

Organisation

AIRPOLIFE had a successful full assembly in March in Copenhagen in relation to the Third Nordic Workshop on Air Pollution, and including presentation and discussion of all WPs as well as 15 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, 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 2006. However, intense collaboration has been established with Statens Seruminstitut (Paal Skytt Andersen, WP3C/D) and The Pharmaceutical Faculty of Copenhagen University (Majid Sheykhzade, WP4D). A few WPs are still a little behind the original plans and maternity leaves will postpone some work. A minor part of the budget will be transferred to 2007 and 2008. For 2006 and 2007 a part of the budget for WP4A will be transferred from UCDP to UCIPH, whereas part of the budget for WP3C and WP4D for 2007 will be transferred from UCIPH to RHMG due to maternity leave of the PhD student.

Dissemination of results and knowledge and research education

AIRPOLIFE has continued the web page (www.airpolife.dk), with presentation of the entire project and new results as well as the Nordic Workshop and PhD course in English and Danish. The PhD course (1 week with 28 participants) and Workshop (2 days with 80 participants) on health effects of air pollution both organised by AIRPOLIFE were successfully carried out in the spring of 2006. Currently, 1 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, e.g. at the Swedish sister program SNAP (www.snap.se) also in 2006. AIRPOLIFE and its partners have published a number of articles and in science communication journals, given public lectures and participated in media work in relation to the program (e.g. Steffen Loft has been interviewed in radio, television or national newspapers more than 15 times in 2006, www.infomedia.dk, and together with other AIRPOLIFE members given evidence to the Ministry of Energy and Transport 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: Marianne Glasius^{NERI AE}, *key researchers:* Matthias Ketzel^{NERI AE}, Peter Wåhlin^{NERI AE}, Finn Palmgren^{NERI AE}, Jacob G. Mønster^{NERI AE}, Rossana Bossi^{NERI AE}, Keld Alstrup Jensen^{NIOH}

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 preparation for publication. A MSc-study is currently undertaken to quantify the relationships between water-soluble elements in indoor-outdoor and personal PM_{2.5} samples in collaboration with the Danish Cancer Society. Additionally metal analysis of size-fractioned authentic indoor and outdoor air-pollution samples previously collected by MOUDI is currently being finalized using various advanced electron microscopy methods (EM). Additionally a detailed study of the metals speciation using chemical extraction techniques and EM as well as the water-solubility of diesel particle samples SRM1649a and a VW-1600TD tail-pipe deposits is in preparation combining result from in vitro toxicological analysis. The 2006 campaign for collecting brake-wear particles and their characterization has been postponed until a 2007 summer-campaign and will be completed by NRCWE (formerly NIOH-DK).

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: Q2 2007. Status: 85% 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. This work is still ongoing. Completed: Q2 2007. Status: 85% 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: Q2 2007 Status: 90% 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 Q3 2007 Status 75% completed.

Remaining activities: Completion of the traffic data set. Expected May 2007. Testing batch mode capability to process large cohort input. Expected May 2007. Adjusting the tools to generate "proxi" estimates, to meet the requirements from the epidemiological studies. June 2007

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: The interaction between exercise and exposure has been studied in a 2x2 design on 30 healthy young non-smoking subjects in indoor exposure chambers with traffic generated air pollutants by use of a ventilator facing a

busy street and extensive monitoring in the laboratory. Biological effects included alveolar integrity, mucociliar, lung and endothelial function, deposition of ultrafine particles, biomarkers of oxidative stress, inflammation, DNA damage and gene regulatory responses. A paper on deposition and a paper showing that ultrafine particles induce oxidative damage to DNA have been accepted and papers on cardiovascular functions is being submitted and on lung function is in preparation. Elderly subjects (41) have been studied in 2006 in their home with and without filtering the indoor air for ultrafine particles. Supplementary financing (1.3 mill kr) for this part has been achieved from Velux and 100.000 from the Heart Association. The first paper showing that removing particles improves endothelial function will be submitted soon.

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 has been completed late in 2006 and in early 2007. The cognitive function assessment of offspring are underway in 2007. Offspring will also be used for study of genotoxic endpoints and reproductive effects in 2007.

WP2C Target organ exposure in humans

PI Lisbeth E. Knudsen^{UCIPH}, Marie Pedersen (new PhD student)^{UCIPH}, Tina Dam Mikkelsen PhD student^{UCIPH}, Elvira Vaclavik^{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, DNA damage and gene regulation in target tissue (placenta and cord blood) in relation to planned caesarean section in 50 pregnant women. A protocol has been developed and approved by the ethics committee and sampling has been initiated in 2007. 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 -07: The study still only awaits the air pollution modeling system to be ready to produce exposure estimates in order to perform the data analysis and reporting.

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 are being analyzed and a paper prepared. 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

Status 10/3-07: A manuscript is almost ready for submission.

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. Due to limitations in power pointed out by the IAB, focus has moved toward study of candidate genes involved in oxidative stress and metabolism as effect modifiers in the National Birth Cohort in close collaboration with WP3D. Polymorphisms in 5 of the 8 planned genes based on genomically amplified DNA have been measured, whereas the remaining 3 genes required original DNA. Analysis of these is ongoing in 2007.

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 31/3-07: 1000 cases and 1000 controls have been selected. DNA has been purified from blood samples. 8 polymorphisms in inflammation genes have been analysed. Gene effects and interactions with ETS have been analyzed and a paper submitted. Estimation of air pollution at residential addresses awaits the modeling system to be ready. We still wait for the modeling system to deliver estimates for outdoor air pollution concentration at the addresses of the study participants. Post doc Mette Sørensen (daily head of project) is on maternity leave.

WP4A. Cardiovascular disease models

PI: Peter Møller, key researchers: Janne Kjærgaard^{UCIPH} coming PhD student^{UCIPH+}, Christian Stevns-Hansen^{UCIPH+DP}, Steffen Loft^{UCIPH}, Thomas Jonassen^{UCDP}, Ole Amtorp^{UCDP}, Håkan Wallin^{NIOH}

Aim: study cardiovascular effects of particles in animal models

Status: Studies of 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 after exposure to diesel particles and 3 papers have been accepted in high ranking journals. American groups have now published long term studies in ApoE^{-/-} mice and WP4A will continue to focus on short-term effects in ApoE^{-/-} mice and diabetic rats. Intratracheal instillation studies with different particles are ongoing. Studies of NFκB reporter mice will continue after a new camera has been purchased.

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 by 31/3-07: Status 10/3-07: Traffic data from the municipalities has been collected and entering these data into the digital maps of the Danish road network is almost completed. The study can proceed when the modeling system delivers estimates for outdoor air pollution at the addresses of cohort members.

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 31.3.07: Associations have been shown between daily levels of particles (PM10) and traffic related gases and all admissions for cardiovascular and lung disease in elderly and asthma in children during 1999-2004 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 accepted and another submitted. The study of daily airway symptoms among 411 children with high risk of atopic disease has been expanded to their first 36 months of life. A paper on associations between symptoms and monitor data has been submitted. 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}, Lars Dragsted^{IFN}, 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 31.3.07: Address history of the cohort has been established. Exposure assessment see WP1AB and WP4B. Target genes have been selected: GSTM1, GSTT1 and GSTP1. A new high throughput analysis for the allele number of M1 and T1 has been developed and a paper for publication of this is being prepared. Genotyping of M1, T1 and P1 has been completed for the whole cohort. The PhD student has been on maternity leave a major part of 2006 continuing in 2007 and progress awaits her return

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: Two papers on the limited role of TNF in particle-induced inflammation based on TNF^{-/-} mice have been published. Three 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 and a third submitted. Tandem repeat mutations in germ cells induced by particle exposure in vivo have been studied and a paper on mutations induced by carbon black in vitro 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 31/3-07: The second on DNA repair polymorphisms and colorectal tumors has been published and a third submitted on interactions between genes and environmental factors (smoking, alcohol consumption, diet, others). 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. Rikke has measured GPX activity in red blood cells and she is currently analyzing the results regarding GPX1 polymorphism, GPX activity and interaction with diet, alcohol and smoking in relation to risk of colorectal cancer. Estimation of air pollution at the residential addresses awaits the modeling system to be ready.

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 31/3-07: Papers describing the results for associations between lung cancer risk and mRNA quantifications of some DNA repair genes (1 paper) 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 published/accepted and 1 on polymorphisms in NER genes is under preparation. 1 paper on DNA adducts has been published and 1 on metabolic polymorphisms accepted. Estimation of air pollution at the residential addresses awaits the modelling system to be ready

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.

The theoretical part of the WP will consist of a derivation and theoretical discussion of a possible foundation for valuing a change in life expectancy. The point of departure for this discussion will be the VSL-theory. However the main focus will be on the life-cycle-consumption models. (Cropper 1990).

WP6 will present empirical results from two different Contingent Valuation surveys carried out in order to examine the Willingness to Pay (WTP) for changes in Life Expectancy (LE). The first survey will consist of face-to-face interviews carried out in Denmark in cooperation with the EU project NEEDS (New Energy Externalities Developments for Sustainability). The second survey will apply the questionnaire developed in the NEEDS-project in a Danish web-based survey. The results from the two surveys will provide us with a rare opportunity to compare different survey Contingent Valuation survey modes. Cropper, M. S. F. G. 1990, "Valuing future risks to life", *Journal of Environmental Economics and Management* pp. 160-174. Drèze, J. H. 1962, "L'Utilite Sociale D'une vie Humaine", *Revue francaise de recherche operationnelle*, vol. 6, pp. 93-118, Jones-Lee, M. W. 1974, "The Value of Changes in the Probability of Death or Injury", *The Journal of Political Economy*, vol. 82, no. 4, pp. 835-849. Rabl, A. 2003, "Interpretation of Air Pollution Mortality. Number of Deaths or Years of Life Lost.", *Journal of Air Waste and Management.*, vol. 53, no. 1, pp. 41-50.