

Organisation

AIRPOLIFE had a successful full assembly in June in Copenhagen with more than 50 participants, including 3 international. The program included presentation and discussion of all WPs as well as 3 international presentations.

AIRPOLIFE has had running contact including several personal meetings with the International Advisory Board (IAB, Paul Borm, Gerard Hoek, Paolo Vineis), who have commented the status report of 2006, WP progress and given further advice. The steering committee has had four coordination meetings in 2006 and discussed revision and progress in the WPs. The PI and partner committee has met twice in 2006. The scientific forums have served as discussion forums and researcher educations with frequent meetings with discussion of WP details, progress and results as well as related projects and relevant literature.

There has been no change in formal partners in 2007. The intense collaboration with Statens Seruminstitut (Paal Skytt Andersen, WP3C/D), The Pharmaceutical Faculty of Copenhagen University (Majid Sheykhzade, WP4D), the Building Research Institute (WP1B), Lund, Gothenburg and Leuven Universities (WP1B) has continued. A few WPs are still behind the original plans due to the 7 maternity leaves and delayed delivery of exposure data for most of the epidemiological work packages, which will postpone some work. A part of the budget will be transferred to 2008-9 and we ask for continuation of the whole program through 2009. For 2008 a small part of the budget will be transferred from UCIPH to ICE due to post.doc. work.

Dissemination of results and knowledge and research education

AIRPOLIFE has continued the web page (www.airpolife.dk), with presentation of the entire project, new results and general information on health effects of air pollution. In 2007 3 PhD student from AIRPOLIFE successfully defended their thesis. Currently, 3 finished and 12 ongoing or coming PhD students, 5 postdocs and 6 masters students are associated with AIRPOLIFE.

AIRPOLIFE has been presented at a number of international occasions,. AIRPOLIFE and its partners have published a number of articles and in science communication journals, given public lectures and participated extensively in media work in relation to the program. E.g. Steffen Loft has been interviewed in radio, television or national newspapers more than 20 times in 2007, www.infomedia.dk, and recently three 3-10 min interviews on the program results have been given. Together with other AIRPOLIFE members Steffen Loft has given evidence to the Danish EPA and the Environmental committee of the Danish Parliament.

Progress, revision and status of work packages

The detailed descriptions of each work package with time schedules have been followed up with frequent status updates and milestone monitoring as a dynamic tool to monitor progression. A summary of each is presented below. Full descriptions are available.

WP1AA. Physical-chemical characterization of particulate air pollution.

PI: Peter Wählin^{NERI AE}, key researchers: Matthias Ketzl^{NERI AE}, Finn Palmgren^{NERI AE}, Jacob G. Mønster^{NERI AE}, Rossana Bossi^{NERI AE}, Keld Alstrup Jensen^{NRCWE}

Aim: To provide detailed physico-chemical characterization particulate air-pollution from specific sources and input on particle composition and source contributions for epidemiological and toxicological studies on adverse health effects from particulate air-pollution.

External Partners: University of Lund (volatility measurements), University of Copenhagen (XRD and DMPS measurements); Aarhus University (Electron Microprobe Analysis); University of Michigan (HAADF STEM); EC Joint Research Centre, Ispra, Italy (PAH and nitro-PAH analysis).

Status of the project March 2007.

Metal Speciation: The indoor-outdoor study of PM_{2.5}, PAHs and metals combined with OSPM modeling of PM_{2.5} was completed and the MSc. thesis was successfully defended in 2006. The work is currently in final preparation for publication. A MSc-study was established in 2005 to quantify the relationships between water-soluble elements in indoor, outdoor and personal PM_{2.5} samples in collaboration with the Danish Cancer Society. Unfortunately the MSC. candidate finally had to terminate the project owing to disease. The project is now completed by the NRCWE staff. Another analysis of the particle characteristics and indoor-outdoor relationships between particle types and elements in size-fractioned authentic air-pollution samples at an uninhabited apartment has been finalized using various advanced electron microscopy methods (EM) and will be submitted spring 2008. Similarly a detailed study of the particle characteristics, metals speciation and water-solubility of elements in diesel particle samples SRM1649a and a VW-1600TD tail-pipe deposits will be submitted for publication in the spring 2008 combining results from in vitro toxicological analysis. Finally, the originally planned 2006 campaign for collecting brake-wear particles and subsequent chemical and in vitro toxicological characterization has been postponed until a spring and summer 2008 and will be completed by NRCWE.

EC/OC: The investigations using soot monitors were continued. The monitors were successfully used to study indoor and outdoor air pollution from residential wood combustion. Specific organic tracers were analysed in particle samples from areas with wood combustion and traffic. The results have been published or are in the process of being published in peer-reviewed journals. In addition two master thesis projects based on the project have been finished in addition to one thesis applying methods developed within the project. Currently the MSc.-study focusing on the the indoor-outdoor concentration of PM_{2.5}, PAH's and elements in shops along high traffic streets is in preparation for publication. The results show an important contribution to elements and PM_{2.5} from indoor sources, especially during the winter campaign.

In-vitro bioassays: We have completed bioassays of diesel emission particles. The results from that study will be published in conjunction with the physico-chemical analysis, mentioned above. The in vitro study of break-wear particles is postponed until early fall 2007, owing to the delayed field-campaign for collection of brake-wear particles. Due to the delay, the results from this study will not be submitted for publication before 2008.

WPIAB Exposure assessment.

PI: Martin Hvidberg key researchers: Martin Hvidberg, Steen Solvang Jensen, Ruwim Berkowicz, Ole Hertel, Matthias Ketzel, all NERIAE.

Aim: "Development of model based assessment of historical air pollution exposure with high capacity and accuracy"

Status:

1) "Data will be established to describe developments in road network, traffic density, building erection and hight." Completed: Q4 2007. Status: 100% complete

1a) Completed data on road network development and traffic density was evaluated and a decision was made to allocate additional resources, beyond the original WP description, to improve the result. Especially the information on medium size roads seemed to be too evenly distributed. Part of the resources for these improvements are drawn from this WP, by removing task 3. The remaining resource demands are sponsored by the partners. Completed: Q4 2007. Status: 100% complete

1b) Data on building erection and hight. Completed Q1 2006. Status 100%

2) "The AirGIS system will be further developed to take into account the historical changes in urban building and street structure and propagation in time using information from the building and housing registry as well as the developed street data base." Completed: Q1 2005. Status: 100% complete.

3) "Historical records for regional and urban background levels of fine and ultra fine particle concentrations are derived together with historical records of emissions factors." Analysis of what is available to establish information about temporal development in the levels fine and ultra fine particles in Denmark have led to the conclusion that the information is insufficient to establish trustworthy time series. The available information it is not sufficient for deriving realistic model estimates of the levels and exposure nor for further comparison with human health outcome. This part has therefore been excluded from the WP. Resources used for task 1b. Status: 0% completed

4) "As the composition of the car fleet has changed considerably over time, data are collected in order to improve emission estimates". Completed: Ultimo 2005 Status: 100% completed

5) "For the regional background, emission inventories are available back to the 1980'ties. Best available estimates are applied for going back to the 1960'ties. Completed: Q2 2005 Status 100%

6) "The AirGIS system will be optimised for exposure assessments in a human lifetime perspective." Finalisation of the batch-mode modules are still outstanding. Completed: Q4 2007 Status: 100% complete

7) "The spatial distribution of traffic on the urban street network is modelled roughly based on counts in specific locations and an assumption that streets of same class carry same load of traffic. These estimates will be sought verified and improved by use of remote sensing and spatial statistics." This part have been excluded to allow the resources to be allocated to part 1a. Status: 0% complete

8) "During model simplification, these assessments are compared to relatively simple assessment of local exposure based on one or more parameters as; distance to (busy) streets, address density within a buffer, traffic intensity within a buffer, number of (high trafficked) streets within a buffer, etc. all inferred from GIS operation. "Some estimated have been delivered, others are to be developed. Completed Q2 2008 Status 75% completed.

Remaining activities. Adjusting the tools to generate "proxi" estimates, to meet the requirements from the epidemiological studies. Q2 2008

WPIB Personal Monitoring

PI: Steffen Loft^{UCIPH} *key researchers:* _Elvira Vaclavik^{UCIPH}, Peter Vinzents^{UCIPH}, Peter Møller^{UCIPH}, Lars Dragsted^{IFN}, Herman Autrup^{AU}, Jann Mortensen^{RHPET}, Ole Hertel^{NERIAE}, Marianne Glasius^{NERIAE}, Finn Palmgren^{NERIAE}, Peter Wählin^{NERIAE}, Matthias Ketzel^{NERIAE}, Mette Sørensen^{UCIPH+ICE}, Ole Raaschou-Nielsen^{ICE}.

External Partners: Lars Gunnarsen, Danish Building and Urban Research; Erik Swietlicki and Jakob Löndahl, Lund University (LU), Lars Barregård, Gotenburg University, Alfred Bernard, Leuven University

Aim: To study associations between controlled exposure to ultrafine particles and biological effects.

Status 08: The effect of traffic-generated particles in 30 healthy young non-smoking subjects in exposure chambers on alveolar integrity, mucociliar, lung and endothelial function, deposition of ultrafine particles, biomarkers of oxidative stress, inflammation, DNA damage and gene regulatory responses resulted in published papers on deposition and oxidative damage to DNA, whereas papers on cardiovascular functions and lung function have been submitted. The paper on improved endothelial function among 41 elderly subjects by filtering the indoor air for ultrafine particles has been accepted. New biomarkers for inflammatory gene expression responses have been developed and applied on the material. The data are under analysis.

WP2A Placenta particle transfer

PI Lisbeth E. Knudsen^{UCIPH}, key researcher Tina Dam Mikkelsen^{UCIPH} PhD student.

Aim: To study passage of ultrafine particles and function in human placenta

Status: The placental perfusion system is well established and functional. It has been validated by concurrent experiments in Kuopio and Copenhagen. Passage of ultrafine goldlabelled particles through the placenta barrier was to be detected by electron microscopy. However, due to lack of suitable methods to quantitate particles the WP cannot be completed.

WP2B Intrauterine exposure models

PI Håkan Wallin^{AMI}, key researcher post.doc. Karin Sørig Hougård^{AMI}, Anja Wellejus^{UCIPH}

Aim: Study effects of intrauterine exposure to air pollution particles on cognitive function.

Status: The exposure was completed late in 2006 and in early 2007. A paper has been accepted on postnatal development, behavior, genotoxicity, and inflammation has been accepted. Reproductive effects in male offspring have been studied and this has continued in 2008.

WP2C Target organ exposure in humans

PI Lisbeth E. Knudsen^{UCIPH}, Marie Pedersen PhD student^{UCIPH}, Tina Dam Mikkelsen PhD student^{UCIPH}, Sanne^{UCIPH}, Steffen Loft^{UCIPH}, Peter Møller^{UCIPH} Peter Wählin^{NERIAE}, Herman Autrup^{AU}, Ole Hertel^{NERIAE}

Aim: Study associations between personal exposure to particles assessed by monitors and biomarker responses related to oxidative stress.

Status Sampling of blood and tissue and monitoring of air pollutants in their home for 4 days prior to caesarean section has been for 43 pregnant women. Nitrogen oxides, size distribution and chemical analysis of particles fractions have been measured. DNA repair capacity has been measured in the first 20 women. WP2C collaborate with NewGeneris an EU FP6 project and a Research Council program on exposure to flame retardants.

WP2D Early exposure, birth weight, perinatal/infant mortality and early childhood airway disease

PI: Ole Raaschou-Nielsen^{ICE}

Aims: To study the hypotheses that exposure to air pollution decreases birth weight, increase infant mortality and increases early childhood airway disease by means of the National Birth Cohort.

Status 10/3 -08: The exposure data are now ready and data analysis will commence.

WP3A. Indoor air pollution and childhood asthma

PI: Ole Raaschou-Nielsen^{ICE}

Aims: To investigate a possible influence of indoor air pollution on airway symptoms in 400 young children at risk of atopic disease.

Status 14/2-06: The 1200 performed sets of indoor measurements of air pollution have been analyzed. Airway episodes during the first 18 months of life has been registered and included in the measurement data file. When ready the modeled data of outdoor air pollution will be included in 2008.

Status 31/3-08: A paper on association between measured exposure and symptoms has been submitted and a paper related to predictors of exposure is under preparation.

WP3C Gene-environment interactions in childhood asthma

PIs: Herman Autrup and Steffen Loft. *key researchers:* Marianne Poulsen PhD student^{RHMG+UCIPH} Anne Tybjærg-Hansen^{RHMG}, Ruth Frikke-Schmidt^{RHMG} Participants: Ole Raaschou-Nielsen^{ICE}, Mette Sørensen^{ICE}, Ulla Vogel^{NIOH}, Ole Hertel^{NERIAE}, Steen Solvang Jensen^{NERIAE}

Status 31.3.08. The genotyping of the set of 1000 cases of airway disease and 1000 controls from the National Birth Cohort in close collaboration with WP3D for SNPs in metabolism and oxidative stress genes has been completed based on genomically amplified DNA. The copy number variation in GSTs has required good quality original DNA, which is being isolated currently.

WP3D. Airway symptoms in children: inflammation genes, air pollution and ETS (replaces WP3B) PI Ole Raaschou-Nielsen^{ICE}, *key researchers:* Mette Sørensen^{ICE}, Leila Allermann Møller^{NIOH}, Ulla Vogel^{NIOH}, Steffen Loft^{UCIPH}, Ole Hertel^{NERIAE}, Steen Solvang Jensen^{NERIAE}

Aims. To study associations between polymorphisms in inflammation genes and interactions with air pollution, in association with airway symptoms in 18 months old children from the National Birth Cohort.

Status 31/3-08: 1000 cases and 1000 controls have been selected. DNA has been purified from blood samples. 8 polymorphisms in inflammation genes have been analysed. A manuscript on polymorphisms in inflammation genes, exposure to tobacco smoke and furred pets and risk of recurrent wheeze in children has been submitted. We expect air pollution exposure data in first half of 2008 for analysis.

WP4A. Cardiovascular disease models

PI: Peter Møller, key researchers: Janne Kjærgaard PhD student^{UCIPH}, Lone Mikkelsen PhD student^{UCIPH}, Lise Vesterdal coming PhD student^{UCIPH}, Christian Stevns-Hansen^{UCIPH+DP}, Steffen Loft^{UCIPH}, Majid Sheykzade Pharmaceutical Faculty, Thomas Jonassen^{UCDP}, Håkan Wallin^{NIOH}

Aim: study cardiovascular effects of particles in animal models

Status: Studies of short-term effect in ApoE^{-/-} and ApoE^{+/+} mice have been continued with respect to inflammation, gene expression and oxidative stress in aorta and non-vascular target organs and endothelial function. Intratracheal instillation and systemic administration studies with a variety of nanosized particles have shown that ApoE^{-/-} mice are also more susceptible to airway exposure for the pulmonary effects, although no effect on endothelial function was found, whereas systemic administration of engineered nanoparticles induced endothelial dysfunction as diesel particles do. Studies of different *luc* reporter mice will continue with a new camera. A paper on lung effects has been submitted and another paper on vascular effects is almost ready for submission.

WP4B Mortality, cancer and hospital admission in relation to air pollution – a cohort study

PI : Ole Raaschou-Nielsen^{ICE}, key researchers: Martin Hvidberg^{NERIAE}, Steen Solvang Jensen^{NERIAE}, Ole Hertel^{NERIAE}, Anne Tjønneland^{ICE}, Mette Sørensen^{ICE}

Aims: To study the hypotheses that exposure to ambient air pollution assessed by modelling at the address increases mortality, cancer and hospital admissions in the Diet Cancer and Health Cohort of 57.000 individuals recruited 1993-1997.

Status per 29/2-2008: Air pollution data was delivered by January 2008. Presently, we control these data and collect/clean up cancer incidence data for the cohort, to prepare the cancer risk analyses.

WP4C. Time-series analysis of CVD and respiratory disease

PI Steffen Loft. Key researchers Zorana Andersen^{UCIPH} (PhD student), Finn Palmgren^{NERIAE}, Peter Wählin^{NERIAE}, Marianne Glasius^{NERIAE}, Thomas Scheike^{UCIPH}, Ole Raaschou-Nielsen^{ICE}

Aim: study associations between daily levels of air pollutants and health outcomes in Danish cities.

Status per 31.3.08: Associations have been shown between daily levels of particles (PM10) and traffic related gases and all admissions for cardiovascular, lung disease and stroke in elderly and asthma in children during 1999-2006 in Copenhagen as well as for specific sources of PM10 and size distribution of ultrafine particles in the last part of this period. One paper has been published and another accepted. A case-cross over study on stroke and daily air pollutant levels is close to being ready for submission. A case-cross-over study on admissions among a cohort of 100.000 related to monitor and modelled exposure data at the address is ongoing. The paper on daily airway symptoms among 411 children with high risk of atopic disease associated with monitor data during their first 36 months of life has been accepted. Analysis of symptoms in relation to daily modelled levels of air pollution at home and day care address and their proximity to busy streets is ongoing.

WP4D. Gene-environment interactions and oxidative stress in acute CVD and airway disease

PIs Anne Tybjaerg-Hansen and Steffen Loft. Key researchers: Marianne Poulsen (PhD student 1.2.05)^{RHMG+UCIPH}, Ruth Frikke-Schmidt^{RHMG}, Mette Sørensen^{UCIPH+ICE}, Zorana Andersen^{UCIPH}, Thomas Scheike^{UCIPH}, Ole Raaschou-Nielsen^{ICE}, Martin Hvidberg^{NERIAE}, Ole Hertel^{NERIAE}, Steen Solvang Jensen^{NERIAE}

Aim: To study effect modification by genes related to metabolism, oxidative stress, inflammation and airway defence on CVD and airway disease among 9.200 from the Copenhagen City Heart Study and in a case-cohort design based on the Diet Cancer and Health Cohort as well as case-cross over design with respect to acute events in both cohorts.

Status per 31.3.08: Address history of the cohort has been established. Exposure data based on WP1AB and WP4B have been received early 2008. Target genes have been selected: GSTM1, GSTT1 and GSTP1. A new high throughput analysis for the allele copy number of M1 and T1 has been developed and a paper submitted for publication. Genotyping of M1, T1 and P1 has been completed for the whole cohort as well as in several verification cohorts related to interesting findings on risks of gender specific cancers. The PhD student has returned from maternity second half of 2007.

WP5A. Experimental study of cancer mechanisms

PI: Håkan Wallin^{NIOH}, key researchers Niklas Raun Jensen (PhD student)^{NIOH+UCIPH}, Herman Autrup^{AU}, Steffen Loft^{UCIPH}, Peter Møller^{UCIPH}, post.doc. Lotte Risom^{UCIPH}, Anne Thoustrup Saber (PhD student)^{NIOH}, Anoop Sharma^{NIOH}, Pernille Høegh Christensen^{UCIPH}

Aim: To study cancer mechanism of air pollution particles by means of (transgenic) animal models

Status by 31.3.08: Two papers have been published and three papers accepted on mutagenicity, oxidative stress induction and DNA damaging capacity of diesel, ambient air and engineered nanoparticles in vitro. Five papers on the role of OGG1 in DNA damage induced in lungs, liver and colon by particle exposure by inhalation, in feed, and single oral and i.p. dose in OGG1-/- mice and rats have been published/accepted. Study of tandem repeat mutations in germ cells induced by particle exposure in vivo have continued in collaboration with researchers from Ottawa, Canada, has been accepted. Studies with reporter mice of NFκB and HO-1-luciferase are ongoing.

WP5B_Case-cohort study of colorectal cancer

PI: Ole Raaschou-Nielsen^{ICE}, key researchers: Ulla Vogel^{NIOH}, Rikke Hansen^{ICE+NIOH} (new PhD student), Anne Tjønneland^{ICE}, Anja Olsen^{ICE}, Mette Sørensen^{ICE}, Ole Hertel^{NERIAE}, Bjørn A. Nexø^{IHG}, Herman Autrup^{AU}

Aim: To study associations between colorectal cancer and genotypes of selected polymorphisms in DNA repair enzymes, RAI and metabolism enzymes as well as effect modification in relation to association between cancer risk and exposure to air pollution assessed in WP4B.

Status by 31/3-08: Genotypes have been determined for 9 SNPs in the following genes; XPA, XPC, XPD, ERCC1, GPX, OGG1, RAI, ASE-1 and for 9 SNP's in metabolism genes for the 1200 samples. The third paper on DNA repair polymorphisms and colorectal tumors has been published and a fourth accepted on interactions between genes and environmental factors (smoking, alcohol consumption, diet, others). A paper on GPX activity, genotype and interaction with diet, alcohol and smoking in relation to risk of colorectal cancer is in preparation. A paper on interaction between meat consumption and metabolic polymorphisms has been resubmitted. Study of air pollution at the residential addresses will be possible in 2008 as the data have been delivered in January. Rikke Dalgaard Hansen finished her PhD entitled: 'Molecular Epidemiology of Colorectal Cancer' in December 2007.

WP5C_Case-cohort study of lung cancer

PI: Ulla Vogel^{NIOH} key researchers: Ole Raaschou-Nielsen^{ICE}, Anne Tjønneland^{ICE}, Mette Sørensen^{ICE}, Bjørn A. Nexø^{IHG}, Herman Autrup^{AU}, Ole Hertel^{NERIAE}, Steffen Loft^{UCIPH}, Lars Dragsted^{IFN}

Aims: To study possible associations and interactions between air pollution, gene polymorphisms, biomarkers for exposure and susceptibility, and diet and smoking in the development of lung cancer in the Diet Cancer and Health Cohorts

Status by 31/3-08: Papers describing the results for associations between lung cancer risk and mRNA quantifications of some DNA repair genes (2 papers) and urinary excretion of DNA repair products (2 papers) have been published or accepted and two more papers are under preparation. Nine genotypes in DNA repair genes and genotypes of metabolism genes have been determined. We have analysed gene effects and interactions with smoking and diet. 3 papers concerning DNA repair genes have been published/accepted. 3 papers on DNA adducts and 2 on metabolic polymorphisms have been published or accepted. Risk associated with estimated air pollution at the residential addresses will be carried out in 2008 as the exposure data has been supplied in January.

WP6A. socio-economic aspects of air pollution

Mikael Skou Andersen^{NERIPA}.

WP6a will deal will theoretical as well as empirical aspect of the economic valuation of changes in mortality risk. Based on the works in (Drèze 1962; Jones-Lee 1974) the theoretical basis for estimation of the value of a change in the probability of dying has been known for a long time. The aggregation of individuals' values has been named "Value of a Statistical Life" (VSL) and this measure has been used for cost benefit analysis within for instance the traffic sector. However, when valuing premature mortality caused by a change in air pollution it has been suggested to value a change in life expectancy instead of the probability of dying (Rabl 2003). This approach potentially can capture, among other things, the fact that most impacts from an elevated level of air pollution have some kind of latency period. However, there are considerable challenges, both theoretically and empirically, before we can have a clear cut approach to valuing changes in life expectancy.

WP6 will present empirical results from two different Contingent Valuation surveys carried out in order to examine the Willingness to Pay (WTP) for a gain in Life Expectancy (LE). The first survey will consist of face-to-face interviews and the second survey will apply the questionnaire in a Danish web-based survey. The results contribute by providing an opportunity to compare different survey modes in a stated preference setting. In addition WP6 will present results from an experimental-based research project developed to ensure stated preference surveys on life expectancy gains describe and communicate life expectancy gains more accurate.