



Childhood Leukemia International Consortium (CLIC)

1

**PATRICIA A. BUFFLER, PHD, MPH, CPH
UNIVERSITY OF CALIFORNIA, BERKELEY
SCHOOL OF PUBLIC HEALTH
DIVISION OF EPIDEMIOLOGY**

**CHILDREN WITH CANCER SCIENTIFIC CONFERENCE
APRIL 26, 2012**

**WEBSITE: [HTTPS://CLIC.BERKELEY.EDU](https://clic.berkeley.edu)
CLIC_CENTRALOFFICE@BERKELEY.EDU**

History of CLIC

The Children with Cancer UK, the National Cancer Institute, the National Institutes of Environmental Health Sciences (NIEHS), and Environmental Protection Agency (EPA), US and the Cancer Council Western Australia have provided support for CLIC organization and/or pooled analyses.

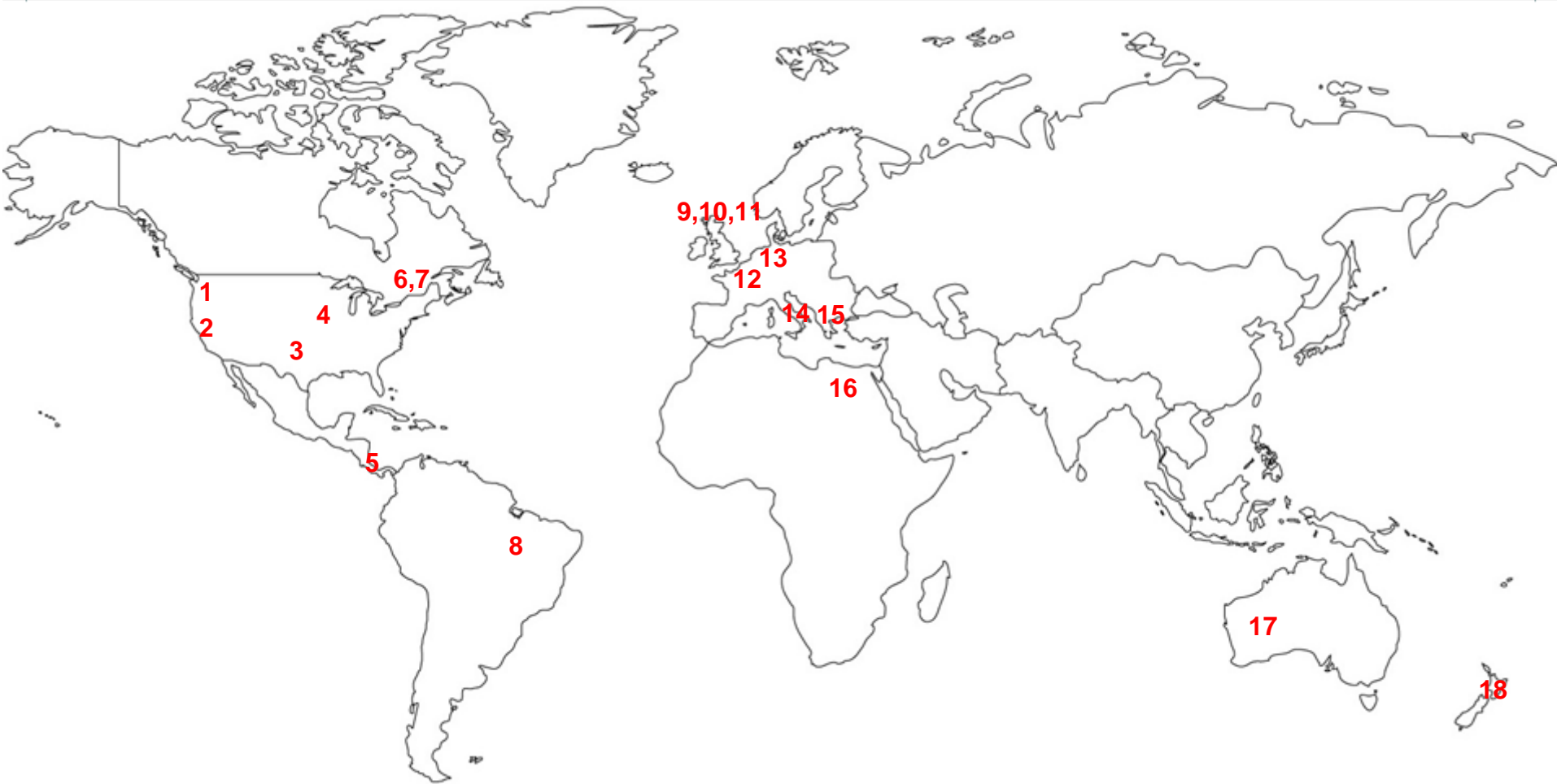
2005	Meeting at the International Agency for Research on Cancer (IARC) to introduce the concept
2006	First informal meeting with Principal Investigators (PIs) from Australia, France, Canada, and United States (California)
2007	<p>CLIC is officially established. Two pooled analyses were undertaken as proof of principle:</p> <ul style="list-style-type: none">▪ Maternal vitamin & folate intake and <i>MTHFR</i> variants and risk of childhood leukemia.▪ Fetal growth and childhood ALL

Mission of CLIC

3

- **Develop and support collaborations between scientists involved in CL research to accelerate knowledge on factors that influence the risk of childhood leukemia through epidemiological studies and related research.**
- **Encourage free exchange of results (published or unpublished) and ideas in a collegial environment without fear of competition.**

Map of Childhood Leukemia Studies participating in CLIC



Principal Investigators/designated co-investigators, study area (from left to right): 1) Beth Mueller, Parveen Bhatti, Washington State, USA; 2) Patricia Buffer, Catherine Metayer, California State, USA; 3) Michael Scheurer, Melissa Bondy, Texas State, USA; 4) Logan Spector, USA; 5) Patricia Monge, Costa Rica; 6) Claire Infante-Rivard, Quebec, Canada; 7) Daniel Sinnett, Quebec, Canada; 8) Maria Pombo-de-Oliveira, Sergio Koifman, Brazil; 9) Eve Roman, Jill Simpson, UK; 10) Jill Birch, Malcolm Taylor, Manchester, UK; 11) Michael Murphy, UK; 12) Jacqueline Clavel, France; 13) Joachim Schüz, Peter Kaatsch, Germany; 14) Corrado Magnani, Italy; 15) Eleni Petridou, Nick Dissypris, Greece; 16) Sameera Ezzat, Egypt; 17) Elizabeth Milne, Bruce Armstrong, Australia; 18) John Dockerty, New Zealand.

Outstanding Research Questions

5

- What are the critical windows of exposure?
- What are the “environmental” (or non-genetic) risk factors for rarer childhood leukemia subtypes like AML, APL, T-cell ALL?
- What risk factors are specific to childhood leukemia cytogenetic/molecular subtypes of ALL and AML, or other tumor characteristics?
- What role does genetics play in CL etiology?
- What is the contribution of gene-environment (GxE) interaction?

Summary of CLIC Member Studies

6

- As of 2012, CLIC has 18 Principal Investigators (PIs) representing 22 childhood leukemia studies from mid 1970's to present
- ~50% of the studies have biospecimens

	Number of Leukemia Cases and Controls					
	All Cases combined	ALL	B-cell ALL	T-cell ALL	AML	Controls
Studies w/ detailed epi data	13,112	11,145	8,167	994	1,870	21,132
Studies w/ limited epi data	13,767	10,188	540 <small>More can be available upon request</small>	60	1,868	24,510
Total (All CLIC Studies)	26,879	21,333	8,707	1,054	3,738	45,642

Organization of the CLIC

7

Management Group

Facilitates overall coordination of CLIC collaboration and communication

Core Logistics Groups

Advise and facilitate cross-cutting research administration

Coordination Group

Principal investigators and/or co-investigators of each childhood leukemia study participating in CLIC

Interest Groups

Promote collaborative projects in specific areas of childhood leukemia research

Working Groups

Pursue proposed research

CLIC Management Group

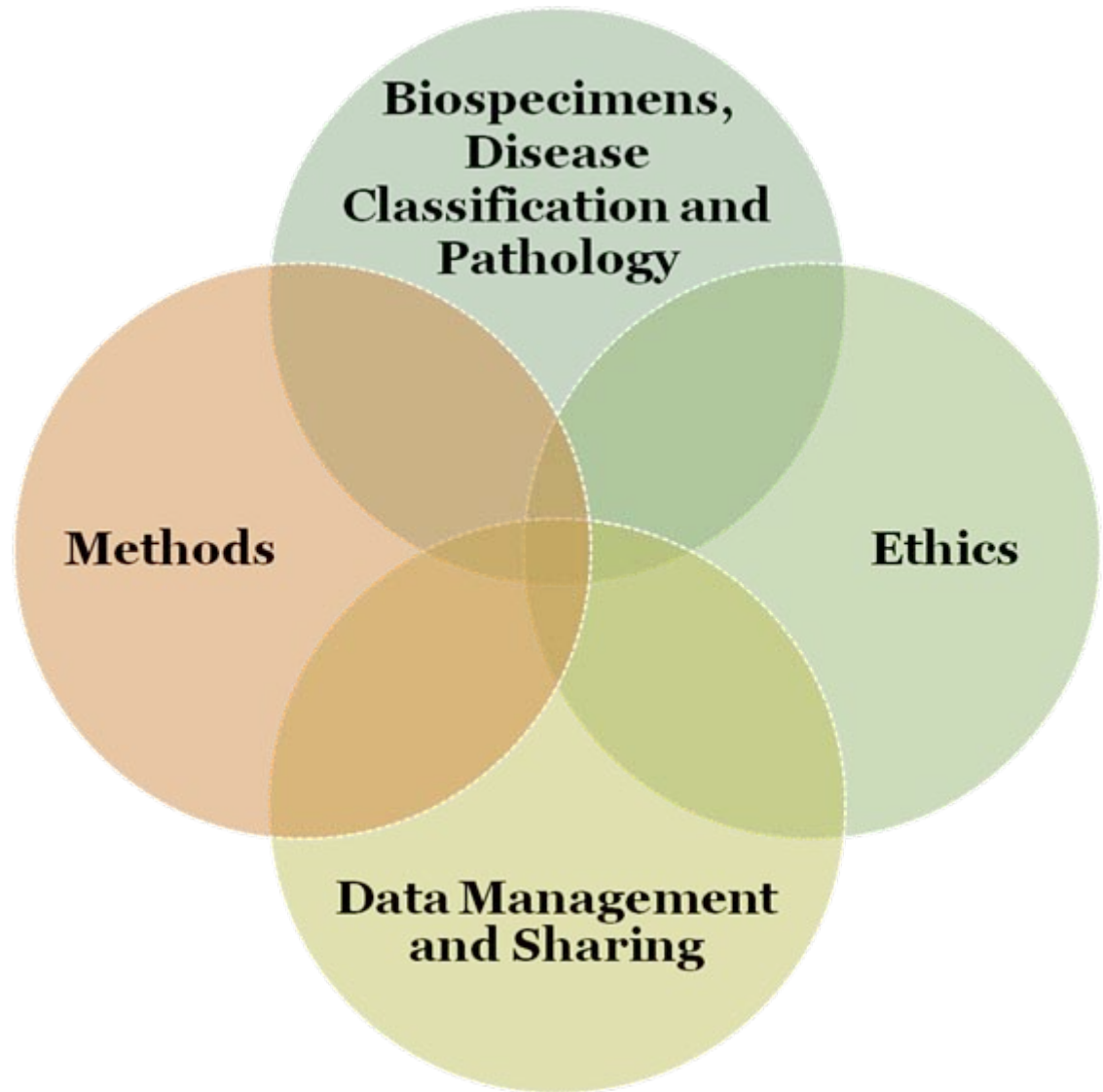
A Management Group (Executive Committee) is elected by the Coordination Group every two years.

Acting Members of the Management Group

Patricia A. Buffler (Chair)	University of California, Berkeley, USA
Elizabeth Milne (Deputy Chair)	University of Western Australia, Australia
Jacqueline Clavel	INSERM, France
Claire Infante-Rivard	McGill University, Canada
Catherine Metayer	University of California, Berkeley, USA
Logan Spector	University of Minnesota, USA
Joachim Schüz	International Agency for Research on Cancer, France

CLIC Core Logistics Groups

Core Logistics Groups advise and facilitate cross-cutting issues within the consortium. There are four groups.



CLIC Interest Groups

The Interest Groups will promote collaborative projects in specific areas of childhood leukemia research.

There are nine Interest Groups in CLIC.

- 1. AML/APL**
- 2. Birth Characteristics**
- 3. Environmental Exposures**
- 4. Family History**
- 5. Genetics**
- 6. Infant Leukemia**
- 7. Infection and Immunity**
- 8. Occupational Exposures**
- 9. Outcomes**

CLIC Procedures

11

**Call for Expressions of
Interest**

**Full Proposal and
Agreement of Pooled
Analyses**

**Data
Transfer**



CLIC Working Groups – Pooled Analyses

12

Name of Proposal

1. Maternal Folate and Alcohol Consumption, MTHFR Gene Variants and Risk of Childhood Leukemia
2. Fetal Growth and Other Perinatal and Birth Characteristics and Risk of Childhood Leukemia
3. Parental smoking and xenobiotic-metabolizing gene variants
4. Early Infections, Day Care, Birth Order, and Childhood Leukemia
5. Time-to-Pregnancy and Acute Lymphoblastic Leukemia
6. Benzene-related Home Exposures and Risk of Childhood Acute Myeloid Leukemia and Subtypes
7. Maternal Coffee and Tea Consumption During Pregnancy and Risk of Childhood Leukemia
8. Demographic, Disease and Socio-economic Status (SES) Characteristics in Relation to Childhood Leukemia Outcomes
9. Exposure to Paints and the Risk of Childhood ALL
10. Exposure to Pesticides and the Risk of Childhood Leukemia
11. Geographical Distribution of Childhood AML Cytogenetic Subtypes

Challenges

13

- Specificity of studies regarding prevalence of exposure, design, confounders (e.g. socio-economic status, ethnicity, etc.)
- Meta-data analyses vs. pooling of raw data
- Recognize potential for selection bias in observational studies that require data access, subject consent, and importance of assessing the representativeness of study participants
- Data harmonization

“Lessons Learned”

14

- **FUNDING** is imperative to support a consortium.
- Regular communication and timely feedback between steering committee members and PIs allow for accountability and progress.
- In person meetings are invaluable.
- Importance of flexibility.

Opportunities of Collaborations with the International Childhood Cancer Cohort Consortium (I4C)

15

- **Exchanges of ideas**
 - Genetic, epigenetic and tumor biology studies
 - Exposure assessment
 - Ethical issues
 - Emerging hypotheses
- **Exchanges of procedures**
 - Standardize data
 - Develop background information on exposure by country, time and activity patterns.

Acknowledgements

16

- **Families of CLIC Member Studies**
- **CLIC Coordination Group (Principal Investigators) and Management Group**
- **Other CLIC Collaborators (Researchers, Clinicians, Advisors)**
- **Our sponsors at the National Cancer Institute US, Children with Cancer UK, National Institute of Environmental Health Sciences (NIEHS) US, Environmental Protection Agency (EPA) US, Telethon Institute for Child Health Research, Australia**

Thank you!

17

CLIC is an open consortium and welcomes individuals interested in childhood leukemia research. Membership applications and other CLIC guidelines can be found online at the CLIC website, <https://clic.berkeley.edu>.

If you have any questions regarding the Consortium and/or difficulty accessing any of the documents, please contact Alice Kang at clic_centraloffice@berkeley.edu.

Additional Slides

18

CLIC Website – clic.berkeley.edu

19



Childhood Leukemia International Consortium

Google Custom Search

Search

Home

About

Organization

Pooled Analyses

Links

Contact Us

Members Only Login

The Childhood Leukemia International Consortium (CLIC) is an international group of researchers established in 2006 in collaboration with the University of California at Berkeley and the International Agency for Research on Cancer, with the aim of sharing comparable data from case-control and family-based trio studies on childhood leukemia. Through this joint research, we will coordinate scientific efforts and achieve greater power to elucidate the role of a variety of clinical, infectious, environmental, and genetic risk factors in the etiology of childhood leukemia.

Childhood Leukemia International Consortium News

CLIC Membership

Please contact the CLIC Central Office at CLIC_centraloffice@berkeley.edu for any questions about the CLIC membership application process. Application forms will be emailed to you.

2012 CLIC Interest Group Workshop

The 2012 Childhood Leukemia International Consortium (CLIC) Interest Group Workshop will be held in London, United Kingdom on April 27, 2012 at the Church House Conference Centre. Minutes from the workshop will be uploaded in the Documents section of the Member's Only website in May, 2012.

2012 CLIC Annual Meeting

We are delighted to announce the General Meeting of the 2012 Childhood Leukemia International Consortium (CLIC) Annual Meeting will be held in Berkeley, CA, USA on October 2 -3, 2012 at the Hotel Shattuck in (<http://www.hotelshattuckplaza.com/>).

You are welcomed to stay at any hotel in the Berkeley/San Francisco (Bay) area as the venue is easily accessible by all major modes of transportation (e.g. car, Bart-metro, or by foot). However, if you wish to stay at the same place as the venue, we created a group room block at the Hotel Shattuck. The Hotel is ready to accept reservations for the dates of Sunday, Sept 30, 2012, Monday, Oct 1, 2012, and Tuesday, Oct 2, 2012.

To make reservations at the Hotel Shattuck, you are welcomed to either call the hotel directly – (510) 845-7300 or toll free (866) 466-9199 and ask for the Childhood Leukemia Study (UCB) group, OR book online using the link provided below.

Online booking

Group Code (in hotel system): 1209CHLDH_001

Online Link: https://reservations.ihotelier.com/crs/g_reservation.cfm?groupID=767828&hotelID=17233

[If you wish to book days before or after the above contracted dates, please contact the hotel directly either by phone ((510) 845-7300 or toll free (866) 466-9199) or email (reservations@hotelshattuckplaza.com).]

The contracted cut-off date for our participants to book reservations is Friday, Aug 31, 2012.

Reservations may be made after this date, but there is no guarantee.

Please send any questions/concerns regarding the meeting to CLIC_centraloffice@berkeley.edu.

Thank you. We hope you are available to attend and look forward to seeing you in Berkeley!

Past Events

CLIC 2011 Meeting

Saturday & Sunday, September 17-18, 2011
Hotel Fira Palace, Barcelona, Spain

CLIC Coordination Group

20

- **The Coordination Group includes the Principal Investigator (PI) of each childhood leukemia study that will contribute data (and possibly additional co-PI for large studies). In the event the PI cannot be in the Coordination Group, s/he will nominate an authorized designate to represent her/his study.**

Active Members of the CLIC Coordination Group

21

Africa

Children's Cancer Hospital, Egypt

PI: Sameera Ezzat

Americas (North)

Costa Rica

PI: Catharina Wesseling

California Childhood Leukemia Study
(CCLS), USA

PI: Patricia Buffler
co-PI: Catherine Metayer

Childhood Cancer Epidemiology and
Prevention Center, Texas, USA

PI: Michael Scheurer

Children's Oncology Group (COG) (CCG
E-14, CCG E-15), USA

PI: Logan Spector

Active Members of the CLIC Coordination Group

(continued)

22

Americas (North, continued)

Collaborative Childhood Leukemia
Studies, Washington, USA

PI: Beth Mueller
co-PI: Parveen Bhatti

Quebec, Canada

PI: Claire Infante-Rivard

Qc-ALL, Quebec, Canada

PI: Daniel Sinnett

Americas (South)

Brazil-IAL, Brazil

PI: Maria Pombo-de-Oliveira
Authorized Delegate: Sergio Koifman

Active Members of the CLIC Coordination Group

(continued)

23

Europe

ADELE, ELECTRE, ESCALE, ESTELLE, France	PI: Jacqueline Clavel
Childhood Cancer Research Group (CCRG), UK	PI: Michael Murphy
German Childhood Cancer Registry (GCCR) (LSP, NIP, WGP), Germany	PIs: Peter Kaatsch, Joachim Schüz
NaReCHeM, Greece	PI: Eleni Petridou
Italy	PI: Corrado Magnani
Manchester, UK	PIs: Jillian Birch, Malcolm Taylor
United Kingdom Childhood Cancer Study (UKCCS), UK	PI: Eve Roman Authorized Delegate: Jill Simpson

Active Members of the CLIC Coordination Group

(continued)

24

Oceania

AUS-ALL, Australia

PIs: Elizabeth Milne, Bruce
Armstrong

New Zealand Childhood Case Control
Study

PI: John Dockerty

Proposed Childhood Leukemia Studies

25

Childhood Leukemia Studies in Planning Phases

Florida (Planning Phase)	PI: Mehmet Tevfik Dorak
Germany (Planning)	Bernd Grosche, Federal Office for Radiation Protection (BFS)
Guatemala (Planning Phase)	PI: Libby Morimoto
Japan (Planning Phase)	PIs: Yasushi Ishida, Shuki Mizutani

Proposed CLIC Papers

26

1. **Introductory Paper on CLIC**
2. **Fetal growth and risk of childhood acute lymphoblastic leukemia (ALL)**
3. **Vitamin/folate supplementation before and during pregnancy, MTHFR variants and risk of childhood ALL and acute myeloid leukemia (AML)**
4. **Parental smoking and xenobiotic-metabolizing gene variants**

Biospecimens in CLIC Studies

27

Bio-specimens for DNA Extraction	Number of <u>Studies</u> with Sources of DNA						
	Case-Child	Control-Child	Case-Mother	Case-Father	Control-Mother	Control-Father	Case Grand-parents
Blood	12	11	10	8	4	2	1
Saliva	5	5	5	4	2	1	1
Buccal Cells	4	4	4	3	3	2	2
ANBS	3	3	1	0	1	0	0

CLIC Database

28

- **Web-based inventory under development**
- **Surveys for availability of biospecimen, genetic, and cytogenetic data**
- **Seek additional funding to complete and maintain CLIC data harmonization**

CLIC Pooled Analyses

29

Name of Proposal (Year Proposed)	Lead Investigator
Maternal Folate and Alcohol Consumption, MTHFR Gene Variants and Risk of Childhood Leukemia (2007)	Catherine Metayer
Fetal Growth and Other Perinatal and Birth Characteristics and Risk of Childhood Leukemia (2009)	Elizabeth Milne
Parental smoking and xenobiotic-metabolizing gene variants (2009)	Claire Infante-Rivard
Early Infections, Day Care, Birth Order, and Childhood Leukemia (2009)	Jacqueline Clavel
Time-to-Pregnancy and Acute Lymphoblastic Leukemia (2011)	Claire Infante-Rivard
Benzene-related Home Exposures and Risk of Childhood Acute Myeloid Leukemia and Subtypes (2011)	Catherine Metayer

CLIC Pooled Analyses (continued)

30

Name of Proposal (Year Proposed)	Lead Investigator
Maternal Coffee and Tea Consumption During Pregnancy and Risk of Childhood Leukemia (2011)	Elizabeth Milne
Demographic, Disease and Socio-economic Status (SES) Characteristics in Relation to Childhood Leukemia Outcomes (2011)	Eleni Petridou
Exposure to Paints and the Risk of Childhood ALL (2011)	Joachim Schüz
Exposure to Pesticides and the Risk of Childhood Leukemia (2011)	Joachim Schüz
Geographical Distribution of Childhood AML Cytogenetic Subtypes (2011)	Luoping Zhang