

# Coordination and implementation of the Plan



From AIEOP. Credit Attilio Rossetti photographer, Italy

SIOPE is the European Society of Paediatric Oncology and is dedicated to care, research and training in paediatric haematology-oncology as well as policy-making for decisions that impact on cancer ('oncopolicy').

Its mission is to ensure the best possible care and outcome for all children and young people with cancer in Europe, by increasing the cure rate and the quality of cure of children with cancer. More specifically, SIOPE is in charge of:

- Coordinating the implementation of the European Strategic Plan;
- Steering the integration of research, care and education, and increase funding levels;
- Ensuring that the EU legislative framework facilitates the implementation of the Strategic Plan;
- Strengthening partnerships with all stakeholders.

SIOPE is the European branch of the International Society of Paediatric Oncology (SIOP) and a founding member of the European Cancer Organization (ECCO).

Currently there are 19 European Clinical Trial Groups (ECTGs) developing clinical and translational research either by an individual disease type (15 groups) or across multiple diseases (4 groups), who define and run their own research strategy according to the SIOPE Strategic Plan. In Europe there are also 25 National Paediatric Haematology-Oncology Societies (NaPHOS). The Chairs of ECTGs and NaPHOS form the SIOPE Clinical Research Council (CRC, formerly ECRC).

*“Children are desperate to enrol in new clinical trials, that in some cases can be the only hope for survival.” (Glenis Willmott, Member of the European Parliament, UK)*

## The European Clinical Trial Groups

Tumour Name	Group Name	Website
<b>Brain Tumour</b>	SIOPE Brain Tumour Group	<a href="http://www.siope.eu/european-research-and-standards/european-clinical-research-council/ecrc/siope-brain-tumour-group">www.siope.eu/european-research-and-standards/european-clinical-research-council/ecrc/siope-brain-tumour-group</a>
<b>Ewing Tumour</b>	EURO- E.W.I.N.G.	<a href="http://www.euroewing.eu/clinical-trials/ee2012-trial">www.euroewing.eu/clinical-trials/ee2012-trial</a>
<b>Germ Cell Tumours</b>	Germ Cell Tumours	
<b>Hodgkin's Lymphoma</b>	EHL – European Hodgkins Consortium, EuroNet-PHL	<a href="http://www.kinderkrebsinfo.de/index_eng.html">www.kinderkrebsinfo.de/index_eng.html</a>
<b>Langerhans Cell Histiocytosis</b>	Histiocyte Society	<a href="http://www.histiocytesociety.org">www.histiocytesociety.org</a>
<b>Leukemias and Lymphomas</b>	I-BFM – The International BFM Study GROUP	<a href="http://www.bfm-international.org">www.bfm-international.org</a>
<b>Liver Tumours</b>	SIOPEL – SIOPE-Epithelial Liver Tumour Study Group	<a href="http://www.siope.org">www.siope.org</a>
<b>Myelodysplasia</b>	EWOG-MDS	<a href="http://ewog-mds.de">ewog-mds.de</a>
<b>Neuroblastoma</b>	SIOPEN – SIOP Europe Neuroblastoma Group	<a href="http://www.siopen.org">www.siopen.org</a>
<b>Non-Hodgkin Lymphoma</b>	EICNHL – European Inter-group Cooperation on Childhood and Adolescent Non Hodgkin	
<b>Osteosarcoma</b>	EURAMOS – European and American Osteosarcoma Study Group	<a href="http://www.euramos.org">www.euramos.org</a>
<b>Renal Tumours</b>	SIOP-RTSG – SIOP Renal Tumours Study Group	<a href="http://www.siop-rtsg.eu">www.siop-rtsg.eu</a>
<b>Retinoblastoma</b>	EURbSG – European RetinoBlastoma Group	
<b>Soft Tissue Sarcoma</b>	CWS – Cooperative Weichteilsarkom Studiengruppe or Cooperative soft Tissue Sarcoma StudyGroup	
<b>Soft Tissue Sarcoma</b>	EpSSG – European Paediatric Soft Tissue Sarcoma Study Group	<a href="http://www.epssgassociation.it">www.epssgassociation.it</a>

## Across diseases:

Topic	Group Name	Website
<b>New Anticancer Agents</b>	ITCC – Innovative Therapies for Children with Cancer	<a href="http://www.itcc-consortium.org">www.itcc-consortium.org</a>
<b>Stem Cell Transplantation</b>	EBMT – European Group for Bone Marrow and Stem Cell Transplantation Paediatric Working Party	<a href="http://www.ebmt.org">www.ebmt.org</a>
<b>Survivorship and Late Effects</b>	PanCare – Pan-European Network of for Care of Survivors after Childhood and Adolescent Cancer	<a href="http://www.pancare.eu/en">www.pancare.eu/en</a>
<b>Very Rare Paediatric Tumours</b>	EXPeRT – European Cooperative Study Group on Paediatric Rare Tumours)	

## The National Paediatric Haematology-Oncology Societies (NaPHOS)

Country	NaPHOS/Group	Website
<b>Austria</b>	AGPHO (Austrian Group for Paediatric Haemato-Oncology)	<a href="http://www.docs4you.at">www.docs4you.at</a>
<b>Belgium</b>	BSPHO (Belgian Society of Paediatric Haematology Oncology)	<a href="http://www.bspho.be">www.bspho.be</a>
<b>Bulgaria</b>	Bulgarian Society of Paediatric Oncology	
<b>Croatia</b>	Croatian National Group	
<b>Czech Republic</b>	CPH (Czech Working Group for Paediatric Oncology)	
<b>France</b>	SFCE (Société Française de lutte contre les Cancers et leucémies de l'Enfant et l'adolescent)	<a href="http://sfce.sfpediatrie.com">sfce.sfpediatrie.com</a>
<b>Germany</b>	GPOH (Gesellschaft für Pädiatrische Onkologie und Hämatologie)	<a href="http://www.kinderkrebsinfo.de/gpoh_society/gpoh_who_we_are/index_eng.html">www.kinderkrebsinfo.de/gpoh_society/gpoh_who_we_are/index_eng.html</a>
<b>Greece</b>	Hellenic society of Pediatric Haematology-Oncology	<a href="http://www.eepao.gr">www.eepao.gr</a>
<b>Hungary</b>	HPOG (Hungarian Paediatric Oncology Network)	
<b>Israel</b>	ISPHO (Israel Society of Pediatric Hematology and Oncology)	<a href="http://www.ispho.org.il/english">www.ispho.org.il/english</a>
<b>Italy</b>	AIEOP (Associazione Italiana Ematologia Oncologia Pediatrica)	<a href="http://www.aieop.org">www.aieop.org</a>
<b>Latvia</b>	Latvian Society of Paediatric Oncology	<a href="http://www.ihot.lt/lt/bspoh">www.ihot.lt/lt/bspoh</a>

Country	NaPHOS/Group	Website
Luxembourg (SIOPE institutional membership)	Foundation Kriibskrank Kanner	www.fondatioun.lu
The Netherlands	SKION (Stichting Kinderoncologie Nederland)	www.skion.nl
Nordic countries (Denmark, Norway, Sweden, Iceland, Finland) + Lithuania	NOPHO (Nordic Society of Paediatric Haematology & Oncology)	www.nopho.org
Poland	Polish Society of Paediatric Oncology and Haematology	
Portugal	SHOP (Sociedade de Hematologia e Oncologia Pediatrica)	www.spp.pt
Romania	Romanian Society of Paediatric Haematology-Oncology	
Serbia	Serbian Society of Haematology and Oncology	
Slovak Republic	Slovak Paediatric Association – Section of Paediatric Haemato-Oncology	
Slovenia	Slovenian Society of Paediatric Oncology	
Spain	SEHOP (Sociedad Española de Hematología y Oncología Pediátricas)	www.sehop.org
Switzerland	SPOG (Schweizerischen Pädiatrischen Onkologie Gruppe)	www.spog.ch
Turkey	TPOG (Turkish Paediatric Oncology Group)	www.tpog.org.tr
United Kingdom & Ireland	CCLG (Children’s Cancer and Leukaemia Group)	www.cclg.org.uk



*“Researchers are an essential driving force in making successful cure for childhood cancer possible.” (Hermann van Rompuy, former President of the EU Council, Belgium)*

# Childhood cancer from a societal perspective

From an international perspective, paediatric oncology research in Europe is in good standing. Between 2005 and 2014, there were 32,785 academic papers about paediatric oncology, representing 4.6% of all oncology papers and 7.1% of all paediatric papers. 22% of those articles came from Europe and 32% from the US [19].

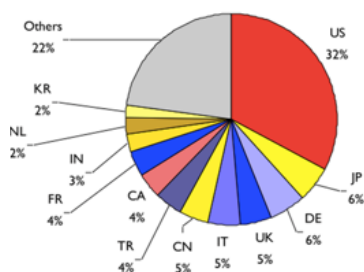


Figure 5: Pie chart of national contributions to paediatric oncology research, 2005-14; fractional counts. European countries coloured blue with shading; North American countries red with shading; Asian countries yellow with shading. Credit: Institute of Cancer Policy, London, UK



Credit Institut Gustave Roussy, France

In 2008, funding for paediatric oncology research was estimated, using previously validated econometric analysis of research activity [20], to be 1,229 USD millions, with more than 50% from public funding, including international funding such as European framework funding and just under 20% from the pharmaceutical industry [21]. In 2013, this has been estimated to have dropped to 900 USD millions, a decline over 25% over five years.

Research output is growing, particularly in clinical research, but availability of short-term funding is getting worse despite more European programmes. In addition, most of the public policy discourse has been focused on an ageing European society and the needs of children with cancer are not high on the political radar, despite the fact that cancer is the leading cause of death by disease in the young population. Globally, childhood cancer is being heavily marginalised.

The SIOPE objectives are:

- To improve public, political and policy visibility of childhood cancer research;
- To show the existing linkage between research activity and better outcomes for children with cancer in Europe;
- To develop strategies in order to broaden research engagement;
- To address both pan-European research funding and national funding streams, as well as funding from charities.

# Facilitating platforms and cross-tumour research projects



Credit University of Nottingham, Children's Brain Tumour Research Centre, United Kingdom



From AIEOP. Credit Attilio Rossetti photographer, Italy

## Platform to facilitate the implementation of ECTGs research strategy: the Clinical Trial Facility (CTF) Platform

This platform will help institutions to set up international clinical trials in the framework of the new EU Clinical Trials Regulation (536/2014/EU), and will allow researchers to share their experiences and solutions to issues related to the Regulation's implementation. It will provide templates and advice for the hurdles faced (e.g. practicalities and contracts) when implementing non-commercial clinical trials across multiple countries and sites, including the specific issues arising when trials are run in partnership with the pharmaceutical industry. Within ENCCA, a consortium of five European academic institutions has been created to speed up the implementation of early phase investigator supported trials.

## Clinical epidemiology platform for outcome research – The PICORET project

The Population Improvement in Childhood Cancer Outcomes through Research,

Evaluation and Training project (PICORET) will address the needs of clinical epidemiology and outcome research in paediatric haematology-oncology. Several paediatric cancers have a high survival rate with treatments that have been established through prospective European randomised trials. Population-based cancer registries measure overall but not relapse-free survival, and so there isn't sufficient information on the effectiveness of first line therapy at a population level.

PICORET will monitor the survival of all children and adolescents with cancer in Europe and evaluate progress across Europe using information from registries and observational studies that use standard treatments. Such 'non-interventional' clinical studies can assess effectiveness of biomarkers, which can be used for prognosis, and allow analysis of traditionally hard-to-research areas, such as surgical and imaging techniques.



Credit Attilio Rossetti photographer, Italy



Credit Institut Gustave Roussy, France



Credit Sociedade de Hemato-Oncologia Pediátrica (SHOP), Portugal

Through building enhanced clinical registry capabilities, PICORET will prospectively collect detailed clinical and biological information that can be used for quality improvement of diagnostics and treatment pathways for patients treated by a standard treatment outside of clinical trials. PICORET will monitor the survival of all children and adolescents with cancer in Europe, and will evaluate and compare the quality and effectiveness of treatments. High resolution studies will be run.

Initially, PICORET will focus on renal tumours, neuroblastoma and medulloblastoma as its first exemplars. It will develop standardised clinical guidelines as well as a standardisation and quality programme in standard care, with a special focus on infant dosing. Twinning between institutions in countries with higher and lower survival rates will be introduced. Data privacy will be carefully monitored, and the project's impact will be assessed.

### Platform for quality assurance in radiotherapy – The QUARTET project

Quality assurance and quality control are mandatory when patients receive radiation therapy. This is to make sure that each patient gets the best treatment in terms of maximising effectiveness and minimising long-term side effects. However, they are not systematically performed within clinical trials and various programmes are implemented only in a limited number of EU countries.

The QUARTET project ('QUALity and excellence in RadioTherapy and imaging for children and adolescents with cancer across Europe in clinical Trials') aims to build a radiation therapy quality assurance programme across all paediatric malignancies. It will be run in partnership with the European Organisation for Research on Treatment of Cancer (EORTC) and Aquilab for patients participating in clinical trials using radiation therapy and run by ECTGs. Eventually, the platform will expand its activity to patients treated outside of clinical trials.

## Multi-stakeholder platform for new paediatric oncology drug development – The CDDF-SIOPE-ITCC platform

This multi-stakeholder platform was created in December 2013 by Cancer Drug Development Forum (CDDF), SIOPE and ITCC as a deliverable of the ENCCA project to improve oncology drug development for children and adolescents [8]. Academia, parents and survivors, industry and regulators are equally represented and work together on the following objectives:

- To set up drug prioritisation and enable drug development, based on the mechanism of action of the drug as well as biological factors;
- To propose changes in the EU Paediatric Medicine Regulation to better address the needs of those with life threatening diseases;
- To propose new incentives for the development of specific paediatric drugs and repurposing of existing drugs;
- To implement long-term follow up measures for new oncology drugs for children and adolescents.

## Ethics, Social Sciences and Humanities programme

This is a natural development of the ethics programme set-up within ENCCA to maintain and improve the level of expertise on ethics in the field of paediatric cancer care and research. It is based on two priorities, namely to reflect the multidisciplinary nature of social sciences and humanities where suitable to paediatric oncology, and to facilitate access to appropriate expert views from professionals and from patients' representatives on ethical issues.

Following these priorities, “ethics” is meant as a multidisciplinary approach to the non-technical issues related to the care, protection, and self-realisation of paediatric oncology-haematology patients (or former patients). It is proposed to develop a non-prescriptive, participatory and outcomes-oriented approach to these issues, harnessing the relevant knowledge and expertise in the Social Sciences and Humanities (SSH) field.

Four main topics will be addressed by this programme: i) return of research results, ii) personal data in care and research environments, iii) access to medical innovation, iv) care and healthcare pathways. The programme will be performed through objective assessment of the non-technical issues related to the care and quality of survival of children and adolescents with cancer, as well as through community-based participatory research actions within the paediatric oncology community.

In accordance with the successful implementation within ENCCA, the programme will be steered and run by a permanent contact point along with ad-hoc academic collaborations. A steering Legal and Ethical Advisory Board will peer-review the projects and the results. The following tools will be set up: i) a thematic database of ethics expertise in Europe, identifying expert individuals and centres in Western and Eastern European Universities, ii) a database of local initiatives for bedside and benchside ethics, accessible to professionals and patients, iii) an initiative to establish multi-centre collaborations on non-technical interventions (fostering experience-sharing and multicentre evaluation).



All this is expected to generate sustained community dialogue, concerted evidence generation as well as transverse capacity-building on non-technical domains, first of all on ethical issues.

## The SIOPE portal

The portal set-up within the ENCCA project will be transferred to SIOPE after the end of the ENCCA project (December 2015). This online 'one-stop-shop' portal will support communication and interaction between everyone involved in implementing the strategic research agenda. It will serve as a resource for documentation and as a platform for information exchange.

Each patient will have a unique ID (EUPID) so that their data can be anonymised and shared between different databases. A pilot project for an integrated IT structure that will allow information to be linked between sources (such as registries, clinical trial databases, hospital electronic health records) and users (such as researchers and analysts) is being developed by the IT providers of ENCCA.

Within ENCCA, a consultation IT platform has been developed for patients with haepatoblastoma (a very rare disease) by SIOPEL along with CINECA. This platform (including pathology slides and images) facilitates access to expert advice for diagnosis and treatment, including indications of liver transplant. This IT tool is further developed within the ExPO-r-Net project for retinoblastoma and extremely rare paediatric tumours, and will eventually be adapted for other diseases within the Paediatric Oncology Europe Reference Network.

In addition, an IT platform for virtual tumour boards will be developed.

Based on these experiences and following those pilot projects, SIOPE and ECTGs will define how to structure the best IT environment that will allow the implementation of the Strategic Plan.

## Network of biobanks

Samples from patients and tumours, which are labelled with additional clinical information, are vital for the success of the SIOPE Strategic Plan. The aim of SIOPE is therefore to support a network of biobanks that can share data electronically, in keeping with EU data protection laws. The difficulty of the task is not underestimated.

A vital step in the development of such a network within SIOPE is the introduction of a unique patient identifier (the above mentioned EUPID) for every paediatric cancer patient treated in Europe, as well as the development of standardised patient consent forms. These must be in line with national data protection laws in European countries, and allow for new developments in molecular analysis of tumour samples (particularly next-generation sequencing), as well as the wishes of patients and parents and other ethical considerations.

In addition to this, ENCCA guidelines are currently being finalised on the standards for tumour and other patient samples (e.g. blood and plasma) as well as related materials like DNA and RNA, and on the process of access and use.

# Cross-tumour programmes

## Oncopolicy programme

Several regulatory initiatives are of direct concern to paediatric haematology-oncology and the implementation of the SIOPE Strategic Plan. SIOPE has developed expertise and skills to monitor and influence the development of relevant European cancer health and research policy themes, and to ensure that the needs of the paediatric haematology-oncology community are taken into account when regulations are drafted or revised:

- Each **National Cancer Plan** should address the needs of children and adolescents with cancer, according to the European Cancer Plan.
- The **Cross Border Healthcare Directive** (2011/24/EU) was established in 2010. This is the framework for the development of the future paediatric oncology European Reference Network (via the ExPO-r-Net project).
- The **Clinical Trials Regulation** (536/2014/EU) is expected to enter into force in 2016 and to facilitate academic trials, and SIOPE will help European institutions and ECTGs to implement their trials within the new Regulation (through the CTF platform, see above) and ensure that experiences, issues and hurdles encountered in paediatric haematology-oncology are fed back to the relevant bodies.
- The **Data Protection Regulation** (2012/0011(COD)) is under discussion at the time of the publication. In its current form, it would be detrimental to outcome



Credit Joke Emmerechts Photographer for SIOPE, Belgium

research in paediatric oncology – a major objective of the SIOPE Strategic Plan – as well as to the interdisciplinary research collaborations involving different institutions, in order to ensure the best quality of care to the patient. SIOPE is joining oncology stakeholders to ensure that the needs of academic research and epidemiology are taken into account.

- The **Paediatric Medicine Regulation** (1901/2006/EC and 1902/2006/EC) entered into force in 2007. The European paediatric oncology community is engaged in pushing for immediate changes to its implementation, in order to better address the unmet needs of children and adolescents with cancer. Because cooperation between all stakeholders (patients, survivors, parents, academia, industry, regulators) is crucial, the CDDF-SIOPE-ITCC multi-stakeholder paediatric platform (see above) was created to propose the immediate changes and to prepare for the revision of the Regulation, which could occur in 2017.

- In the 2015 Health programme, the European Commission called for a **Joint Action on Rare Cancers** that will be implemented jointly with EU Member States. This will provide the framework for the implementation of part of the SIOPE Strategic Plan and for cooperation with adult oncology in the field of rare cancers.

In 2014, SIOPE effectively obtained the commitment of EU institutions and civil society representatives to support young people with cancer, through their endorsement of the SIOPE-ENCCA-ICCCPO Manifesto for Paediatric Oncology. This document was signed by 20 members of the European Parliament, setting up objectives to advance childhood cancer research, treatment and care. After the European elections, this document became an even stronger advocacy document for SIOPE on the long-term.

Additionally SIOPE and the European paediatric haematology-oncology community will contribute to the development of oncology in Europe in the fields of multidisciplinary care, access to innovation and development of e-Health. SIOPE will join efforts with the European Cancer Organisation (ECCO) along with European Society for Medical Oncology (ESMO) and other European societies.

## Training and education programme

The aim of this programme is to encourage high quality clinical and basic research as well as the delivery of high quality care in paediatric oncology throughout Europe. This is a remit of SIOPE and focuses on the organisation of educational courses and on the revision of the training syllabus in paediatric oncology.

SIOPE is involved in several training courses to develop the knowledge of health professionals on new and state-of-the-art therapies and allow them to gain more practical skills in the treatment of paediatric malignancies:

- The SIOPE-ESO Masterclass in paediatric oncology: practice-oriented training with a focus on the application of the most recent research findings to clinical practice;
- The ECCO-AACR-ASCO workshop on “Methods in clinical cancer research” in Flims, Switzerland: introduction of junior clinical oncologists to the principles of good and innovative clinical trial design and methods;
- The SIOPE-ENCCA-ENTYAC European Course on the treatment of teenagers and young adults (TYA) with cancer: centred around multiple disciplines;
- The joint SIOPE-ESMO training programme on TYA.

*“The EU Data Protection Regulation is a debatable piece of legislation which could threaten childhood cancer clinical research” (Nikolaus Forgó, Institute for Legal Informatics, DE)*

As part of the work of the European Academy of Paediatrics, SIOPE revised its previous syllabus with the aim of having a comprehensive document for the whole of the EU that details the requirements expected from a trainee in paediatric haematology-oncology. The new version of the syllabus proposes a programme

containing core knowledge and practical aspects related to approaches for diagnosis and treatment that are essential for all trainees in paediatric haematology-oncology (available on the SIOPE website: [www.siope.eu](http://www.siope.eu)).

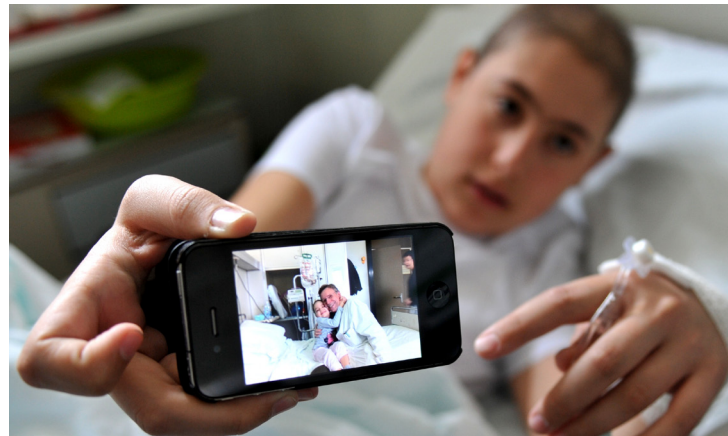
*“Europe should have a European Paediatric Cancer Plan addressing both care and research.”  
(Participants at the SIOPE-ENCCA Conference, 18-19 September 2014)*

## Communication

The SIOPE Strategic Plan relies on timely, relevant and tailored communication to target stakeholders. Based on its expertise of information-sharing with members and leading EU projects’ dissemination, SIOPE has set up a communication strategy, encompassing the pan-European haematology-oncology community, decision-makers and the general public.

The communication objectives are:

1. **Uniting the community:** further increasing the profile of SIOPE as the main reference point for paediatric haematology-oncology in Europe, to stimulate cross-border exchange of best practices, to strengthen existing collaborations and to develop new ones;



From AIEOP. Credit Attilio Rossetti photographer, Italy

2. **Raising awareness:** by fostering the well-informed involvement and commitment of target stakeholders and by raising awareness of paediatric cancers across Europe in partnership with parents and survivors.
3. **Generating action:** translating the needs of the Strategic Plan as well as the SIOPE position and requests into legislative, funding, advocacy, partnership-building and further communication initiatives.



# Partnerships



Credit Europe Regional Committee of Childhood Cancer International (CCI)

## Partnership with patients, survivors and parents

Building a partnership with patients, survivors, and parents' organisations is essential to achieve the goals of SIOPE in terms of research, equal access to standard care and expertise, advocacy when new policies are developed and strategic decisions made at the national and European levels.

**Childhood Cancer International (CCI)** is a worldwide childhood cancer organisation that represents families of children with cancer and childhood cancer survivor groups. SIOPE has been working with the CCI Europe Regional Committee for several years, including partnerships in several European projects and initiatives.

In 2011 the **Parent and Patient Advocacy Committee (PPAC)** within ENCCA was created with CCI Europe Region Committee members, and consists of representatives from different national parents and survivors organisations. Since then, they have been building networks between parent and survivor groups and organisations, disseminating health policy-related issues within Europe and improving the training of representatives of patients survivors and parents in clinical research to make them powerful advocates and partners in this field. ENCCA, SIOPE and PPAC also worked together in joint research and dissemination activities, as well as the development of a long-term sustainable strategy for paediatric oncology in Europe, the present SIOPE Strategic Plan and the seven medical and scientific objectives.

SIOPE and the CCI Europe Regional Committee entered into a co-operative relationship in order to implement the European long-term Strategic Plan and to raise awareness on cancer in children and adolescents. They signed a **Memorandum of Understanding** that sets out the specific areas of cooperation along with the principles by which both parties will run the partnership. The four areas are: i) ethics and social sciences and humanities, ii) access to standard of care and expertise, iii) improvements to the regulatory and political environment at the pan-European and national level, iv) research and development.



Credit Hellenic Society of Paediatric Haematology-Oncology (HeSPhO), Greece

## Partnership with adult oncology

During the last 50 years, paediatric oncology has developed in relative isolation. Improving the cooperation of all paediatric haematologists and oncologists was the crucial objective so that an effective European clinical research programme could be set up and address the very specific needs of children with cancers without reference to adult cancer services.

It is now recognised that adult and paediatric oncology have a lot to share and learn from each other, and that collaboration is beneficial in order to address common goals and challenges:

- Care and research for rare cancers, in terms of innovative methodology to evaluate new treatments and in terms of health care organisation models to provide access to expertise for patients suffering from rare and extremely rare cancers;
- Care and research for TYA (see above);
- Access to essential medicines, since most anti-cancer drugs are used to treat both adult and paediatric cancers, even though there are differences in the tumours;

- European initiatives on care and research oncopolicies.

SIOPE and ESMO (the European Society of Medical Oncology) have decided to develop a joint initiative to address those topics, and established a Memorandum of Understanding to help this collaboration.

## Partnership with paediatric haematology-oncology in other continents

SIOPE is part of the global paediatric oncology agenda run by the International Society of Paediatric Oncology (SIOP). Several European-centred study groups have an international scope, and bring together global investigators to participate in a common clinical trials portfolio.

The IBFM-study group is international, and patients from countries outside Europe participate to its leukaemia trials and translational research projects.

More than a hundred institutions from Europe, Asia, Central and South America, Australia and New Zealand collaborate in SIOPEL, the SIOPE-liver study group. Early drug trial groups such as ITCC in Europe, the Paediatric Oncology Experimental Therapeutics Investigator's Consortium (POETIC) and Therapeutic Advances in Childhood Leukemia and Lymphoma (TACL) in North America, the Canadian C17 network, the Australia Children's Cancer Trials group and the Children Oncology Group (COG) phase I consortium are working together to speed up the development of new anticancer agents.

SIOPEX has built with COG and neuroblastoma groups from Japan, China and Australia a large clinical and biological database of more than 9,000 neuroblastoma patients in order to define and validate new staging system and new biological prognostic biomarkers through the International Neuroblastoma Research Group [9] [22].

Groups such as the SIOPEX-Renal Tumours Study Group support clinical trials groups in other continents that run studies using the same standard treatment backbones, adapted to local circumstances.

The COG and the European Inter-group for Childhood non Hodgkin lymphoma (EICNHL) are currently running a randomised phase III clinical trial to evaluate the addition of rituximab, an anti CD20 monoclonal antibody, on standard intensive chemotherapy treatment in high-risk Burkitt's lymphoma.

The European and American Osteosarcoma Study Group (EURAMOS) has successfully completed a large phase III study with partners, which included the COG, the European Osteosarcoma Intergroup, the Cooperative Osteosarcoma Study Group, and the Scandinavian Sarcoma Group. The EURAMOS Strategy Group, made up of these four multi-national groups, as well as the relevant Australasian, French, Italian, Japanese, and Spanish osteosarcoma groups, is exploring options for collaboration on an even larger platform.

In the next 10 years, international cooperation will be reinforced to evaluate innovative targeted drugs within extremely small and rare groups (defined by biomarkers), such as children with B-RAF mutated malignancies. Even in less rare clinical situations, international randomised clinical trials will be considered more regularly to speed up evaluation of innovative therapies.



## Partnership with industry

For the last 50 years, progress has been made in curing paediatric cancers by running academic trials using anti-cancer drugs that are available in hospital pharmacy departments. Pharmaceutical companies have not developed their anti-cancer agents in the paediatric population, and nearly half of drugs used daily to cure cancer in children and adolescents do not have the regulatory official authorisation, stated in the 'Summary of Product Characteristics'.

In Europe this situation has significantly changed over the last five years because regulatory initiatives, first in the U.S. and then in Europe, obliged pharmaceutical companies to test their drugs in the paediatric population when relevant.

There was indeed an urgent need to access new drugs developed by pharmaceutical companies as early as possible during their development in adults, and to avoid families moving to the US to get access to innovative therapies in development.

Thanks to the EU Paediatric Medicine Regulation, pharmaceutical companies and academia have started to work together, to evaluate oncology drugs within paediatric investigation plans. This is a learning curve for everyone since pharmaceutical companies are not accustomed to working with paediatric oncologists and vice versa.

The goal is to develop **‘intelligent and transparent’ partnerships** that recognise the specificities of paediatric haematology-oncology, i.e. a well-structured arena for clinical research, dealing with rare and complex situations, while the paediatric development of oncology drugs is, by definition, a pre-competitive research activity for pharmaceutical companies and competition to access rare patients makes no sense.

A new model of cooperation between pharmaceutical companies, academia and public-private partnership needs to be developed in order to adequately address the needs of children and adolescents with cancer and regulatory requirements. This is being addressed in the CDDF-SIOPE-ITCC paediatric oncology platform. In addition, a strategy will be implemented to encourage investment and partnership with small pharmaceutical companies to develop drugs against specific paediatric targets.



Credit Czech Working Group for Paediatric Oncology, Czech Republic

## Partnership with charities

In several EU Member States, charities are extremely efficient at fundraising to support research and care for children and adolescents with cancer. These efforts are developed at the national level and can be fragmented, with significant differences between countries.

Most research programmes are run at the European level, and there is a need to figure out how charities from different countries can be more efficient at jointly funding large and ambitious European programmes.

SIOPE will propose to charities to fund and co-fund European projects and programmes. By defining, implementing and coordinating a long term sustainable Strategic Plan, SIOPE and the European paediatric haematology-oncology are willing to provide a transparent and clear visibility to the projects that will be run within a well-defined and integrated framework.



# Funding strategy

By definition, funding of the now established European strategy in paediatric haematology-oncology will come necessarily from several sources: the European Commission, national funding bodies, charities and foundations, industry as well as anyone willing to invest in paediatric oncology research and development.

European funding is available for research projects through Horizon 2020 calls. Projects in paediatric haematology oncology will be submitted to relevant European calls by SIOPE, groups and institutions as part of the implementation of the SIOPE Strategic Plan and referred as such in their application.

The critical hurdle encountered in paediatric haematology-oncology, as well as in other research areas, is the lack of funding for structures that are needed to run a coordinated and integrated research agenda. To this extent, in 2011 the European Commission provided €12m to structure oncology research into children and adolescents. One of the best examples of the goals achieved is the long-term sustainable Strategic Plan described in this document. ENCCA illustrates how funding for a permanent structure is essential to achieve progress and deliver success.

ENCCA will finish on December 2015 and the decision was taken that SIOPE will run the on-going agenda. The key question is how to fund the projects, the programmes and the structures that are needed to implement the long-term sustainable strategy.

At the end of the SIOPE-ENCCA event, which shared the European Strategic Plan with all stakeholders in Brussels in September 2014, the participants proposed to develop a **European Cancer Plan for Children and Adolescents**. This plan would show the commitment of the EU and its Member States to address childhood and adolescent cancers as a priority and a strategic objective for the European Union. Specific European initiatives would be set up to join efforts from the EU and its Member States for funding. In addition, it would allow other co-funding bodies to contribute to a pan-European initiative.

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# List of acronyms/glossary

- Biobank: A type of biorepository that stores biological samples (usually human) for use in research
- Biomarker: Generally refers to a measurable indicator of some biological state or condition
- CCI: Childhood Cancer International
- CDDF: Cancer Drug Development Forum
- CNS: Central Nervous System
- COG: Children Oncology Group
- CRC/ECRC: European Clinical Research Council for paediatric and adolescent oncology
- CTF: Clinical Trial Facilitating platform
- DG SANTE: Directorate General for Health and Food Safety, European Commission
- EAC: (ENCCA) Ethics Advisory Committee
- EAC: (ENCCA) Ethics Advisory Committee
- ECCO: European CanCer Organisation
- ECTGs: European Clinical Trial group(s) in paediatric oncology
- EICNHL: European Inter-group Cooperation on Childhood and Adolescent Non Hodgkin Lymphoma
- ENCCA: European Network for Cancer research in Children and Adolescents
- EORTC: European Organisation for Research and Treatment of Cancer
- EPAAC: European Partnership for Action Against Cancer
- ERN: European Reference Network(s)
- ESMO: European Society for Medical Oncology
- EU: European Union
- EURAMOS: European and American Osteosarcoma Study Group
- FP5, FP6, FP7: EU 5th/ 6th/ 7th Framework Programmes for research and innovation
- Horizon 2020: EU Programme for research and innovation (2014-2020)
- I-BFM: International BFM Study Group
- ITCC: Innovative Therapies for Children with Cancer
- LTS: (ENCCA) Long-Term Sustainability (working group)
- MAC: Members of the Parliament (MEPs) Against Cancer group
- MOA: Mechanism(s) Of Action
- NaPHOS: National Paediatric Haematology-Oncology Society-ies
- PanCare: Pan-European network for Care of survivors after childhood and adolescent cancer
- PanCareSurFup: PanCare childhood and adolescent cancer SURvivor care and Follow-UP studies
- PICORET: Population Improvement in Childhood cancer Outcomes through Research, Evaluation and Training
- PIP: Paediatric Investigation Plan(s)
- POETIC: Pediatric Oncology Experimental Therapeutics Investigators' Consortium
- PPAC: (ENCCA) Parent and Patient Advocacy Committee
- QUARTET: QUALity and excellence in RadioTherapy and imaging for children and adolescents with cancer across Europe in clinical Trials
- SAB: (ENCCA) Scientific Advisory Board
- SIOPE: SIOP Europe, the European Society for Paediatric Oncology
- SIOPEL: SIOPE-Epithelial Liver Tumour Study Group
- SIOPEN: SIOP Europe Neuroblastoma Group
- SSH: Social Sciences and Humanities project
- TACL: Therapeutic Advances in Childhood Leukemia and Lymphoma
- TYA: Teenagers and Young Adults

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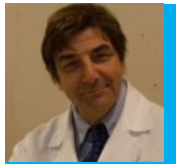
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Italy



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International Society of Paediatric  
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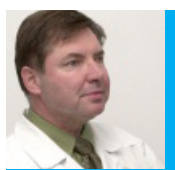
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University College London  
United Kingdom



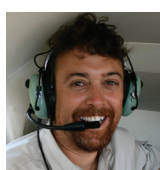
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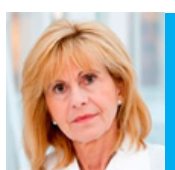
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SIOPE  
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Brussels, Belgium

## ENCCA Project Manager

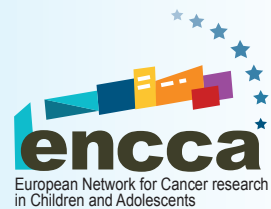


Zoltan Dobai (HU)  
ENCCA Project Manager  
St. Anna's Children's Hospital  
Vienna, Austria





Avenue E. Mounier 83  
B-1200 Brussels, Belgium  
Website: [www.siope.eu](http://www.siope.eu)  
E-mail: [office@siope.eu](mailto:office@siope.eu)  
Tel: +32 2 775 02 12



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