



EUROPEAN COMMISSION
RESEARCH & INNOVATION DG

Periodic Report

Project No: 226285

Project Acronym: ENRIECO

Project Full Name: ENVIRONMENTAL HEALTH RISKS IN
EUROPEAN BIRTH COHORTS

Periodic Report

Period covered: from 01/03/2010 to 28/02/2011

Date of preparation: 29/04/2011

Start date of project: 01/03/2009

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Project coordinator name:

Prof. Mark Nieuwenhuijsen

Project coordinator organisation name:

FUNDACIO CENTRE DE RECERCA EN
EPIDEMIOLOGIA AMBIENTAL - CREAL

Version: 1

Periodic Report

PROJECT PERIODIC REPORT

Grant Agreement number:	226285
Project acronym:	ENRIECO
Project title:	ENVIRONMENTAL HEALTH RISKS IN EUROPEAN BIRTH COHORTS
Funding Scheme:	FP7-CSA-CA
Date of latest version of Annex I against which the assessment will be made:	07/09/2010
Period number:	2nd
Period covered - start date:	01/03/2010
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Declaration by the scientific representative of the project coordinator (1)

I, Prof. Mark Nieuwenhuijsen FUNDACIO CENTRE DE RECERCA EN EPIDEMIOLOGIA AMBIENTAL - CREAL , as scientific representative of the coordinator of the project ENRIECO and in line with the obligations as stated in Article II.2.3 of the Grant Agreement declare that:

The project has fully achieved its objectives and technical goals for the period.

The attached periodic report represents an accurate description of the work carried out in this project for this reporting period.

The public website is up to date.

To my best knowledge, the financial statements which are being submitted as part of this report are in line with the actual work carried out and are consistent with the report on the resources used for the project (section 6) and if applicable with the certificate on financial statement.

All beneficiaries, in particular non-profit public bodies, secondary and higher education establishments, research organisations and SMEs, have declared to have verified their legal status. Any changes have been reported under section 5 (Project Management) in accordance with Article II.3.f of the Grant Agreement.

Name	Prof. Mark Nieuwenhuijsen FUNDACIO CENTRE DE RECERCA EN EPIDEMIOLOGIA AMBIENTAL - CREAL
Date	29/04/2011

This declaration was visaed electronically by Diana VAN GENT (ECAS user name nvangedi) on 29/04/2011 at 29/04/2011 16:02:26 CET

1. Publishable summary

Summary description of project context and objectives

Epidemiological studies have shown associations between environmental pollutants and adverse child health outcomes, which may result in substantial economic and societal costs. There are many pregnancy and birth cohorts in Europe with information on environment and health. However, the wealth of available information has only been partially exploited, and there is a lack of statistical power in single studies which study rare health outcomes or exposures with a low prevalence. Therefore, an urgent need exists to evaluate, and where possible combine, the existing environmental exposure and health data, methods and tools from European birth cohort studies in order to evaluate any causal links between exposing agents and health and to provide recommendations for effective policy decisions to improve children's environmental health and reduce economic and societal costs.

The overall aim of ENRIECO is to advance our knowledge on specific environment and health causal relationships in pregnancy and birth cohorts by providing support to exploitation of the wealth of data generated by past or ongoing studies funded by the EC and national programmes. Specific objectives are to make inventories of birth cohorts, assure quality and interoperability of exposure, health and exposure-response data, obtain data access, build databases, conduct analysis, make recommendations for data collection in the future to improve environment-health linkages and information, and disseminate this information. The project intended to bring together over 30 pregnancy and birth cohorts and information on around 250,000 newborns, infants and children from across Europe. The anticipated outcome was the structuring and consolidation of often fragmented data from various studies undertaken throughout Europe, which will improve the knowledge base for FP 7 Cooperation Work Programme 2008: Environment (including climate change) environment and health linkages. Furthermore, data regarding environment-health causal relationships were set to be more readily available in a form useful for policy makers.

To achieve the above, specific objectives determined by work packages were to:

- Make inventories of birth cohorts, including; health data; exposure data; biological samples; environmental exposure response functions; expertise and access.
- Assure quality and interoperability and validate exposure, health and exposure-response data through extraction and rigorous evaluation of quality of the data, (including developing protocols describing the strategic approach); evaluation of opportunities and validation/testing studies (through case studies).
- Obtain data access, build databases, and conduct analysis including setting up protocols for data access database building and analyses; setting up protocols for exposure response analyses; conducting specific analyses on exposure and health data to obtain exposure response functions (through case studies) and conducting specific meta/pooled analyses to obtain exposure response functions (through case studies).
- Make recommendations for data collection in the future to improve environment-health linkages and information for data collection (exposure, health etc), possible analyses (laboratory and statistical) and exchange of knowledge between older and newer cohorts.
- Disseminate information to the scientific community, policy makers and general public through a project website, virtual network, workshops, easy accessible info and a database with exposure response functions.

To this end, the project was divided into scientific workpackages: WP1 - Inventory of birth cohorts; WP2 - Evaluation of health outcomes; WP3 - Evaluation of health outcomes; WP4 - Evaluation of exposure-response relationships; WP5 - Database building; WP6 - Dissemination. Within these, 27 topical working groups and three case studies were established. Details of this structure are provided in Table 1 of Annex I.

The overall management of the work is led by CREAL (WP7).

Description of work performed and main results

The foundation of the project formed the development of a searchable cohort database as a major resource. Birth cohorts included were selected on basis of a set of criteria: studies had to be based in a European country and cover at least 200 mother-child pairs; include collected data on at least one

environmental exposure topic; enrolment started during pregnancy or at birth and required at least one follow-up point after birth. An inventory questionnaire was developed and used for information collection. Enquiries were made regarding basic protocol details and exposure and outcome assessments, including specific contaminants, methods and samples, timing, and number of subjects. The full inventory is publicly available as a searchable database at www.birthcohortsenrieco.net. Questionnaires were completed by 36 cohorts in 19 European countries that are studying a total of more than 350,000 mother-child pairs. All cohorts collected biological specimens of children or parents. Many cohorts collected information on passive smoking (n=35), maternal occupation (n=32), outdoor air pollution (n=26) and allergens/biological organisms (n=26). Fewer cohorts (n=12 to 16) collected information on water contamination, ionizing or non-ionizing radiation exposures, noise, metals, persistent organic pollutants, or other pollutants. All cohorts have information on birth outcomes, nearly all on asthma, allergies, childhood growth and obesity, and 25 collect information on child neurodevelopment.

The ENRIECO inventory is the first to make this information publicly available. It is intended to facilitate collaborations between birth cohort researchers in this field and can be searched to identify cohorts relevant for comparison and replication studies, or for combined analyses with pooled or non-pooled data. Moreover, it may be used by policy makers and other stakeholders to identify birth cohorts that can provide specific information on environmental exposures or related outcomes. The inventory should form the basis for a long-term cohort coordination infrastructure.

The aims of WP2 were to evaluate existing environmental exposure information of the cohorts, to assure quality and interoperability and to make recommendations for future analyses either as individual cohorts or by pooling cohorts, and for exposure assessment methods. Working groups (WGs) consisting of experts in the field evaluated the information from the inventory regarding different exposures and made recommendations for future research. During the first months of the project, the different working groups developed short questionnaires to collect the relevant information regarding exposure assessment methods and tools from the cohorts for the inventory. Then, protocols for the evaluation were developed and tasks were distributed among working group members.

During the following months the WGs performed reviewed the exposure information that is available in the cohort studies and wrote concise informative reports. Reviews included a description of the current available data of European birth cohorts; details on protocols; and evaluations of assessment methods including the comparability of methods and protocols between studies and were largely based on the inventory. The recommendations for future research in European birth cohorts given by the working groups to a large extent depend on expert judgement. Included are recommendations for individual cohorts as well as recommendations for pooling cohorts and for exposure assessment methods. Suggestions have also been made for potential further use of methods and tools in cohorts where they did not exist or where there had been insufficient use with an emphasis on methods that are appropriate and feasible within the context of birth cohort studies.

WP3 focused on health outcomes available within the existing birth cohorts in EU countries. The health outcomes covered are pregnancy related outcomes, childhood allergy and asthma, neurobehavioral/cognitive function, cancer and child growth, metabolic and endocrine disorder. For each type of health outcome a WG evaluated the existing diagnostic criteria, the corresponding assessment tools and source of measurement error. Then, each WG proposed homogeneous groups of cohorts in term of assessment of the health outcome and calculated the numbers of participants in each group to highlight further combined analyses between outcomes and exposures and made recommendations for new analyses of existing cohorts, future follow up and data collection in the future cohort studies. A previous defined framework allowed harmonizing work between the WGs. Each WG was able to go to the end of the protocol for at least two health outcomes. The WP included a case-study on Persistent Organic Pollutants (POPs) and reproductive outcomes or children's health. Results of these have been published separately.

WP4 systematically collected information from the existing exposure response data including the methods and tools that were used from European birth- and pregnancy cohorts. Based on systematic reviews in each WG, the current status of existing environmental exposure-response data was presented and recommendations for further use of the data were made. The exposure of interest

within the twelve participating working groups varied considerably. The majority of the WGs were focused on the association between environmental exposure and birth outcomes such as still birth, prematurity and growth, followed by allergy and neurobehavioral function. Based on the results, there was good evidence that exposure to second hand smoke (SHS), ambient air pollution and domestic visible mould was associated with adverse birth outcomes and allergic respiratory diseases in infants and children.

The amount of published data on each specific exposure-response relationships differed considerably between the single WGs:

There was good evidence for an association between exposure to second hand smoke (SHS) in relation to adverse birth outcomes, ambient air pollutions caused by traffic in relation to asthma and domestic visible mould in relation to wheeze, asthma and rhinitis symptoms in European and non-European investigations. Further, occupational hazards including pesticides can adversely affect reproduction and pregnancy outcomes and recent studies observed that exposure to Persistent Organic Pollutants (POPs) were related to harmful impact on neurodevelopment impairment in children. Literature indicated some evidence for an association between ambient air pollution, drinking water exposure to disinfection by-products (DBPs), metals and polychlorinated biphenyls (PCBs) and a number of birth and pregnancy outcomes. In terms of neurobehavioral impairments, there is evidence that high exposure to metals might have neurotoxic effects in children, but effects at low levels are less well understood. Lastly, there was no evidence that chronic noise exposure of pregnant women was related to adverse birth outcomes, but the available body of evidence is limited.

The WPs produced details including methodology and topic specific recommendations. These have been submitted to the EC and are also available through the project website: www.enrieco.org.

To establish and reinforce links with participating cohorts, a kick-off meeting and cohort workshop were organised in Barcelona, Spain, in 2009 and the follow-up workshop in Utrecht, The Netherlands, in 2010 in collaboration with the management team. Extensive reports outlining the discussions have been published following the meetings.

Dissemination of project activities and results are the responsibility of WP5 which launched an active tiered website at the start of the project (www.enrieco.org).

A Dissemination Strategy was prepared describing the principles of the dissemination strategy, as well as its tools and plan for effective dissemination of project results. For this, project branding, including a logo (see Annex I, Fig. 3) was created. Written materials included a web-based project brochure with general information about ENRIECO for interested parties, newsletters, supplement and a leaflet summarizing final outcomes (Annex I, Fig. 4 & 5). Aside from oral and poster presentations during scientific meetings, to which all partners contributed, an article was published about ENRIECO in The Parliament Magazine.

Final results of the project will be disseminated to international media through a press release by the Coordinator.

Expected final results and potential impacts

ENRIECO has proven to provide a much needed resource for cohort experts in environmental health. The project has brought together environmental data information of 36 birth cohorts in the publicly available online ENRIECO Inventory: www.birthcohortsenrieco.net. It forms an extensive cohort data resource together with the earlier established www.birthcohorts.net.

We have shown that many pregnancy and birth cohorts exist with information on environmental exposures and health outcomes, covering Europe fairly well, to a lesser extend Eastern Europe. Considerable expertise and experience is associated with these cohorts, complimented by great effort. Overall, greater and more efficient use needs to be made of the existing cohort data at the European level to provide timely response to key policy questions and concerns about "new" environmental exposures, to improve methodology and power, understanding of geographical and cultural inequalities in disease, exposure and health related behaviours. Replication of findings with important public health implications in different settings should be addressed, as well as improvement of statistical power through combined analysis. Cohorts should also improve links with routinely collected environmental and health data, as much data is currently available, but unused.

Follow-up of existing cohorts is essential to determine health effects in later life of pre natal and early childhood exposure, for which there is some but not conclusive evidence. New environmental exposures, or existing environmental exposures under new conditions would benefit from new pregnancy and birth cohorts to enable evaluation of any potential health effects.

Cohorts provide important environmental exposure, health and environmental exposure-response data, yet the amount and detail of information provided on environment and health varies considerably. Cohorts tend to report individually, but recent initiatives have tried to combine data from various cohorts to increase e.g. power (overall and subgroups). Existing European birth and mother-child cohorts provide a real potential for combined analyses on pregnancy-related outcomes and child health outcomes in relation to environmental exposures.

Combining data from various cohorts requires careful consideration of the aims, protocols, data, ethical issues, analyses and management, and it is time and labour intensive but potential fruitful. There are currently limited resources for this.

Methodological and scientific developments and substantive results of this project are being disseminated to a wide user community of academics, public health departments, and policy makers throughout Europe. Every effort was made to ensure that interim results of the project were made widely available and accessible to all such user-groups. Long-term uptake and use of the project outcomes requires that knowledge about the project is invested in a wide range of both end users and intermediate users (e.g. service providers). To this aim, the ENRIECO website will be actively managed and updated for the next 2 years (March 2011 - February 2013) with new ENRIECO reports and partner publications. It will continue to provide regularly news, reports, and publications related to the project and share these with the scientific community, the policy makers, NGOs, the general public, and all related stakeholders. The project activities and results are summarized in a final newsletter and a leaflet for distribution to the target audiences. We will release information to international and national media with the intention to achieve broad coverage through non-scientific means in particular.

ENRIECO findings will be published in leading, international, peer-reviewed journals in the key fields of interest, including exposure assessment, water, epidemiological, and public health journals, including: Nature and Science for high level, overview papers; Epidemiology, British Medical Journal, Lancet, European Journal of Public Health and Environmental Health Perspectives for results relating to environmental epidemiology and public health; Environmental Science and Technology, Environmental Toxicology and Chemistry and Environmental Pollution for results relating to environmental monitoring, biomonitoring and environmental systems; Biostatistics, Statistics in Medicine and Journal of the Royal Statistical Society for statistical methodologies; and Risk Analysis and Environmental Modelling and Assessment for more general results on risk assessment methodologies. See Annex I for a list of anticipated scientific publications. Further efforts will be made to raise awareness about the project and its outcomes, and to encourage their use, through the many policy networks with which partners are involved at national and international level. Inter alia, these include the various Directorates of the EU, the European Environment Agency and its topic centres, Members States' environmental and health ministries, and regional and local authorities.

Contact will be pursued with other EU and non-EU funded research projects and ENRIECO project's findings forwarded, such as CHICOS, HIWATE, ESCAPE, EnviroGenoMarkers, MeDALL, Ga2len and The National Children's Study (USA)

Project public website address:

www.enrieco.org

2. Core of the report

Project objectives, Work progress and achievements, and project management during the period

The Project Summary Pdf document contains the core of the report.

3. Deliverables and milestones tables

Deliverables (excluding the periodic and final reports)										
Del. no.	Deliverable name	Version	WP no.	Lead beneficiary	Nature	Dissemination level	Delivery date from Annex I (proj month)	Actual / Forecast delivery date	Status	Comments
10	Periodic Report Year 1	1.0					0	28/04/2010	Submitted	
11	Report for Workshop for User Groups	1.0					0	27/07/2010	Submitted	
22	D17_WP3_report.pdf	1.0					0	09/12/2010	Submitted	
23	D18_WP3_P OPs_case_study_report_presub.pdf	1.0					0	09/12/2010	Submitted	
24	D19_WP4_report.pdf	1.0					0	09/12/2010	Submitted	
13	Searchable database of birth cohorts	1.0	1	FUNDACIO CENTRE DE RECERCA EN EPIDEMIOLOGIA AMBIENTAL - CREAL	Other	PU	21	30/11/2010	Submitted	
14	Scientific paper with and inventory of European birth cohorts on environment and health	1.0	1	FUNDACIO CENTRE DE RECERCA EN EPIDEMIOLOGIA AMBIENTAL - CREAL	Report	PU	21	30/11/2010	Submitted	
26	Scientific paper with	1.0	1	FUNDACIO CENTRE DE	Report	PU	21	28/02/2011	Submitted	

	h and inventory of European birth cohorts on environment and health			RECERCA EN EPIDEMIOLOGIA AMBIENTAL - CREAL						
3	Protocol for evaluation of environmental exposure information	1.0	2				0	25/03/2010	Submitted	
15	Report with evaluation of environmental information and recommendations	1.0	2	UNIVERSITEIT UTRECHT	Report	PU	21	30/11/2010	Submitted	
16	Report of methods and approaches of evaluating occupational exposures in European birth cohorts	1.0	2	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)	Report	PU	21	30/11/2010	Submitted	
25	Evaluation of Environmental Information and Recommendations	1.0	2	UNIVERSITEIT UTRECHT	Report	PU	21	28/02/2011	Submitted	
4	Protocol for evaluation of health inform	1.0	3				0	25/03/2010	Submitted	

	ation									
17	Persistent Organic Pollutant (POP) Case Study	1.0	3	AARHUS UNIVERSITETSHOSPITAL, AARHUS SYGEHUS	Report	PU	21	30/11/2010	Submitted	
18	Report with evaluation of health information and recommendations in European birth cohorts	1.0	3	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)	Report	PU	21	30/11/2010	Submitted	
27	Report with evaluation of health information and recommendations in European birth cohorts	1.0	3	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)	Report	PU	21	28/02/2011	Submitted	
28	Persistent Organic Pollutant (POP) Case Study	1.0	3	AARHUS UNIVERSITETSHOSPITAL, AARHUS SYGEHUS	Report	PU	21	28/02/2011	Submitted	
5	Protocol for evaluation of environmental exposure response information	1.0	4				0	25/03/2010	Submitted	
21	Report with evaluation of environmental exposure-response in	1.0	4	HELMHOLTZ ZENTRUM MUENCHEN DEUTSCHES FORSCHUNGSZENTRUM FUER	Report	PU	21	30/11/2010	Submitted	

	formation and recommendations in European birth cohorts			GESUNDHEIT UND UMWELT GMBH						
29	Report with evaluation of environmental exposure-response in formation and recommendations in European birth cohorts	1.0	4	HELMHOLTZ ZENTRUM MUENCHEN DEUTSCHES FORSCHUNGSZENTRUM FUER GESUNDHEIT UND UMWELT GMBH	Report	PU	21	28/02/2011	Submitted	
6	Protocol for database building	1.0	5				0	25/03/2010	Submitted	
7	Protocols for indoor exposures and allergy and asthma case study	1.0	5				0	25/03/2010	Submitted	
20	Report on exposure-response relationships for the case studies on indoor exposures (ETS and dampness) and allergy and as	1.0	5	CHARITE - UNIVERSITAETSMEDIZIN BERLIN	Report	PU	21	30/11/2010	Submitted	

	thma									
30	Report on exposure-response relationships for the case studies on indoor exposures (ETS and dampness) and allergy and asthma	1.0	5	CHARITE - UNIVERSITAETS MEDIZIN BERLIN	Report	PU	21	28/02/2011	Submitted	
1	Project Website - www.enrieco.org	1.0	6				0	25/03/2010	Submitted	
2	Web based project brochure with simple information	1.0	6				0	25/03/2010	Submitted	
8	Dissemination strategy	1.0	6				0	25/03/2010	Submitted	
9	Project newsletter no 1	1.0	6				0	25/03/2010	Submitted	
12	Project Newsletter	1.0	6	PANEPISTIMIO KRITIS (UNIVERSITY OF CRETE)	Other	PU	20	29/11/2010	Submitted	
19	Dissemination material	1.0	6	PANEPISTIMIO KRITIS (UNIVERSITY OF CRETE)	Other	PU	21	30/11/2010	Submitted	
31	Project Newsletter n	1.0	6	PANEPISTIMIO KRITIS	Report	PU	18	19/04/2011	Submitted	

	o 2			(UNIVERSITY OF CRETE)						
32	Dissemination material	1.0	6	PANEPISTIMIO KRITIS (UNIVERSITY OF CRETE)	Other	PU	21	19/04/2011	Submitted	

Milestones

Milestone no.	Milestone name	Work package no	Lead beneficiary	Delivery date from Annex I	Achieved Yes/No	Actual / Forecast achievement date	Comments
1	First workshop	6	UoC	31/07/2009	Yes	28/05/2009	Moved forward to benefit early development of work strategies
2	Presentation and discussion of overall strategy and protocols at first workshop.	1	CREAL	31/07/2009	Yes	29/05/2009	
3	Periodic report for year 1	1	CREAL	27/02/2010	Yes	28/04/2010	Within required reporting period
4	Second workshop	6	UoC	31/08/2010	Yes	26/05/2010	
5	Searchable database of birth cohorts on internet	1	CREAL	30/11/2011	Yes	30/11/2010	
6	Final Report	7	CREAL	28/02/2011	Yes	29/04/2011	Within required reporting period

Attachments	ENRIECO_Project_Summary_Annex_I.pdf, ENRIECO_PR2_Core_Report_final.pdf
Grant Agreement number:	226285
Project acronym:	ENRIECO
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Name of the scientific representative of the project's coordinator and organisation:	Prof. Mark Nieuwenhuijsen FUNDACIO CENTRE DE RECERCA EN EPIDEMIOLOGIA AMBIENTAL - CREAL
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