Project no. 282688

ECLIPSE

Evaluating the **Cl**imate and Air Quality **Im**p**a**cts of **S**hort-Liv**e**d Pollutants

Collaborative Project

Work programme: Climate forcing of non UnFCCC gases, aerosols and black carbon
Activity code: ENV.2011.1.1.2-2
Coordinator: Andreas Stohl, NILU - Norsk institutt for luftforskning

Start date of project: November 1st, 2011
Duration: 36 months

Deliverable D 5.7 Health effects descriptors for the exposure to short -lived pollutants (SLCF) (R)

Due date of deliverable: project month 24
Actual submission date: project month 29

Organisation name of lead contractor for this deliverable: NILU
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Revision 1

Project co-funded by the European Commission within the Seventh Framework Programme (2007-2013)		
Dissemination Level		
PU	Public	
PP	Restricted to other programme participants (including the Commission Services)	X
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

Objectives of task 5.3 Interface between air quality indicators and health benefits according to Description of work

For aerosols, air quality legislation is based on the concept of particulate matter (PM), in particular PM2.5 (the mass of PM smaller than 2.5 µm). However, PM is a complex mixture of aerosol components and it is possible that differences in PM composition could have different impacts on human health, just as the climate effects of aerosols depend on the radiative properties and, thus, the chemical composition of the aerosol. This task will provide a review of existing air quality standards and guideline values from the National Ambient Air Quality Standards (NAAQS) of the U.S. Environmental Protection Agency (EPA), the new Directive 2008/50/EC of the European Parliament on ambient air quality and cleaner air for Europe and the 2005 WHO Air Quality Guidelines (AQGs) of the World Health Organization (WHO) as well as of the latest literature, in order to summarize the weight given to the individual SLCF components (e.g., BC, sulfate) with respect to acute and chronic human health effects, especially respiratory diseases, cardiovascular diseases and lung cancer. The output of this task will feed into WP 7, where potential sensitivities of abatement measure optimization to the definition of air quality standard definition will be considered.

1 Introduction

Ambient air pollution was classified as carcinogenic to humans (group 1) in October 2013 at the meeting of experts at the International Agency for Research on Cancer (IARC), (IARC, in press, Gross, 2013). Outdoor air pollution is a mixture of multiple pollutants originating from natural and anthropogenic sources. Transport, power generation, industrial activity, biomass burning, and domestic heating and cooking are the predominant anthropogenic sources in many locations (Gross et al. 2013). Typically recorded pollutants are respirable particulate matter (PM10), fine particulate matter (PM2·5), NO_2, SO_2, and ozone (O_3). PM2.5 is increasingly used as an indicator pollutant, with annual average concentrations ranging from less than 10 to more than 100 $\mu g/m^3$ globally. WHO and national air quality guidelines for PM2.5 and other pollutants in many countries are routinely and substantially exceeded.

2 Health effects of organic aerosols

Carbonaceous aerosol is a heterogeneous mixture in the form of organic carbon (OC) and elemental carbon (EC or Black Carbon (BC)) and is a major component of PM, gases and vapors in the atmosphere. Organic aerosol includes non-PM components such as VOCs, SVOCs and particulate species.

There is an association between organic fractions of ambient PM and adverse health effect on the respiration and cardiovascular system (Mauderly and Chow, 2008). However, recent epidemiological and other studies are insufficient to support a quantitative relationship for the aggregate risk of these heterogeneous organic air contaminants to human health. Mauderly and Chow (2008) suggest that risk assessment should be done for individual species or mixtures and suggests that a common SRM should be used for both organic speciation but also for health response assays and that additional biomarkers should be added linking organic aerosols to health effects to promote research for in vitro human cells study and in vivo animal studies in the development of exposure-response relationships.

Still there are plenty of epidemiological studies showing evidence that organic aerosols adversely affect public health but the information is diverse and largely indirect (Mauderly and Chow, 2008). Generally, epidemiological studies are concerned with adverse effects of PM10 or PM2.5 but in many studies a deeper characterization of the non-PM carbonaceous compounds which have only sparse direct evidence of associations to adverse outcomes. The weight of evidence is high from epidemiological studies and laboratory studies on biological systems showing that carbonaceous pollutants affect health.

In a hospital admission study in London, Atkinson et al. (1999) found that both PM10 and BS - a filter darkening method, crudely reflecting Black Carbon levels (BC) - was significantly linked to cardiovascular effects.

Mar et al. (2000) studied the association between organic aerosols and total non-accidental mortality and cardiovascular mortality in Phoenix (1995-1997) and compared concentrations of PM10, PM2.5, and criteria pollutant gases and the PM2.5 was analyzed for organic (OC) and elemental carbon (EC, Black Carbon) and reported positive significant association between cardiovascular mortality and PM10, PM2.5, OC, EC and inorganic components. Daily mortality data from 1992 to 1995 from the seven-county Philadelphia, PA, metropolitan area were analyzed in a single pollutant and multiple-pollutant models in relation to weather and a variety of ambient air quality parameters such as size-classified PM, SO4(2-), and H+ (Lipfert et al. (2000)). Significant associations were found between daily mortality and air pollution, especially for peak O_3 and associations with PM metrics.

Ostro et al. (2006) examined the daily mortality in nine California counties. Significant associations were found between cardiovascular mortality and levels of PM2.5, OC and EC. Similar studies have been performed by Klemm et al. (2004) and Tolbert et al. (2000).

Health effects of individual particulate matter (PM) components

Composition of fine particulate matter (PM2.5) plays a significant role for their attributing acute and chronic health effects on humans which is the general consensus of the scientific community (Rohr and Wyzga, 2012 and Lippmann and Chen 2009a,b).
Epidemiological studies, controlled human exposure studies and toxicological studies are the general basis of the current knowledge of health effects of PM. The conclusion is that health effects of PM and its components do not exonerate any major component of PM as each have been implicated in studies (Rohr and Wyzga, 2012). However, the reviewers suggest that there is a particular importance of the carbonaceous fraction of PM on human health while model results from only PM2.5 is not as strong. The reviewers stated that as a whole the literature suggests that "EC and/or OC being potentially more important than other PM components". However, as this fraction are themselves a complex mixture this fraction of PM needs to be thoroughly examined.

In a review of Janssen et al. (2011), they suggested the use of black carbon (BC) as an additional indicator on the associations between health effects and particulate matter (PM10 and PM2.5). They estimated that there would be an increase in life expectancy four to nine times for a hypothetical traffic abatement when expressed in BC compared with an equivalent change in PM2.5 mass and they concluded, "BCP is a valuable additional air quality indicator to evaluate the health risks of air quality dominated by primary combustion particles."
Lippmann and Chen (2009a,b) reviewed CAPs (Collected Ambient Particles) in animal and human studies and concluded that there is emerging evidence that PM is associated with adverse health effects close to current ambient PM2.5 mass concentrations. The components with the most casual correlation with health effects includes EC, Ni, V and Pb and a

suggestive relationship for Al, Zn and OC. Kelly and Fussell (2007) concluded that combustion derived components of PM such as the ultrafine particles, and possibly metals and PAHs (and other OCs) are responsible for the health effects while Kelly et al. 2004 reported less compelling evidence on the effects of secondary particles such as ammonium sulphate and nitrate.

Epidemiological studies and controlled exposures to humans and animals on traffic related exposures, Grahame and Schlesinger (2010) concluded that diesel emissions, diesel exhaust particles, or ambient air close to highways near major cities found associations of cardiovascular mortality and morbidity with black carbon (BC). The review by Maulderly and Show (2008), on the health effects associated with organic aerosols concluded that even if organic aerosols might be more important to human health, current data is insufficient to support a quantitative characterization of the cumulative risk from aerosols. In a review of Stanek et al. 2011, they summarized the source apportionment studies of PM2.5 on the human health to pinpoint if different sources might be closely and unequivocally related to health effects. The review concluded that not enough evidence based on the current studies exist to assert specific factors to health effects.

Epidemiological studies

Rohr and Wyzga (2012) considered 48 independent epidemiological studies on different components and concentrations of PM. They concluded that "No major components of PM studied, however, was unequivocally not associated with health responses." More attention have been given to the carbon containing particles which have greater associations with cardiovascular than respiratory outcomes. Only a few studies have been considering elemental species and only giving mixed results. Components including copper, vanadium, zinc, copper, silicon and potassium have shown to have the most significant results while the results for sulphate are very mixed.

Controlled human exposure

There are only two studies according to Rohr and Wyzga (2012) where they studied individual PM components but results showed that for cardiovascular outcomes EC and OC showed the greatest significant correlation.

Toxicological studies

Rohr and Wyzga (2012) considered 20 toxicological studies, studies incorporating in vivo CAPs or *in vitro* studies using collected PM. These studies included PM components such as EC, OC and different elements. V and Ni have been associated with cardiovascular and respiratory outcomes while Fe, Zn, S and Pb have shown fewer associations. Carbonaceous compounds have been observed for both outcomes while sulphate were associated in less than half of 18 studies.

Summary of component specific adverse health effects

PM2.5

Effects on the respiratory, cardiovascular, immune and neural systems, which can lead to premature mortality or morbidity. The mechanism of PM for the cardiovascular and cerebrovascular diseases are thought to be through systemic inflammation, direct and indirect coagulation activation and direct translocation into systemic circulation. PM causes

respiratory morbidity and mortality by creating oxidative stress and inflammation that leads to pulmonary anatomic and physiological remodeling (Anderson et al 2012).

Mortality

- Premature attributable death (all-causes), acute 1 or more days of exposure
- Attributable death (all causes or cardiovascular or cardiopulmonary or lung cancer)
- Years of life lost in association with long-term exposure >30years
- Attributable infant mortality (0-1 years)

Morbidity outcomes

- Bronchitis symtoms in children <18 years
- Chronic bronchitis > 30 years
- Asthma attacks
- Cardiovascular, cerebrovascular and respiratory hospital admissions
- Urgent care visits due to asthma and cardiovascular diseases
- Restricted activity (days)

Short Lived Climate Forcing Agents (SLCF)

The more important Short lived climate forcing air pollutants includes BC, methane, ozone and Hydrofluorocarbons (HFC).

Health effects of black carbon (BC)

PM is the most important air pollutant and BC is a part of this heterogeneous pollutant mixture and is a major component of diesel soot which has shown to cause cancer (WHO 2012). PM penetrate deep into sensitive regions of the respiratory system. BC belongs to the ultrafine fraction of PM0.1 and penetrates into the alveolar region and through the bloodstream to organs (Status of black carbon monitoring in ambient air in Europe, EEA Technical report, no 18/2013). WHO have summarized the current health effects of BC and conclude that short-term epidemiological studies provide sufficient evidence of an association of daily variation in BC concentrations with short term changes in health such as all-cause, cardiovascular mortality and cardiopulmonary hospital admissions. Cohort studies provide sufficient evidence of association of all-cause and cardiopulmonary mortality with long term BC exposures. Also BC seems to be a better indicator of harmful particulate substances than PM mass alone when comparing combustion sources.

In 2006, an IARC Monographs Working Group reevaluated the carcinogenic hazards to humans of carbon black, titanium dioxide, and talc (WHO 2010). Epidemiological studies among workers in carbon black production and in the rubber industry provided inadequate evidence of carcinogenicity. In an epidemiological case control study of lung cancer conducted in Montreal, Canada, the authors were able to assess possible relationships between exposure to these substances and subsequent lung cancer risks with the result that no detectable excess in lung cancer risk was found for subjects with an occupational exposure to carbon black (Ramanakumar 2007).

The overall data from cancer studies in rodents exposed to carbon black provided sufficient evidence of carcinogenicity. Chronic exposure to inhaled particles at sufficiently high concentrations in experimental animals might lead to impairment of lung function leading to chronic alveolar inflammation with inflammatory responses such as reactive oxygen species (ROS), cell injury, cell proliferation, fibrosis, induction of mutations, and, ultimately, cancer.

In addition, impaired lung clearance in rodents exposed to ultrafine particles occurs at much lower mass concentrations than with fine particles, which adds to the human relevance (Baan 2007).

Ozone

Oxidizing agents may cause respiratory health problems and lead to premature mortality at elevated levels (EEA report no 9, 2013). Adverse effects of short and long-term exposure of O_3 is well documented (WHO 2006) showing that short-term exposure causes exacerbation of existing lung diseases and long-term exposure can produce irreversible changes in the lung function and structure. In a study, air pollutants - total suspended sulfates, sulfur dioxide, ozone (O_3), and nitrogen dioxide - were related to 1977-1992 mortality in a cohort of 6,338 nonsmoking California Seventh-day Adventists. Ozone showed a strong association with lung cancer mortality when O_3 exceeded 100 parts per billion (Abbey et al. 1999). Jerrett et al (2009) reported an association between long-term exposure to O_3 and respiratory mortality in the American Cancer Society cohort showing a 4% increase in relative risk for a 10 ppb increase of O_3. However, these types of studies are difficult to attribute the toxicity solely to the effect of O3 as PM2.5 is a major factor in respiratory mortality.
The conclusions from West et al. (report Ch 5, Impact on health, ecosystem and climate) is that short-term exposure to O_3 is associated with increased daily mortality and morbidity in many studies but the long-term evidence of O_3 impact on cardiovascular mortality and respiratory disease is limited but adverse health effects appears to be linearly correlated to O_3 concentrations with no evident threshold limits, the same conclusion as for PM concentrations.

NOx

Health effects from NOx exposure include inflammation of airways and reduced lung function. Current scientific evidence links short-term NO_2 exposures with adverse respiratory effects including airway inflammation in healthy people and increased respiratory symptoms in people with asthma. Also, studies show a connection between breathing elevated short-term NO_2 concentrations, and increased visits to emergency departments and hospital admissions for respiratory issues, especially asthma. NO_2 concentrations in vehicles and near roadways are appreciably higher than those measured at monitors in the current network. In fact, in-vehicle concentrations can be 2-3 times higher than measured at nearby area-wide monitors. Near-roadway (within about 50 meters) concentrations of NO_2 have been measured to be approximately 30 to 100% higher than concentrations away from roadways. Individuals who spend time on or near major roadways can experience short-term NO2 exposures considerably higher than measured by the current network. NO_2 exposure concentrations near roadways are of particular concern for susceptible individuals, including people with asthma asthmatics, children, and the elderly (US-EPA).

SOx

Current scientific evidence links short-term exposures to SO_2, with an array of adverse respiratory effects including bronchoconstriction and increased asthma symptoms. These effects are particularly important for asthmatics at elevated ventilation rates. Studies also show a connection between short-term exposure and increased visits to emergency departments and hospital admissions for respiratory illnesses, particularly in at-risk populations including children, the elderly, and asthmatics. EPA's National Ambient Air Quality Standard for SO_2 is designed to protect against exposure to the entire group of sulfur

oxides (SOx). SO_2 is the component of greatest concern and is used as the indicator for the larger group of gaseous sulfur oxides (SOx). Other gaseous sulfur oxides (e.g. SO3) are found in the atmosphere at concentrations much lower than SO_2. Emissions that lead to high concentrations of SO_2 generally also lead to the formation of other SOx. Control measures that reduce SO_2 can generally be expected to reduce people's exposures to all gaseous SOx. This may have the important co-benefit of reducing the formation of fine sulfate particles, which pose significant public health threats (US-EPA).

In one study of air pollutants - total suspended sulfates, sulfur dioxide and other air pollutants were studied for the California Seventh-day Adventists (Abbey et al. 1999) - sulfur dioxide showed strong associations with lung cancer mortality for both sexes.

Air quality guidelines of the European Union member states, US-EPA National Air Quality Standards and WHO air quality guidelines

As is stated in the European Union Air Quality Directives 2008/50/EC (EC 2008) "In order to protect human health and the environment as a whole, it is particularly important to combat emissions of pollutants at source and to identify and implement the most effective emission reduction measures at local, national and Community level. Therefore, emissions of harmful air pollutants should be avoided, prevented or reduced and appropriate objectives set for ambient air quality taking into account relevant World Health Organisation standards, guidelines and programmes."

The European Union established directives based on the need to reduce European pollution to levels which minimize harmful effects on human health, especially to sensitive populations and the environment and to improve the monitoring and assessment of air quality (EC 2008).

The European Union Air Quality Directives 2008/50/EC (EC 2008) and 2004/107/EC (EC 2004) set legally binding limits for ground-level concentrations of outdoor air pollutants. Key elements of EU air quality legislation are EU limit values are legally binding concentration thresholds that must not be exceeded. Limit values are set for individual pollutants and are made up of a concentration limit, an averaging time over which a pollutant is to be measured or estimated. Limit values are legally binding on EU Member States. Target values are to be attained where possible by taking all necessary measures not entailing disproportionate costs. Target values are not legally binding. Exposure reduction obligation concentrations are to be reduced by a given per cent depending on the mean triennial PM2.5 urban background concentrations from 2008–2010 to 2018–2020 (EEA 2013). *Table 1* compares the EU reference levels including EU limit or target levels with the WHO Air Quality Guidelines, US-EPA National Ambient Air Quality Standards and the Environmental Quality Standards (EQS) and guideline values for air pollutants in Japan.

In the US it was implemented the "Clean Air Act" which was last amended in 1990. US-EPA was required to set National Ambient Air Quality Standards (40 CFR part 50) for pollutants considered harmful to public health and the environment. The Clean Air Act identified two types of national ambient air quality standards. *Primary standards* provide public health protection, including protecting the health of "sensitive" populations such as asthmatics, children, and the elderly. *Secondary standards* provide public welfare protection, including protection against decreased visibility and damage to animals, crops, vegetation, and buildings. The US-EPA set National Ambient Air Quality Standards for six principal

pollutants, which are called "criteria" pollutants (See *Table 1 (not including BaP and Benzene in their guidelines)*). Units of measure for the standards are parts per million (ppm) by volume, parts per billion (ppb) by volume, and micrograms per cubic meter of air (µg/m^3) (US-EPA 2012).

The WHO air quality guidelines (WHO 2006) was designed to offer guidance in reducing the health impacts of air pollution for all WHO regions and inform policy-makers considering various options for air quality management in different parts of the world about the targets for air quality. These guideline values was based on a review of the accumulated scientific evidence up to 2005 for the most common air pollutants, a part of which is included in *Table 1* for comparison.

The most problematic pollutants are PM and O_3 considering harm to human health (EEA 2013). Pollutants can be ranked according to their relative risk for damage to human health: PM2.5 > PM10 > O_3 > NO_2 > BaP > SO_2 > CO > Pb > benzene

Table 1. Air quality standards for Europe (European Union reference values), WHO air quality guidelines (AQG), US-EPA National Ambient Air Quality Standards (NAAQS) and the Environmental Quality Standards (EQS) and guideline values for air pollutants in Japan

Pollutants	EU reference levels[a]	WHO AQG[b]	USEPA NAAQS[c]	Japan EQS[d]
PM2.5	20 µg/m^3 (Year)	10 µg/m^3 (Year)	12 µg/m^3 (Year)	2.5 µg/m^3 (year)
PM10	50 µg/m^3 (Day)	20 µg/m^3 (Year)	150 µg/m^3 (day)	100 µg/m^3 (day, SPM[e])
O_3	120 µg/m^3 (8-hour)	100 µg/m^3 (8-hour)	0.075 ppm (8-hour)	118 µg/m^3 (1-hour[f])
NO_2	40 µg/m^3 (year)	40 µg/m^3 (Year)	53 ppb (Year)	75-113 µg/m^3 (1-hour)
BaP	1 ng/m^3 (Year)	0.12 ng/m^3 (Year)	-	3 µg/m^3 (year)
SO_2	125 µg/m^3 (day)	20 µg/m^3 (day)	75 ppb (1-hour)	105 µg/m^3 (1-day)
CO	10 mg/m^3 (8-hour)	10 mg/m^3 (8-hour)	9 ppm (8-hour)	10 ppm (1-hour)
Pb	0.5 µg/m^3 (Year)	0.5 µg/m^3 (Year)	0.15 µg/m^3(3-month)	-
Benzene	5 µg/m^3 (Year)	1.7 µg/m^3 (Year)	-	3 µg/m^3 (year)

[a]EEA 2013, Indicator CSI 004
[b]WHO Air Quality Guidelines (WHO 2006)
[c]US-EPA National Ambient Air Quality Standards (http://www.epa.gov/air/criteria.html#3, accessed 16/4/2014).
[d] Environmental Quality Standards (EQS) and guideline values for air pollutants in Japan (Kawamoto et al. 2011).
[e] 100% efficiency cut-off at 10um while PM10 is defined as 50% efficiency cut-off at 10um aerodynamic diameter (Kawamoto et al. 2011)
[f] Photochemical oxidants (Ox) (Kawamoto et al. 2011)

Abatement of PM effects on population health

PM metrics for health outcomes

There are several validated studies were there have been created concentration-response functions generally described as an 10 μg/m^3 decrease in PM levels will give an increase in life expectance from a few months to several years or alternatively an 10 μg/m^3 increase in PM will increase for cardiopulmonary mortality by 9% (Pope et al 1995).

PM health outcomes

- Adult cardiopulmonary mortality PM2.5
- Adult lung cancer mortality from long-term exposure to PM2.5
- Acute respiratory infection mortality for children < 5 years due to short-term exposure to PM10
- All-age all-causes mortality associated with short-term exposure to PM10

Several other endpoints have also been studied (Global burden of disease study 2010).
Other PM metrics for which response functions have been published for at least some health endpoints include PM10, black carbon, sulphate and others (WHO 2013, REVIHAAP project: technical report). Compared to PM2.5 there are fewer studies and fewer health outcomes. BC is an example that can be used as an indicator for traffic-related PM such as the BC concentration-response function for the mortality effects of long-term exposure (Smith KR et al. Lancet, 2009).

Conclusions

The findings regarding the carcinogenicity of outdoor air pollution as a mixture, and of PM specifically, are remarkably consistent in epidemiological research, studies of cancer in experimental animals, and a wide range of studies of mechanistic studies.
Especially, an increased risk of lung cancer was consistently observed in cohort and case-control studies including millions of people and many thousands of lung cancer cases from Europe, North America, and Asia. Many studies estimated quantitative levels of outdoor air pollutants, most often as mass concentration of PM, and adjusted for a wide range of potential confounders including tobacco smoking. The IARC Working Group classified outdoor air pollution and PM from outdoor air pollution as carcinogenic to humans (IARC Group 1).

All of the studies were done in areas where annual average levels of PM2.5 range from about 10 to 30 μg/m^3, which represents the lower exposures worldwide. Nevertheless, increased risk of lung cancer was observed even in those areas where PM2.5 concentrations are less than the current health-based guidelines (Raaschou-Nielsen et al., 2013)

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