gram-negative bacteria

from 2015 until 2021

Penta budget
€ 1,725,013

Total budget
€ 168,679,583

Funder
European Commission – Innovative Medicines Initiative - IMI

Role
PARTNER

PediCAP Trial

Impact of duration of antibiotic therapy and of oral step-down to amoxicillin or co-amoxiclav on effectiveness, safety and selection of antimicrobial resistance in severe and very severe childhood community-acquired pneumonia (CAP): a randomised controlled trial

Purpose

To optimize antibiotic treatment for children aged 3 months to 10 years hospitalized with severe/very severe community-acquired pneumonia in South Africa, Uganda, Zambia and Zimbabwe

from 2019 until 2024

Penta budget
€ 792,756

Total budget
€ 6,779,078

Funder
European Commission – EDCTP 2

Role
COORDINATOR

VALUE-Dx

The value of diagnostics to combat antimicrobial resistance by optimizing antibiotic use

Purpose

To focus on the value of diagnostics to combat antimicrobial resistance by optimising antibiotic use

from 2019 until 2023

Penta budget
€ 298,250

Total budget
€ 10,704,100

Funder
European Commission – Innovative Medicines Initiative - IMI2

Role
PARTNER

NeoOBS

*NeoAMR
Observational Study*

Purpose

To collect high-quality observational data to inform trial design and comparator selection for a clinical trial(s) to assess the efficacy of novel antibiotic regimens in areas with high endemic rates of antimicrobial resistance

from 2017 until 2020

Penta budget
€ 2,497,461

Funder
GARDP

Role
PARTNER

Other Viruses projects

ZIKAction

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

Purpose

To address key knowledge gaps relating to Zika virus epidemiology, natural history and pathogenesis, with a particular emphasis on maternal and child health

Key achievement

The Microcephaly Case-Control Study in Ecuador commenced and patient enrolment completed for the Vertical Transmission cohort studies in Jamaica and Haiti.

from 2016 until 2021

Penta budget
€ 1,061,926

Total budget
€ 6,961,081

Funder
European Commission - Horizon 2020

Role
COORDINATOR

PREPARE

Platform for European Preparedness Against (Re-)emerging Epidemics

Purpose

To harmonize large-scale clinical research studies on infectious diseases, preparing rapid responses to any severe infectious disease outbreak and providing real-time evidence for clinical management of patients

from 2014 until 2021

Penta budget
€ 585,400

Total budget
€ 23,992,375

Funder
European Commission – The Seventh Framework Programme - FP7

Role
PARTNER

RESCEU

Respiratory Syncytial virus Consortium in Europe

Purpose

To gather information on the scale of Respiratory Syncytial Virus (RSV) infection in Europe and its economic impacts, using this information to design best practice guidelines for monitoring of RSV and to shape future vaccination programmes.

from 2017 until 2021

Penta budget
€ 175,000

Total budget
€ 15,016,625

Funder
European Commission – Innovative Medicines Initiative - IMI2

Role
PARTNER

PREPARE / Ped-Mermaids

(Paediatric, Multi-centre, EuRopean study of MAJOR Infectious Disease Syndromes) coordinated by Penta.

Key achievement

The study included 847 children admitted to hospital with a new episode of community-acquired sepsis-like syndrome (SLS) or ARI and age-matched afebrile controls. The study has provided standardized data on the clinical characteristics, management and outcome of children under 6 months of age, who were hospitalized for Acute Respiratory Infections and Sepsis-Like Syndromes in Europe. These data are not only the basis for the drafting of standardized protocols for the management of these infections in the paediatric field but have also provided valuable information for the shaping of new research studies into the new novel Sars-CoV-2 virus.

Clinical research network and infrastructure building

ECRAID

European Clinical Research Alliance on Infectious Diseases

Purpose

To establish a coordinated and permanent European infrastructure for clinical research on infectious diseases

from 2019 until 2020

Penta budget

€ 165,150

Total budget

€ 2,994,560

Funder

European Commission – Horizon 2020

Role

PARTNER

By building paediatric clinical research networks and infrastructures, we can make progress towards our primary objective - to **facilitate the generation of information** needed to ensure that the right drug at the right dose is available for use by children and newborns. Through EU funding, Penta is contributing towards the development of a European network of collaborators which can facilitate the conduct of research concerning child diseases and drug development, together with the pharmaceutical industry.

ID-EPTRI

Infectious Diseases – European Paediatric Translational Research Infrastructure

Purpose

To propose developmental models for paediatric medicines that integrate technology driven aspects with clinical trials

Key achievement

The Consortium positively assessed ten “virtual Feasibility studies” to test its capability of responding to the possible needs of stakeholders

from 2018 until 2019

Penta budget

€ 175,625

Total budget

€ 3,000,000

Funder

European Commission – Horizon 2020

Role

PARTNER

connect4children

Collaborative Network for European Clinical Trials for Children

Purpose

To develop a large, collaborative paediatric network that will facilitate the development of new drugs and other therapies for the entire paediatric population in Europe

Key achievement

c4c Consortium selected the first study portfolio to leverage the expertise of the c4c network, as well as activated the c4c Academy and formed expert groups to strengthen the c4c network.

from 2018 until 2024

Penta budget

€ 10,232,871

Total budget

€ 140,496,816

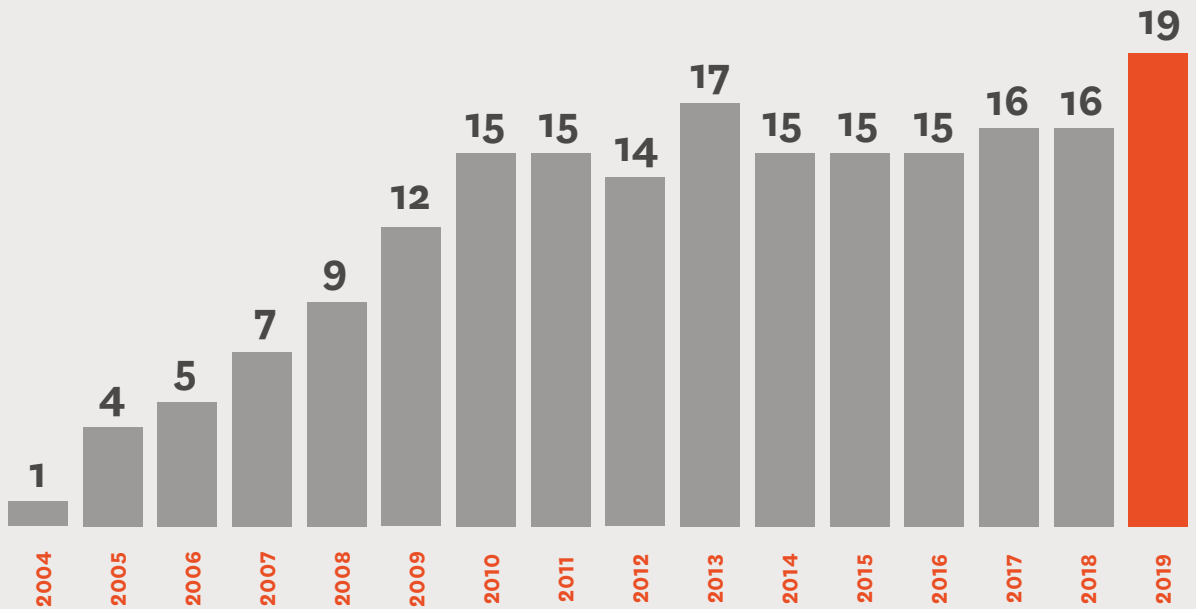
Funder

European Commission – Innovative Medicines Initiative - IMI2

Role

COORDINATOR

Numbers of projects (2004 - 2019)



Other activities



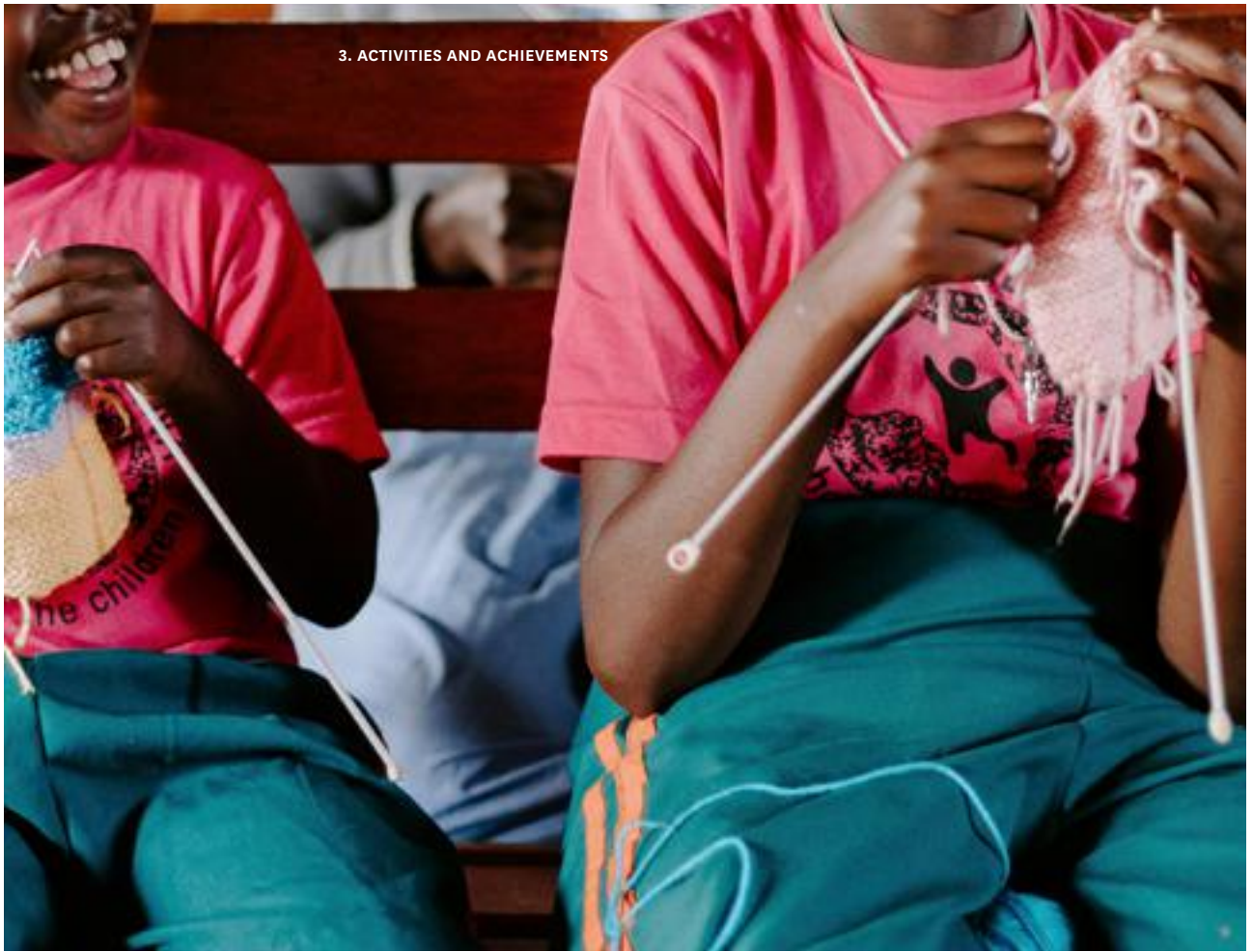
Prescribing Medicines for Children

In 2019, Penta contributed to the development and launch of Prescribing Medicines for Children, the **first international textbook** providing guidance on the principles behind optimal neonatal and paediatric prescribing. This textbook stems from the Global Research in Paediatrics - GRiP project: an EU-funded network of excellence that brings together worldwide paediatricians and pharmacists from Europe, North America and Japan as well as the WHO, for which a number of Penta network members contributed. The textbook covers different **key clinical prescribing areas** related to all paediatric sub-specialties. It perfectly reflects the mission and vision of Penta, and all our efforts aimed at implementing the best ways to prevent, diagnose and treat diseases in children.

Patient involvement

Increasingly it is recognized that patients, including **children and adolescents must be involved in research** – not just as passive beneficiaries. Penta has been pioneering in developing examples of how researchers can engage children and their families in the research work. This includes:

- Sexual and relationship education programmes are aimed at increasing the skills of those working with HIV positive adolescents to be able to have conversations and give clear, factual information on sex and relationships. The delivery of these programmes help improve the wellbeing of adolescents living with HIV, providing them with all the information they need in order to empower them to make informed decisions about their sexuality and relationships freely and responsibly.
- Youth Trial Board is a pilot project nested within the ODYSSEY study to explore ways to meaningfully involve young people living with HIV in the development and delivery of clinical trials. Penta supports an interactive, youth-friendly programme with young people involved in the study across four different countries.
- Patient and Public Involvement is a cross-cutting theme within the c4c project that gives an active role to patients' families and members of patient associations in the design and development of the different clinical trials that c4c will promote and conduct.



Penta involvement in International Cooperation Projects

Since the early 2000s, Penta has been involved in the management of **several international cooperation projects** in low- and middle-income countries, in partnership with different Italian and international NGOs (such as Casa Accoglienza alla Vita Padre Angelo, the Romanian Angel Appeal

Foundation and various hospitals and associations operating in the health and psycho-social care field in Eastern Europe and Sub-Saharan Africa) aiming to provide care to women, children and families in Africa and resource limited settings.

Quality Assurance

Penta takes quality seriously – and we actively establish, manage and monitor systems for Quality Assurance in all our work. Through our quality system, we ensure that the standards for all the study documentation are compliant with Good Clinical Practice procedures and every type of collected personal data are

compliant with the principles of newly approved European Data Protection Regulation. We also require that the same standards are adopted by our collaborators when working with us.

Training

Education is key to our mission. Penta remains committed to providing clinical training in paediatric HIV and other infections as part of its goal to improve clinical care for children, and to ensure robust high-quality clinical assessment as part of its trials. We continually seek to ensure new investigators are trained and supported to run research, are able to design their own studies and we will continue to expand on this type of capacity building. The WHO toolkit for research and development of paediatric antiretroviral drugs and formulations, developed in collaboration with Penta, was a major step towards this.

The network updated its [HIV Treatment guidelines](#) in 2019. These guidelines act as a concise reference document for clinicians to guide antiretroviral choices for children and adolescents with perinatally acquired HIV.

Tr@inforPedHIV started in 2005, as a partnership between Penta and ESPID (*European Society for Paediatric Infectious Diseases*). It is a training programme for healthcare workers caring for HIV infected children, adolescents and pregnant women. This pioneering course has integrated distance learning with interactive residential courses. Having delivered upwards of 60 training courses to date, and with a fully briefed faculty on board, Penta is able to deliver and tailor its innovative and high-quality training for a range of settings.

Since its initiation, more than 4,000 healthcare workers from over 30 countries have benefitted from our training courses. In 2019 alone, we trained over 500 healthcare workers at residential courses in Maputo (Mozambique), Irkutsk (Russian Federation), Dushanbe (Tajikistan), Oxford (UK), Minsk (Belarus), Cuernavaca (Mexico) and Johannesburg (South Africa).

In September 2019, an emergency clinical mentorship training course took place in Ratodero-Larkana, Pakistan following a significant HIV outbreak in the region.

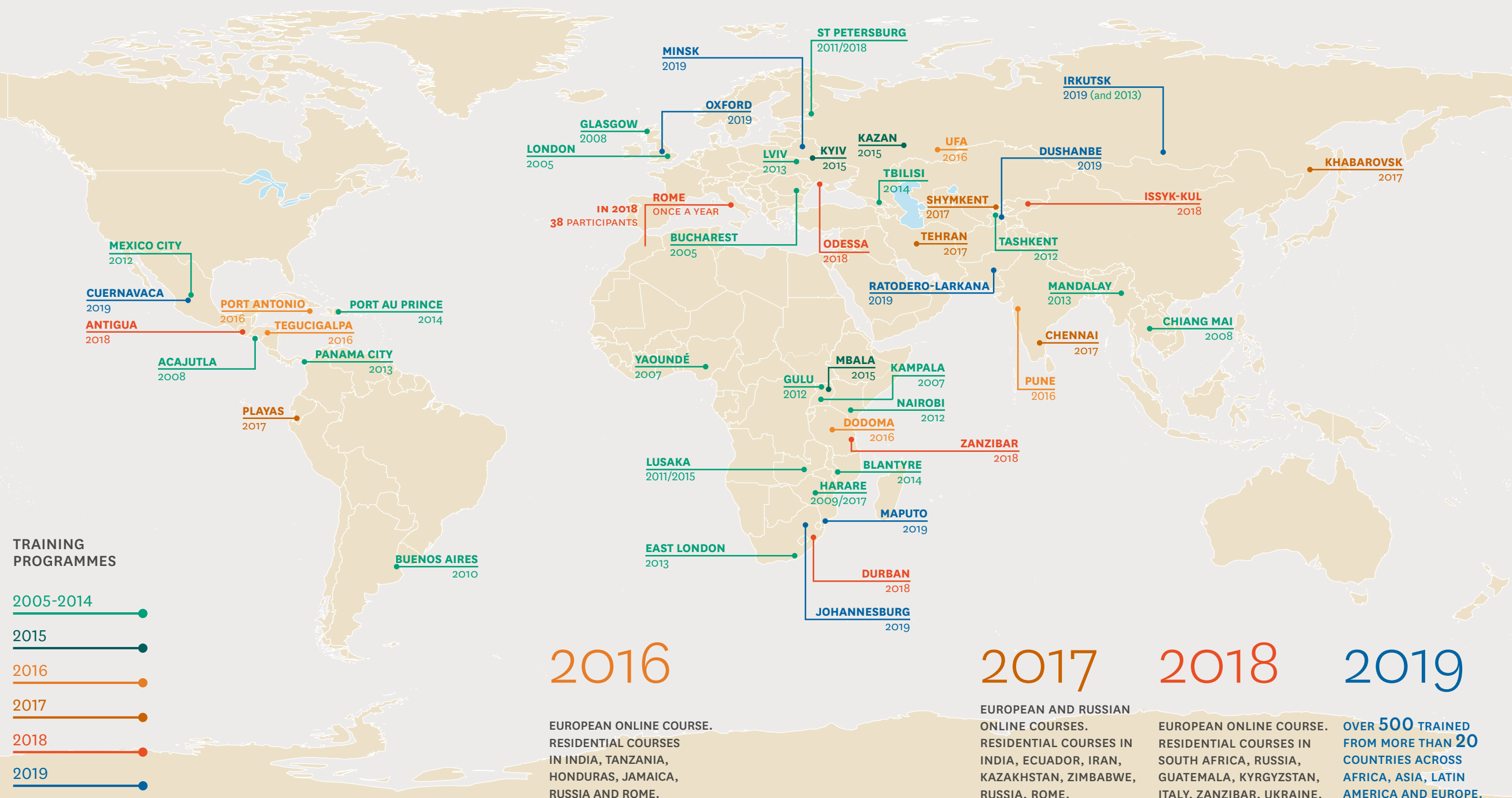
“Unique, irreplaceable, outstanding”

Some words from Penta trainer, Tim Niehues:

Overcoming the stigma of HIV in a sensitive and clever way is the key to treatment success. The Penta Training courses do just that! Apart from educating about drugs and their side-effects, many other non-medical aspects of HIV are challenged and discussed. In addition to the lectures delivered, it is the work in smaller groups that is really special in the Penta courses, helping overcome the barriers that most of the participants have when they want to speak about HIV. The exchanges among participants from different regions within the country is key to building the trust that is needed to formulate national guidelines and a uniform policy towards fighting HIV. The interaction with international doctors and local doctors is highly instructive for both sides, and the participants usually understand very quickly that an open and trustful exchange on sensitive topics in HIV medicine behind closed doors is the most effective way to learn and then treat your patients successfully.

Tr@inforpedHIV has been outstanding because it is more international, more global. Its interactive group discussion work, involving specialists with different expertise and nationalities, make Tr@inforpedHIV better than most other courses I have attended. The spirit of the Penta ID Network has always aimed at successful high-level scientific collaboration. Crucial to this success is the involvement of all kinds of disciplines ranging from paediatrics to adult medicine, from pharmacology to social work to psychologists to immunologists and infectious disease specialists and many more. This mixture of different disciplines is unique to the Penta ID Network.

Tr@inforPedHIV Training courses 2005-2019



4. PIM 2019





Every 2 years we get together for the Penta ID Network Meeting (PIM). Since its initiation in 1999, the PIM has traditionally been the key opportunity to gain an in-depth understanding of **Penta's activities, plans and ...dreams!** It has encouraged the exchange of ideas and proposals within the network and highlighted the importance of all contributions.



The PIM encompasses a rich and multifaceted network of scientists and professionals



Our global collaborators and stakeholders have a common goal: to improve the quality of life of children and their families



We encourage the exchange of data and proposals within the network



We highlight the importance of every contribution and strengthen the sense of belonging within the network



For all of us, sharing is a value, a method and a goal

Our communication through horizontal, two-way, peer-based, participatory exchanges make us unique





**We are cultivating
a new generation
of leaders**



5. THE FUTURE: CHALLENGES AND OPPORTUNITIES





Following a successful year, our activities in 2020 are focused on **organizational growth** and continuing to strengthen **network capabilities**



Penta UK



In line with our growth, the Penta Foundation has **set up a branch office in the UK.**

In 2019 we registered the Penta Foundation in the UK as a charity. The objects of the Charity are for the public benefit:

- to relieve sickness and to preserve health, particularly, but not exclusively, amongst women, children and young people suffering from diseases;
- to advance the education of the general public, including medical professionals and patients and their families, in all areas relating to health science and paediatric diseases, particularly in, but not limited to, vulnerable populations and to promote research for the public benefit in all aspects of that subject and to publish the useful results.

This allows Penta to apply for UK funding for childhood infectious diseases research. The Board will meet and approve the 2020 strategic plan and workplan in early 2020. We feel this will allow us to:

- Strengthen opportunities and collaborations with UK partners
- Expand our portfolio of collaborative research activities.

The UK Foundation will at all times operate with the same strategic priorities as Penta Foundation Italy – but the board may choose to emphasize training or other facets of the network as a focus.

Penta ID innovation

Stemming from the Penta ID Network, Penta ID Innovation is a **site management organization** that utilizes Penta's expert network in paediatric Infectious Diseases, to **reduce the gap between industry and academia** and deliver high-level consultancy services, thus guaranteeing well-performing trial recruitment to the pharmaceutical industry.

To do so, Penta ID Innovation has partnered with CROMSOURCE (a Contract Research Organization). This strategic collaboration combines Penta's expertise in paediatric infectious diseases and CROMSOURCE's capabilities in managing worldwide drug development programmes to address the challenges of bringing new therapies to children.

“We want to accelerate the research that makes a difference to children's health”



Looking forward

Penta will build upon the progress made in paediatric sepsis and antimicrobial resistance research. We have now developed all the methodology and tools to support the NeoOBS study and we will work to develop greater depth and strength in this area throughout 2020. We intend to explore a deeper partnership with CUAMM to develop greater implementation science within our portfolio and work towards securing a more ambitious partnership with GARDP. We plan to **establish a global collaborative network of experts and hospitals** that care for seriously ill babies, to generate critical information on ways to prevent and treat bloodstream infections.

For 2020, we will seek ambitious non-research dependent funding to **expand the Penta network**. We hope this will allow us to take the network's expertise, the

data and evidence we have gathered, and scale this up to enable us to reach our goal of reducing deaths in babies with infections, especially those that are life-threatening.

We will expand collaborative activities with the Penta network, expanding our work in infectious diseases, and our growing experience in **vertical transmission** will be explored further. Our work on Zika has shown we can adapt and provide useful tools and capacities quickly and efficiently, and we will call upon our networks again.

The emergence of the COVID-19 pandemic will both be a huge opportunity for the network and a serious threat. Managing ongoing studies and readjusting to a time when families and children are under lockdown means we may face challenges in the delivery of our studies and the delivery of high quality care to all of our study children.

The COVID-19 pandemic is also playing out very differently in children, with most having mild to moderate infections. We don't know why children appear to have milder disease overall, however it is likely a combination of factors related to body chemistry, immune function, and social factors such as how children are cared for and spend their days. Nevertheless, we urgently need to understand transmission dynamics and therapeutic options.

We also need to understand the public health impact of choices made now in the midst of the epidemic and be sure we understand the implications long after the immediate crisis is over. We must have a **global learning agenda** so that mistakes are not repeated country after country, and secondary population health effects are not overlooked.

We will rapidly **develop the research agenda and deploy the full strength of the network**. We will work tirelessly towards growing, consolidating and expanding our network of investigators and trial sites. We will explore how to bring more countries into the network, especially low - and middle - income countries.

We are working closely with the Global Accelerator for Paediatric Formulations (GAP-f) partnership, and through this collaborative have prioritized products needed for treating, streamlining the generation of clinical evidence, incentivizing manufacturers, and accelerating product development.






2019 has been a busy and productive year for Penta

We also strongly believe that **2020 will be both an exciting and challenging year.**


As this annual report goes to press, we find ourselves in the midst of a global pandemic of COVID-19 disease– caused by a previously unknown coronavirus SARS-CoV-2.

As we set our sights to the years ahead, we are looking forward to:







Further building a network of support, expertise and access to patients to study and generate solutions for children's health - notably infections



Revamping our training and education platform to take advantage of digital developments and reflect our scientific priorities



Optimally managing our ongoing research projects, partnerships and consortia to deliver on the research and impact we have promised



Promoting and sponsoring research on prevention, diagnosis and treatment and management of infections in children - with a priority to respond to the COVID-19 pandemic



We also seek to embed our scientific priorities that have been approved for 2020 into the network – and we want to build a sustainable network that will endure and operate as an open platform for collaboration into the future

6.

FINANCIAL RESULTS





Penta is an independent organization financed by **public and private** contributions from international organizations

5. FINANCIAL RESULTS

■

Last year, the Penta Foundation implemented a new budgeting system with multi-year financial forecasting, as well as an investment plan in order to meet the long-term objectives. In addition to this, our accounting system has been modified in order to better reflect the financial figures of a non-profit organization. This modification should be taken into account when reading the financial figures.

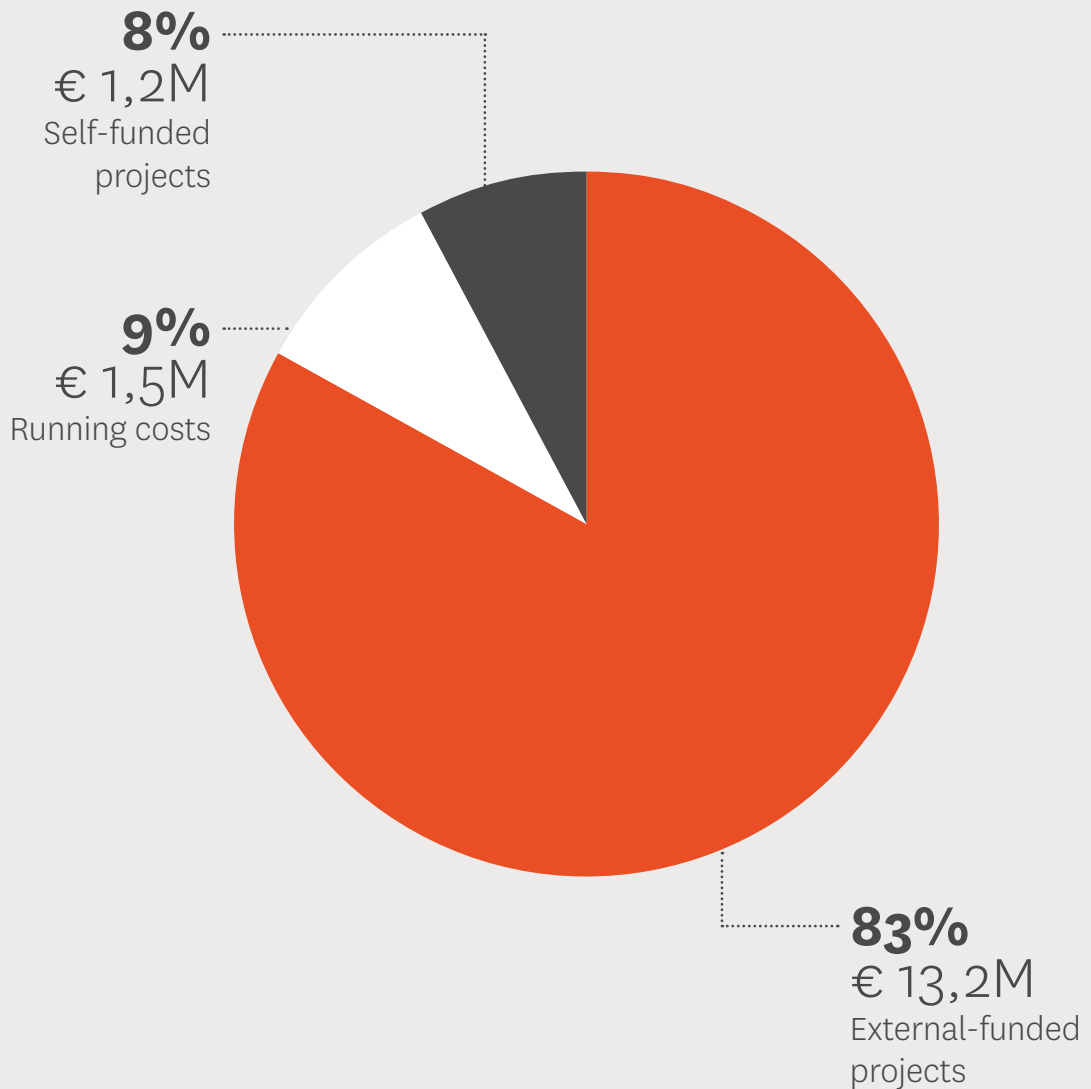
As shown in the following graphs, HIV remains a key focus in the research activities of Penta. Nevertheless, our focus on other areas of research is growing, particularly on Antimicrobials.

In addition, the use of resources is mainly directed to project-related activities while running costs represent a residual percentage.

With regards to funding sources, in 2019 most of the funding received came from private institutions showing the numerous collaborations Penta has in place.

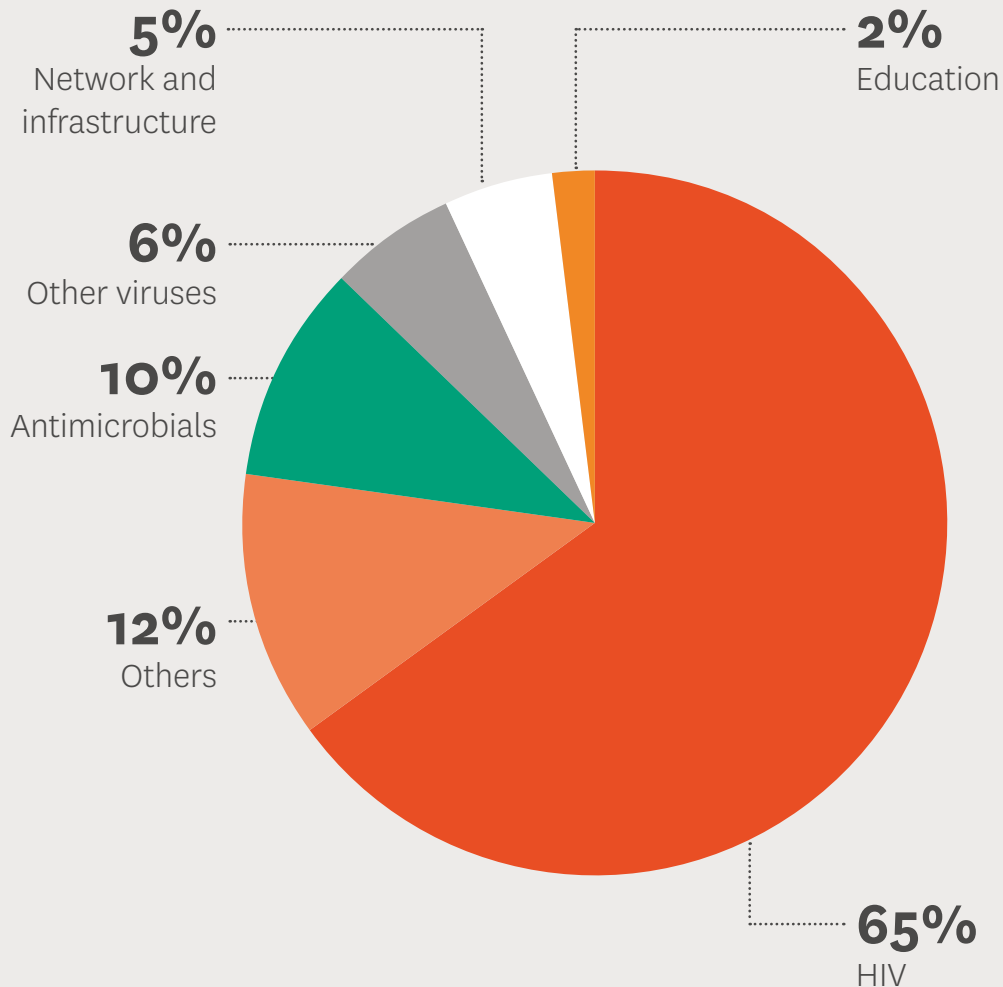


Resource distribution



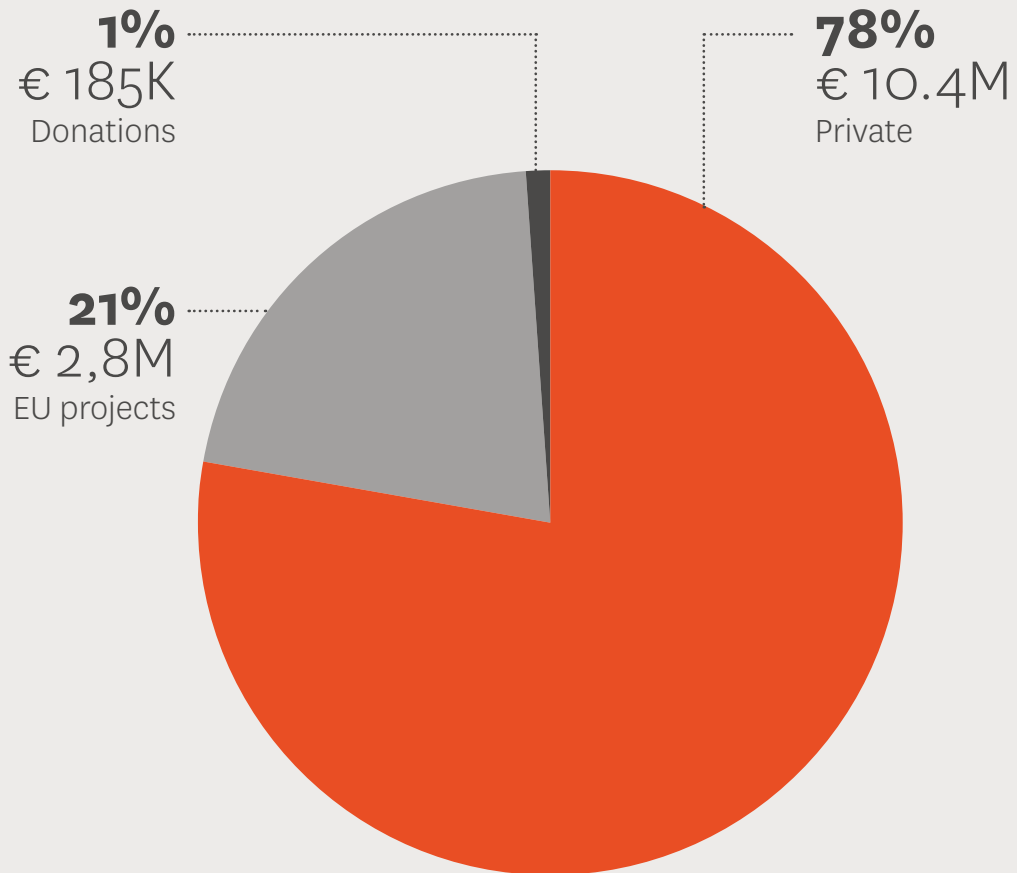
THE ABOVE CHART SHOWS THE PERCENTAGE DISTRIBUTION OF THE RESOURCES BY THE FOUNDATION FOR 2019.

Expenses by research area



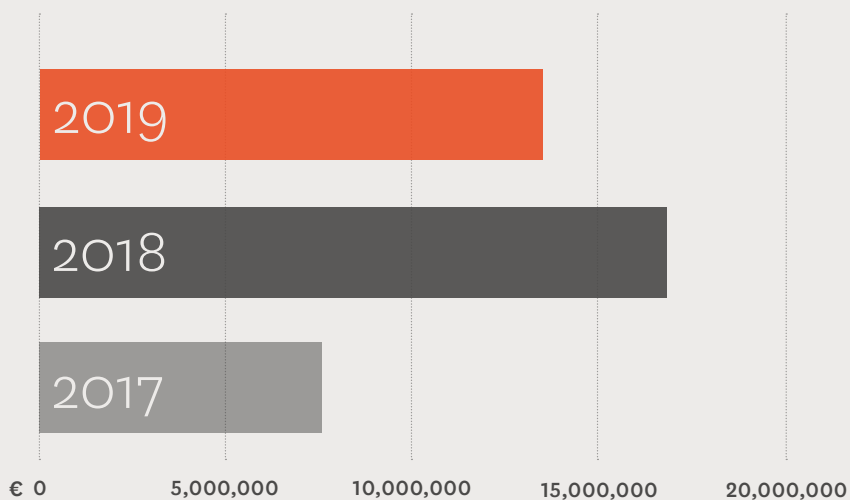
THE CHART ABOVE SHOWS THE PERCENTAGE DISTRIBUTION OF THE EXPENSES INCURRED BY RESEARCH AREAS IN 2019. HIV CONTINUES TO BE THE KEY AREA OF RESEARCH OF THE FOUNDATION. THERE IS A SIGNIFICANT INCREASE IN THE WEIGHT OF THE ANTIMICROBIALS AREA OF RESEARCH SHOWING THE GROWING IMPORTANCE OF THE FIELD.

Incomes by source



THE ABOVE CHART SHOWS THE PERCENTAGE DISTRIBUTION OF THE INCOMES RECEIVED BY SOURCE OF FUNDING IN 2019. THE HIGHEST PROPORTION CORRESPONDS TO PRIVATE SOURCES WHICH SHOWS THE NUMEROUS COLLABORATIONS THE FOUNDATION HAS IN PLACE. DONATIONS ARE NOT A SIGNIFICANT SOURCE OF FUNDING.

Revenues



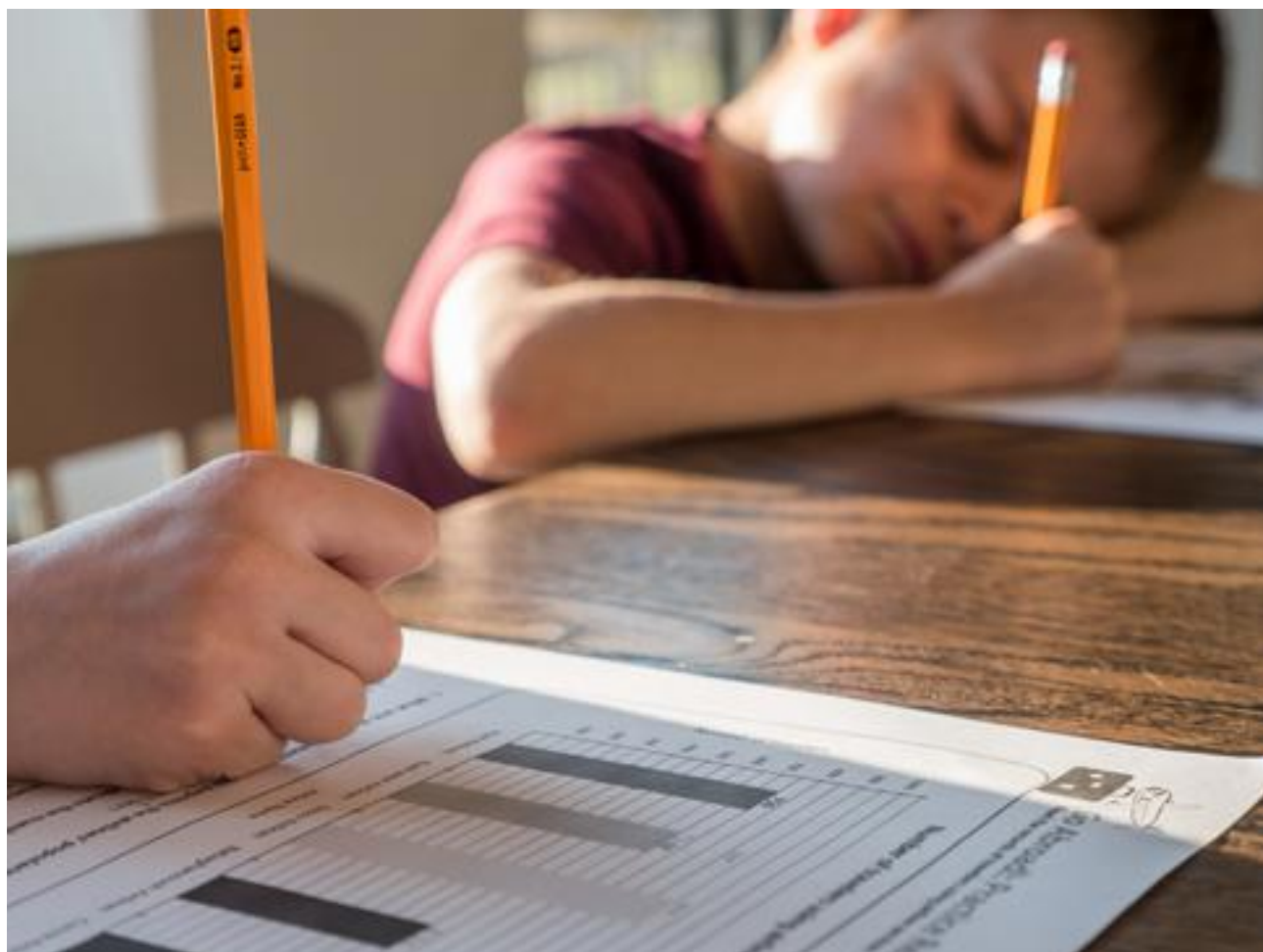
REVENUES HAVE DECREASED BY 19% IN 2019 WHEN COMPARED TO 2018. HOWEVER, AS STATED IN THE INTRODUCTION TO THIS SECTION, THIS NUMBER IS AFFECTED BY THE CHANGES IN THE ACCOUNTING SYSTEM IMPLEMENTED THIS YEAR.

Financial audits



The organization financial statements are regularly audited and certified by the Board of Auditors, which is composed of 3 professionals appointed by the Board of Directors.

For 2019 no irregularities have been identified by the Board of Auditors.



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LISTS OF ACRONYMS

CLEO
Centre for Clinical Epidemiology and Outcome Research
CRO
Contact Research organization
CVBF
Consorzio per Valutazioni Biologiche e Farmacologiche
DNDI
Drugs for Neglected Diseases initiative
EDCTP
European and Developing Countries Clinical Trials Partnership
ENPR-EMA
European Network of Paediatric Research at the European Medicines Agency
GARDP
Global Antibiotic Research & Development Partnership
GAP-F
Global Accelerator for Paediatric Formulations
HCV
Hepatitis C Virus
IMI1/IMI2
Innovative Medicines Initiative
JCRC
Joint Clinical Research Centre
NGO
Non Governmental Organization
OPBG
Ospedale Pediatrico Bambino Gesù
PADO
Paediatric Antiretroviral Drug Optimization
PAWG
Paediatric Antiretroviral Working Group
PIP
Paediatric Investigation Plan
TB
Tuberculosis
UCL
University College London
WHO
World Health Organization



concept and design bcvassociati.it

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