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SAMENVATTING
(Executive summary in Dutch)

Inleiding

In 1991 discussieerde de Tweede Kamer met de Minister van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer over het risico voor de gezondheid van stadsbewoners tijdens wintersmogepisoden over de bijdrage van de uitlaatgassen van verkeer in de stad aan dit risico, en over de herziening van de wintersmogwaarschuwingsregeling. Vanwege de potentiële ernst van het risico en de onzekerheden van de bijdrage van verkeer aan het risico, deed de minister de toezegging onderzoek in deze te laten verrichten. De Kamer zou geïnformeerd worden via een interimrapportage in 1994 en een eindrapportage in 1996. De interimrapportage ligt thans voor U.

De startnotitie "Hoofdlijnen van onderzoek naar acute effecten van wintersmog op de menselijke gezondheid" (51) beschrijft onderzoek dat tenminste moet worden uitgevoerd om de gestelde beleidsvragen te kunnen beantwoorden.
De eerste hoofdlijn betreft bevolkings(epidemiologisch)onderzoek naar de relatie tussen wintersmog en gezondheidseffecten. Dit onderzoek vindt plaats in een grote stad met veel verkeer onder vier groepen uit de bevolking (zogenaamde panels), te weten volwassenen en kinderen met of zonder ziekte van de ademhalingswegen. Het contrast tussen wintersmog met of zonder stadsverkeer wordt gevonden door vergelijking van de stadspanels met panels uit een dorp met weinig verkeer. Dit onderzoek moet aantonen hoe ernstig de gezondheidseffecten zijn, die tijdens wintersmog in Nederland kunnen voorkomen en wat bij benadering de bijdrage van het stadsverkeer aan de effecten is (54, 55).
De tweede hoofdlijn betreft het vaststellen van de blootstelling van de stadsbevolking aan wintersmog en het nader karakteriseren van de bijdrage uit de diverse bronnen (industrie, huisverwarming, verkeer, enz.) aan de stadsluchtverontreiniging (51).
De derde hoofdlijn is dierexperimenteel onderzoek ter onderbouwing van de plausibiliteit van de gegevens verkregen uit het epidemiologisch onderzoek (52) en ter verkrijging van inzicht in het werkingsmechanisme van wintersmog om op basis daarvan de kans op het ontstaan van onherstelbare gezondheidseffecten door herhaalde blootstelling aan wintersmog te kunnen schatten.
Het "Wintersmog en Verkeer" project wordt in opdracht van Directie Lucht & Energie/Directoraat-Generaal Milieubeheer uitgevoerd door de Landbouwuniversiteit Wageningen (LUW) en de Rijksuniversiteit Groningen (RUG), en door het Rijksinstituut voor Volksgezondheid en Milieuhygiëne (RIVM) in het kader van het Meerjaren Activiteiten Programma.

Stand van zaken

In de interimrapportage wordt de huidige stand van zaken beschreven van, hoofdzakelijk, (inter)nationaal epidemiologisch onderzoek naar de relatie tussen PM_{10} en het optreden van gezondheidseffecten. PM_{10} ("particulate matter") is de afkorting van de massa van de in de lucht zwevende

deeltjes (aerosol) met een diameter kleiner dan ongeveer 10 micrometer (10 µm = 0,01 mm). PM_{10} wordt in Nederland ook wel "fijn stof" genoemd en geldt als indicator voor de ernst van het wintersmogmengsel. Daarna wordt verslag gedaan van het onderzoek dat tot nu toe is afgerond.
Uit de literatuur blijkt dat blootstelling aan wintersmog geassocieerd is met een toename van de dagelijkse sterfte, met ziekenhuisopnamen voor ademhalingsklachten, met een toename van medicijngebruik bij astmatici en met longfunctieverslechtering. Er lijkt geen drempelwaarde voor dergelijke associaties te bestaan waar beneden effecten op mortaliteit en morbiditeit niet meer voorkomen. Gelet op de moeilijkheid een drempelwaarde vast te stellen, wordt een schatting van de gezondheidseffecten uitgedrukt als procentuele toename per 100 $\mu g/m^3$ verandering in de daggemiddelde concentratie van PM_{10}. Deze toename is voor dagelijkse sterfte 10-15%, voor toename van ziekenhuisopnamen voor respiratoire aandoeningen 20-40% en voor toename van medicijngebruik bij astmatici ongeveer 30%. De longfunctieverslechtering wordt geschat op 2-4% voor 100 $\mu g/m^3$ toename van de PM_{10} concentratie. De daggemiddelde PM_{10}-concentraties in Nederland kunnen tijdens wintersmogepisoden oplopen tot 140 $\mu g/m^3$ en hoger.
Er zijn weinig toxicologische gegevens beschikbaar omtrent de gezondheidseffecten en het werkingsmechanisme van deeltjesvormige luchtverontreiniging. Enkele proefdierstudies met gecontroleerde inhalatie van verschillende (redelijk onoplosbare) deeltjes suggereren dat de grootte van het oppervlak en de reactiviteit van het oppervlak van ultrafijne deeltjes (< 0,1 µm) een rol spelen in het veroorzaken van pulmonale effecten.
Het grootste deel van de massa van alle deeltjes wordt veroorzaakt door deeltjes met een diameter van enige micrometers (µm) tot enige tientallen micrometers. Omdat de hoogte van de PM_{10}-niveaus afhangt van de massa van de deeltjes worden deze PM_{10}-niveaus vooral bepaald door deeltjes groter dan enkele micrometers in diameter. De ultrafijne deeltjes met diameters van enige honderdsten tot tienden van micrometers vormen wel de grootste aantallen deeltjes, maar dragen vrijwel niet bij aan de PM_{10}-niveaus. Deeltjes van tussenliggende diameters bepalen voor het grootste deel het oppervlak. Zij hebben een verwaarloosbaar effect op de PM_{10}-niveaus. Het is momenteel nog onbekend of het toxische werkingsmechanisme van de deeltjes afhangt van de massa dan wel de chemische samenstelling van de deeltjes, of afhangt van het oppervlak van de deeltjes of juist van de aantallen deeltjes. Daarom is de keuze van het juiste bestrijdingsdoel op dit moment niet eenvoudig.

Resultaten onderzoek uitgevoerd in het kader van "Wintersmog en Verkeer"

Tijdens de winter 92/93 zijn er door de LUW, de RUG en het RIVM epidemiologische panelstudies uitgevoerd in Rotterdam en Bodegraven/Reeuwijk. Deze dragen het karakter van pilotstudies. De resultaten van deze studies bevestigen het voorkomen in Nederland van wintersmogeffecten op de gezondheid zoals op basis van eerder uitgevoerd onderzoek werd verwacht. Er worden verbanden gevonden tussen PM_{10}-concentraties (daggemiddelde) en gezondheidseffecten. Verder komt uit de pilotstudies naar voren dat er verschil bestaat in de mate van het optreden van de gezondheidseffecten tussen de urbane en rurale onderzoekslocatie. De resultaten van de pilotstudies

suggereren dat de urbane populatie sterker reageert op de verhoogde daggemiddelde PM_{10}-concentraties dan de rurale onderzoekspopulatie. Uit de luchtkwaliteitsmetingen van deze studies blijkt dat het verschil tussen urbaan en ruraal in PM_{10}-concentraties tijdens episodes ongeveer 30% bedraagt. Onder niet-episode omstandigheden was de concentratie in stedelijke gebieden tot ongeveer 10% verhoogd. De verschillen in gasvormige componenten als koolmonoxyde, stikstofoxide en zwaveldioxide tussen het urbane en rurale gebied zijn groter dan de hier genoemde percentages. De resultaten van de luchtkwaliteitssmetingen uit deze studies kunnen door het beperkte aantal metingen op enkele meetstations niet worden geëxtrapoleerd naar de landelijke situatie.

Gedurende de winter 93/94 heeft er een luchtkwaliteitsmonitoring project (CHEAP = Characterization of Episodical Air Pollution) plaats gevonden. Analyses van de metingen worden op dit moment uitgevoerd. Voorlopige resultaten suggereren dat tijdens een episode de concentratie ultrafijne deeltjes (met een diameter kleiner dan 0,1 µm) absoluut en procentueel toeneemt t.o.v. de PM_{10}-niveaus.

De universiteit van Californië (USA) in Irvine verricht een literatuurstudie naar mogelijke gezondheidseffecten als gevolg van blootstelling aan uitlaatgassen van diesel-, benzine- en LPG-motoren tijdens wintersmogepisoden. In het interimrapport is een eerste samenvatting opgenomen van deze studie. In deze samenvatting worden twee mogelijke biologische hypothesen genoemd die het mechanisme van de toxicologische werking van deeltjes zouden kunnen verklaren.

Beantwoording beleidsvragen

1) Wat is de stand van zaken (organisatorisch gezien) met betrekking tot het onderzoekprogramma zoals geschetst in de notitie 'Hoofdlijnen van onderzoek naar acute effecten van wintersmog op de menselijke gezondheid'?

Tijdens de winters 92/93 en 93/94 zijn er door LUW, RUG en RIVM epidemiologische panelstudies uitgevoerd. Onderdeel van deze studies is een beschrijving van de luchtkwaliteit op de onderzoekslocaties. De gemeten niveaus aan PM_{10} (5 - 145 $\mu g/m^3$ als daggemiddelde) zijn zodanig dat ze liggen in het gebied waarin in buitenlands epidemiologisch onderzoek associaties met (ernstige) gezondheidseffecten zijn aangetoond. Voorlopige analyse van de resultaten bevestigt de bevindingen uit de literatuur. In een pilotonderzoek gedurende de winter van 93/94 is de uitvoerbaarheid van meting van de persoonlijke blootstelling aan PM_{10} onderzocht. In de winter van 94/95 worden de epidemiologische panelstudies afgerond met extra aandacht voor de persoonlijke blootstelling. De resultaten zijn dermate positief dat de persoonlijke PM_{10} blootstellingsmeting op grotere schaal in de studie wordt geïncorporeerd.
In 1994 wordt een literatuurstudie afgerond naar de mogelijke gezondheidseffecten als gevolg van

blootstelling aan uitlaatgassen van benzine-, diesel- en LPG-motoren tijdens een winterepisode. Toxicologisch onderzoek zal uitgevoerd worden in de vervolg fase van het onderzoekprogramma. Daarnaast wordt een model opgesteld dat de mogelijkheid biedt de blootstelling van de stadsbevolking aan wintersmog te berekenen en de relatieve bijdrage van broncategoriën aan de blootstelling, m.n. de uitstoot door het verkeer, te kunnen kwantificeren.

2) Wat zijn de nieuwste inzichten rondom effecten van wintersmog en relatie met verkeer, aanvullend op RIVM-rapport over wintersmog van februari 1990 (53)?

De gegevens in tabel 2.1 (zie 2.1.5) geven aan dat er een relatie bestaat tussen blootstelling aan deeltjesvormige luchtverontreiniging en vervroegde sterfte, ziekenhuisopnamen, longfunctieveranderingen en luchtwegsymptomen (zie ook de inleiding). Recent zijn uit het buitenland aanwijzingen verkregen dat het wonen aan of nabij drukke verkeerswegen samengaat met een verhoogd voorkomen van luchtwegaandoeningen en een chronisch verlaagde longfunctie. Verschillen in luchtwegaandoeningen en longfunctie zijn door enkele onderzoekers aangetroffen binnen stedelijke gebieden, hetgeen suggereert dat er een mogelijk verband is met verschillen in blootstelling aan verkeersgerelateerde luchtverontreiniging tussen mensen wonend langs of nabij drukke en minder drukke wegen in dezelfde stad. Het onderzoek dat in deze richting wijst is uitgevoerd in Duitsland, Japan, en op beperkte schaal ook in Nederland. Het is hoogst onwaarschijnlijk dat een "worst-case" wintersmogepisode als in 1990, beschreven in het RIVM wintersmograpport (53), nog kan voorkomen. Door succesvolle bronbestrijding in Duitsland en Oosteuropese landen zijn de gemiddelde SO_2-niveaus sterk gedaald. Daardoor is de verhouding waarin SO_2 en PM_{10} in de lucht voorkomen sterk veranderd. Gezien de aangetoonde associaties tussen relatief lage daggemiddelde PM_{10}-concentraties en gezondheidseffecten groeit de bezorgdheid over de invloed op de gezondheid van deeltjesvormige luchtverontreiniging ondanks de sterke daling van de SO_2-concentraties.

3) Kan inzicht gegeven worden in de bijdrage van het verkeer aan de luchtverontreiniging in steden tijdens wintersmogepisoden en het effect van verkeersbeperkende maatregelen op de concentraties van luchtverontreinigende stoffen?

Voor het beantwoorden van deze vraag is kennis nodig over de samenstelling en hoeveelheid gassen en deeltjes uitgestoten door het verkeer in de stad, op het platteland en in het buitenland. Door modellering van de verspreiding van de uitstoot kan de luchtverontreiniging in de stad worden berekend. Na koppeling met informatie over het activiteitenpatroon van de stadsbevolking wordt de luchtkwaliteit gebruikt voor het modelleren van de blootstelling aan verkeersemissie van de stadsbewoners. Indien de keten van bron-luchtkwaliteit-blootstelling bekend is, kan de keten tevens in omgekeerde volgorde worden doorlopen om het effect van verkeersbeperkende maatregelen op de blootstelling door te rekenen. Op beperkte schaal zijn voor gasvormige componenten de noodzakelijke gegevens beschikbaar. Voor deeltjesvormige luchtverontreiniging is met name voor

verkeersgerelateerde deeltjes fragmentarische kennis aanwezig. Voor de vervolgfase van het programma wordt daarom onderzoek voorgesteld om in deze belangrijke leemte te voorzien.
De resultaten van de metingen van de luchtkwaliteit in de epidemiologische studies, gedurende de onderzoeksperiode van 92/93 gemeten op een locatie in een stad en op het platteland, lieten zien dat tijdens 'normale' omstandigheden in de winter de PM_{10}-concentratie in de stad maximaal 10% verhoogd is ten opzichte van het platteland. Tijdens episodes bedroeg het verschil op deze locaties ongeveer 30%. De stofsamenstelling van de bemonsterde filters van de beide lokaties verschilt mogelijk meer dan de gemeten PM_{10}-massa concentraties. Nadere analyses in deze zijn voorzien in de vervolgfase van het project. Voor gasvormige componenten waren de verschillen tussen urbane en rurale concentraties groter.

4) Kan thans reeds een uitspraak worden gedaan of het verkeer tijdens wintersmogepisoden oorzaak kan zijn van ernstige acute gezondheidseffecten zoals aangegeven in het Gezondheidsraadadvies over smog van december 1990 en kan inzicht worden gegeven in de omvang (aantal personen) en ernst van de effecten onder de bevolking en risicogroepen binnen de bevolking?

Wintersmog is een grootschalig fenomeen, optredend tijdens bijzondere weersomstandigheden, waardoor t.o.v. gemiddelde omstandigheden soms sterk verhoogde niveaus van luchtverontreiniging kunnen voorkomen. Als broncategorie draagt verkeer in belangrijke mate bij aan de verhoogde niveaus. Met name geldt dit voor de gasvormige componenten en in mindere mate voor PM_{10}. In welke mate (lokaal) verkeer bijdraagt en welke gevolgen dat heeft voor de gezondheidseffecten is op dit moment niet opgehelderd. Ernstige gezondheidseffecten door blootstelling aan wintersmog zijn te verwachten (zie antwoord op vraag 2 en 3).
Door het RIVM is als interne activiteit een eerste kwantitatieve schatting uitgevoerd van de gezondheidseffecten die met blootstelling aan PM_{10} geassocieerd zijn. Daarmee is een poging gedaan, op basis van bestaande gegevens, de omvang van de effecten onder de Nederlandse bevolking in te schatten.

5) Indien 4 positief kan worden beantwoord kan dan nu reeds worden aangegeven of stillegging van het verkeer in steden tot een belangrijke vermindering van het gezondheidsrisico zal leiden.

Het is nog niet duidelijk welke invloed verkeersemissie in een stad heeft op het verminderen van de blootstelling noch op het optreden van gezondheidseffecten. Het is dus nog niet mogelijk aan te geven of stillegging van het verkeer in steden tot een belangrijke vermindering van de gezondheidseffecten zal leiden.

6) Is de huidige indicator voor wintersmog nog voldoende adequaat; zo nee, is er reeds een bruikbaar alternatief?

De somparameter van daggemiddelde concentraties voor SO_2-PM_{10} zoals die nu bestaat als indicator voor de ernst van een smogepisode is achterhaald (zie antwoord op vraag 2). Recente resultaten van binnen- en buitenlands epidemiologisch onderzoek geven aan dat het PM_{10}-niveau op dit moment een meer geschikte indicator lijkt te zijn.

7) Zijn de thans gehanteerde smogklassen (die zijn gekoppeld aan de ernst van de effecten: gering, matig, ernstig en zeer ernstig) nog bruikbaar of moeten deze worden aangepast?

De themagroep 'Wintersmog en verkeer' is van mening dat, gezien de huidige inzichten omtrent het voorkomen van ernstige gezondheidseffecten tijdens wintersmogepisoden, de noodzaak bestaat de bestaande smogklassen aan te passen.
Gezien het feit dat er geen drempelwaarde voor gezondheidseffecten lijkt te bestaan, kunnen ernstige effecten reeds voorkomen bij relatief lage, niet episodische, niveaus reeds voorkomen. Gradatie van gezondheidseffecten in milde mate en ernstige gezondheidseffecten lijkt daardoor sterk bemoeilijkt of onmogelijk te worden.

8) Is er op grond van de nieuwe inzichten aanleiding om de voorlichting over wintersmog aan de bevolking aan te passen?

Deze vraag zou volgens de themagroep 'Wintersmog en Verkeer' voorgelegd moeten worden aan de commissie 'Gezondheidseffecten luchtverontreiniging' van de Gezondheidsraad.

Werkplan

Kwantitatieve risicoschatting van de gezondheidseffecten veroorzaakt door wintersmog en toebedelen van dat risico aan broncategorieën is van groot belang voor effectief en efficiënt risicobeheer. De kwantitatieve risicoschatting komt, als in de inleiding vermeld, tot stand door koppeling van de blootstelling van de stadsbewoner aan luchtverontreiniging met informatie over de bij die blootstelling te verwachten respons. De werkelijke blootstelling van de stadsbevolking aan wintersmog is gebaseerd op kennis van de luchtkwaliteit en het activiteitenpatroon van de bevolking. Indien de herkomst (bronnen) van wintersmog bekend is, kan worden doorgerekend wat de reductie van de uitstoot van bepaalde broncategorieën moet zijn om het risico tot het gewenste niveau terug te brengen.
Van 1992-1994 is vooral onderzoek uitgevoerd dat voor de Nederlandse situatie aangeeft welke gezondheidseffecten kunnen voorkomen bij gezonde personen en bij personen met een ziekte aan de ademhalingswegen in een gebied met veel of weinig verkeer. Voor de volgende fase wordt ook onderzoek voorzien naar de blootstelling van de stadsbevolking en naar het vergroten van het inzicht in het werkingsmechanisme van wintersmog. Zonder deze informatie kan niet adequaat worden geadviseerd over het te voeren risicobeheersbeleid.

Blootstelling
Voor het opstellen van een model dat de werkelijke blootstelling beschrijft (waaraan wordt een individu blootgesteld en hoeveel inhaleert hij daar als hij zich door de omgeving beweegt), zijn de volgende gegevens nodig:

1) karakterisering van de luchtkwaliteit in de stad;
2) herleiding van de luchtkwaliteit naar broncategorieën in de stad, het platteland en het buitenland. Met name dient aandacht aan de herkomst van de uitstoot door het verkeer te worden geschonken;
3) modellering van de blootstelling van de stadsbevolking aan wintersmog met behulp van het Nationale Blootstellingsmodel;
4) validatie van gemodelleerde blootstelling door bepaling van de persoonlijke blootstelling.

Blootstellings-respons
Het in 1992 gestarte epidemiologisch onderzoek, uitgevoerd door de LUW en de RUG, wordt voortgezet in de winter 94/95.
Onderzoek naar het werkingsmechanisme van wintersmog is nodig ter onderbouwing van de biologische plausabiliteit van de gevonden associaties uit het epidemiologisch onderzoek en het adviseren ten aanzien van het optimale bestrijdingsbeleid.

In de vervolgfase van het onderzoek naar de blootstelling-responsrelatie voor wintersmog wordt het volgende onderzoek voorzien:

1) voortzetting lopend epidemiologisch onderzoek;
2) onderzoek naar de invloed van deeltjesgrootte van het aerosool op het gezondheidseffect;
3) dierexperimenteel en zo mogelijk onderzoek met vrijwilligers met deeltjes zoals deze in stadslucht voorkomen.

Afstemming buitenlands onderzoek
In een aantal landen wordt epidemiologisch onderzoek uitgevoerd naar de relatie tussen blootstelling aan stadslucht met name deeltjes en de mate en ernst van gezondheidseffecten. Echter de aandacht van de Nederlandse ministeries voor de invloed van het verkeer op de gezondheid wordt in deze onderzoeken nog niet of nauwelijks gedeeld.

Onderzoek met vrijwilligers en proefdieren naar het werkingsmechanisme van deeltjesvormige luchtverontreiniging staat in de kinderschoenen. In een beperkt aantal landen verkeert het onderzoek in de fase van het formuleren van de vraagstelling en het opperen van te testen onderzoekhypotheses. Hierbij staat de vraag centraal op welke wijze geringe verhogingen van de concentratie van inadembare deeltjes een cascade van gebeurtenissen kan veroorzaken die vooral

bij oudere personen met cardio/pulmonaire ziekten kan leiden tot ernstige ziekte of vervroegd overlijden. Voor het beleid bruikbare resultaten van dergelijk onderzoek zijn eerst rond de eeuwwisseling te verwachten.

Het belang van het uitvoeren in Nederland van zowel epidemiologisch als toxicologisch onderzoek is dat er in dergelijk onderzoek uitgegaan wordt van de Nederlandse situatie met zijn eigen kenmerken (klein dichtbevolkt land, specifiek klimaat, economisch infrastructuur en bedrijvigheid). De problemen die kunnen ontstaan bij het herleiden van buitenlands onderzoek naar de Nederlandse situatie treden dan niet op. Verder is het van belang dat wanneer het onderzoek in Nederland wordt uitgevoerd (eventueel in samenwerking met buitenland) de resultaten sneller beschikbaar zullen zijn.

SUMMARY

This report presents a halfway score of the research project "Winter smog and Traffic", one of the themes of the research programme "Air Pollution and Health". A state of the art is presented of the health effects associated with exposure to winter smog and of the toxicological effects caused by the inhalation of particles. A summary of the assessment of air quality and the results of epidemiological research is presented. Some policy questions are answered as far as possible at this stage of the project. Finally, an outline of a plan of activities is presented which is based on the policy needs and the most serious gaps in knowledge.

A review of the literature shows that population exposure to episodes of winter smog is associated with morbidity and mortality. There does not appear to be a 'threshold-level' for the occurrence of these health effects. Certain subpopulations are at an increased risk such as people suffering from respiratory and cardiovascular diseases. The consistency and coherence of these findings increases the plausibility that the relationship between exposure to winter smog and the observed health effects is a causative one. Preliminary results of the epidemiological studies suggest that health effects also occur in the Netherlands. Air quality in terms of annual and daily mean particulate matter with a cut-off diameter of ten micrometer (PM_{10} levels) is more or less the same at rural and urban sites. Toxicological research to increase the insight in the pathobiological and mechanism of action of aerosol exposure, has not been performed yet. A feasibility study presents an outline for toxicological research most needed to contribute to the causality of the relationship.

A number of elements are essential for a more quantitative assessment of the health effects and the contribution of traffic exhaust to these effects is still lacking. Quantifying public health risk of acute exposure to winter-type smog with an emphasis on traffic-related air pollution requires the determination of the magnitude of the risk, a generalized insight into the actual exposure of the urban population to winter-type smog and information about the health response originating from such exposure. A model of exposure of the urban and rural population to winter-type smog, including the relationship with emission sources, has not been developed yet. Insight into the working mechanism(s) underlying the exposure-effect relationship is very scanty. Therefore, further research is necessary to quantify the health risk of the population to winter smog.

To corroborate earlier findings the epidemiological research will be continued during the winter 1994/95. Additionally, personal exposure to PM_{10} will be assessed. Further characterization of the air quality and especially the assessment of the contribution of various source categories to the actual population exposure is necessary. Additional characterization of the particulate matter is warranted, both for the epidemiological studies and to gain insight into the actual exposure of the population stratified to particle diameter. A continuation of a CHaracterization of Episodical Air Pollution (CHEAP)-like project is recommended.

In the feasibility study for human and animal toxicological research the following three lines of research are presented:

1) the assessment of a relationship between exposure to concentrated particulate matter and health effects,
2) the development of insight into underlying mechanisms of toxicity,
3) the support of the biological plausibility of the epidemiological findings.

1. INTRODUCTION

In 1991 the Minister of Housing, Physiological Planning and Environmental Protection discussed with the Parliament the pros and cons of limiting traffic in large cities during episodes of winter smog and promised a research programme to find answers to the following policy questions:

1) Can serious adverse health effects be caused by exposing the urban population to air pollution during episodes of severe winter smog?
2) What is the contribution of traffic exhaust emitted in the city to the health effects during such an episode?

To initiate a programme to investigate these questions a number of experts drafted a report recommending research to be performed. According to this group the most needed research was:

- epidemiological research: a panel study was suggested with susceptible and healthy children and adults performed at urban and rural sites to ascertain the health effects of exposure to winter smog and to investigate the potential difference in health effects of exposure in an urban and rural setting.
  Research on activity patterns and exposure on a population and personal level is incorporated in this panel-study;
- air quality research: execution of a detailed monitoring programme at a few selected sites within a city to characterize the complex 'winter-type' smog mixture. Efforts need to be made to define 'tracer' components that can be used to monitor the contribution of traffic exhaust to the total air pollution exposure of the urban population and to support exposure assessment for the epidemiological study;
- toxicological research: exposure of laboratory animals (and cell cultures) to the actual complex mixture of 'winter-type' smog so factors such as concentration, exposure time and recovery and structural and functional changes could be studied in more detail. In addition, instillation studies and studies with exposure of laboratory animals to exhaust of diesel, gasoline and lpg (liquified petroleumgas) powered engines could be performed.

In 1991 parliament requested an interim report of the so-called 'Winter smog and Traffic' research programme to be delivered in 1994. The main topic of this report will be whether it is already possible to provide preliminary answers to some of the policy questions and whether it will be necessary to change the winter smog warning regulation.

At this moment epidemiological panel-studies with the distinct panels in cities and rural areas are being analyzed. Except for the research on activity patterns of the panels, the studies correspond to the description mentioned above.
Air quality research has been performed as a part of the epidemiological studies and in the winter of 93/94 a more detailed monitoring programme was performed in a large city and a small village.

Until now toxicological research has not been executed. In the study 'Feasibility report on human and animal toxicity research to assess health effects of short-term exposure to urban winter-type smog and traffic emissions' (52) a set of research recommendations are described.

This interim report reflects a state of the art of the literature on the 'Winter smog and Traffic' (chapter 2), it describes the research that has been performed and, it gives a description of the development of toxicological research (chapter 3). It presents some preliminary answers to the policy questions (chapter 4), and finally the plan of research activities for the second half of the programme is presented.

Chapter 2 and 3 are written by: B. Brunekreef and members of the department Epidemiology and Public Health, Wageningen Agricultural University (WAU) in cooperation with J.P. Schouten and members of the department of Epidemiology, State University of Groningen (RUG); P. Fischer, department of Chronic diseases and Environmental Epidemiology; H. Bloemen, Laboratory of Air Research, and L. van Bree, Laboratory of Pharmacology and Toxicology, all from the National Institute of Public Health and Environmental Protection (RIVM).

The executive summary, introduction and chapter 4 are written by the Task Force 'Man and Environment' research programme, E. Buringh , S. de Loos, and P. Rombout.

2. STATE OF THE ART

2.1 Recent epidemiological evidence relating exposure to low levels of air pollution to acute effects on health

2.1.1 Introduction

The health effects of particulate matter were evaluated jointly with those of sulphur dioxide (SO_2) in the World Health Organization (WHO) Air Quality Guidelines, on the basis of the observation that they usually occur together representing a complex mixture dominated by products of fossil fuel combustion (1). The discussion of short-term effects led to the evaluation that excess mortality could be expected to occur at 24-hour levels of SO_2 and Black Smoke both exceeding 500 $\mu g/m^3$. Likewise, excess morbidity was suggested to occur at SO_2 and Black Smoke levels both exceeding 250 $\mu g/m^3$, and temporary decrements in lung function were suggested to occur at levels of Total Suspended Particulate matter (TSP) exceeding 180 $\mu g/m^3$, in the presence of elevated concentrations of SO_2 (exact levels not specified). A later WHO evaluation of acute effects on health of smog episodes basically used these same values as a basis for establishing some kind of relationship of exposure and health effects (2). At the time of publication of the WHO Air Quality Guidelines no studies relating health effects to inhalable particles (PM_{10}) had been published. Based on the phenomenology of the occurrence of suspended particulate matter it was suggested that 180 $\mu g/m^3$ of TSP would be equivalent to 110 $\mu g/m^3$ of PM_{10}. Taking into account a margin of protection of 1.5, 24-hour average guidelines of 125 $\mu g/m^3$ for SO_2, in combination with 125 $\mu g/m^3$ of Black Smoke, or 120 $\mu g/m^3$ of TSP, or 70 $\mu g/m^3$ of PM_{10} were proposed. In 1987, the US EPA promulgated a 24-hour PM_{10} National Ambient Air Quality Standard of 150 $\mu g/m^3$ (3), without consideration of concurrent levels of SO_2. In the same year in The Netherlands a 24-hour PM_{10} standard of 140 $\mu g/m^3$ was proposed. The review focuses on studies conducted at 24-hour SO_2 concentrations not exceeding 200 $\mu g/m^3$, Black Smoke and TSP levels not exceeding 200 $\mu g/m^3$ and PM_{10} levels not exceeding 150 $\mu g/m^3$, either alone or in combination.

2.1.2 Mortality

Several recent studies have addressed the relationship between particulate air pollution and daily mortality at low levels of exposure (4-9).

Schwartz and Marcus reanalysed mortality data from London (UK) for the winters of 1958-1972 (4). In a graphic analysis, they found no evidence for a threshold in the relationship between Black Smoke and total daily mortality, down to the lowest levels of 20 $\mu g/m^3$. No interaction between Black Smoke and SO_2 was found, and after adjustment for weather variables and SO_2, the effect of Smoke remained significant whereas there was no independent effect of SO_2 after adjustment for Black Smoke. The graphic analysis suggesting effects at very low levels was not supported by a specific statistical analysis using censored data, so that it remains unclear what the lowest level of Black Smoke was below which significant relationships between air pollution and daily mortality could be found.

Schwartz analyzed the relationship between air pollution and daily mortality in Detroit, for the years 1973-1982 (5). TSP was measured every sixth day, and its value for the other days was estimated from a regression model containing visibility data and other variables. A significant relationship between TSP and mortality was found that was independent of other pollutants (ozone and SO_2) and of weather variables. No independent effects of either ozone or SO_2 were found. A graphic analysis suggested that there was no threshold for this effect. After excluding all TSP values under 46, and over 137 $\mu g/m^3$, the results stayed unchanged, suggesting that effects on mortality are observable at 24-hour average TSP levels below 137 $\mu g/m^3$. The estimated magnitude of the effect was a 6% increase in daily mortality associated with a 100 $\mu g/m^3$ increase in TSP averaged over 24 hours.

Pope et al. studied daily mortality in relationship with PM_{10} pollution in Utah Valley for the period of April 1985 - December 1989 (6). A local steel mill is a major source of particulate air pollution in the area, in which concentrations of ozone, SO_2 and nitrogen dioxide (NO_2) are generally low. Respiratory and cardiovascular mortality were found to be related to PM_{10}. 24-hour average concentrations ranging up to 365 $\mu g/m^3$ during the observation period, but a graphical and tabular analysis suggested that effects on mortality could be seen at levels below 100 $\mu g/m^3$. No statistical evaluation using censored data was made, however.

Schwartz and Dockery studied mortality in Philadelphia, PA, over the years 1973-1980 (7). The second-highest 24-hour average TSP concentration in this period was 222 $\mu g/m^3$. Daily mortality was found to be related to TSP. There was no interaction with SO_2, and the effect of TSP was independent of SO_2. The estimated effects were larger for respiratory and cardiovascular deaths than for other diagnoses, and they were also larger for subjects over 65 years of age than for younger subjects. A graphical analysis suggested that the effect was already detectable at levels below 100 $\mu g/m^3$, but no attempt was made to do an analysis with data censored to below certain cut-off points for TSP.

The same authors have also published a very similar analysis of mortality data from Steubenville (Ohio) (8). Again, a graphical analysis suggested effects of TSP on mortality at levels below 100 $\mu g/m^3$, but no censoring was applied to the data that would permit identification of a threshold level below which no significant relationship between mortality and TSP exists.

Dockery at al. have also published an analysis of daily mortality in St. Louis (Missouri) and the counties surrounding Kingston/Harriman (Tennessee) (9). During the period of observation (September 1985 - August 1986) 24-hour average PM_{10} levels ranged from 1-97 $\mu g/m^3$ in St. Louis, and from 4-67 $\mu g/m^3$ in Kingston/Harriman. Even at these low levels, a relationship between PM_{10} and mortality was found that was statistically significant in St. Louis. The estimated coefficient for Kingston/Harriman was insignificant, but of similar magnitude. A number of gaseous air pollution components (SO_2, NO_2, ozone) were evaluated as well, but none of these was found to be significantly associated with mortality.

2.1.3 Hospital admissions

Schwartz et al. investigated the variation in daily visits to hospitals or pediatricians for croup symptoms and obstructive bronchitis in children (10) in five German towns in the mid-1980s. Maximum pollutant concentrations were not given, but 90-percentiles for 24 hour-TSP ranged from 41 - 118 $\mu g/m^3$ in the five cities, suggesting that the majority if not all of the concentrations were lower than 200 $\mu g/m^3$ in the period of observation. Visits for croup (but not for obstructive bronchitis) were found to be associated with TSP, NO_2 and SO_2 in models containing only one pollutant. In two-pollutant models, SO_2 and NO_2 became insignificant, whereas TSP remained significant in the model also containing SO_2. A graphical analysis suggested that at 24 hour-TSP levels below 100 $\mu g/m^3$, the risk of croup was still increased.

Diaz-Caneja et al. studied hospital admissions for chronic obstructive pulmonary diseases (COPD) in Santander (Spain) in relation with daily SO_2 and Black Smoke concentrations (11). The mean and range of the pollutant concentrations were not given, but COPD admissions were found to be related to both SO_2 and Black Smoke. A graphical analysis suggested that admissions were already increased at 24 hour-BS levels exceeding 40 $\mu g/m^3$. There was also a relationship with SO_2 but this appeared to be less strong than for Black Smoke. No attempt was made to separate the two pollutants in the analysis.

Sunyer et al. studied emergency room admissions for COPD in Barcelona (Spain) (12,13). 24-Hour Black Smoke concentrations ranged from 39 - 310 $\mu g/m^3$, and 24 hour-SO_2 from 17 - 160 $\mu g/m^3$. A significant relationship between the number of emergency room admissions and both SO_2 and Black Smoke was found. The relationship persisted when all SO_2 concentrations above 72 $\mu g/m^3$ were removed from the analysis, and also when all Black Smoke concentrations over 100 $\mu g/m^3$ were removed. The relationships with SO_2 and Black Smoke appeared to be independent from each other, and the relationship with SO_2 was apparent in all seasons, whereas the relationship with Black Smoke was most clear in winter (30).

Schwartz et al. studied hospital emergency room visits for asthma in Seattle over a 13 month period from September 1989 - September 1990 (14). 24-hour average PM_{10} concentrations ranged from 6 - 103 $\mu g/m^3$. Asthma visits by subjects under 65 were significantly associated with PM_{10} measured on the previous day, after adjustment for weather variables and a number of other potential confounders. A graphical and tabular analysis suggested that an increase in asthma visits could already be observed at levels below 24 $\mu g/m^3$. SO_2 and ozone were not found to be related to asthma visits. SO_2 concentrations never exceeded 81 $\mu g/m^3$, and ozone data were only available for a four months period within the period of observation.

Walter et al. (15) studied hospital admissions for asthma and acute respiratory disease over a two year period in Birmingham (UK). Air pollution exposure was expressed as weekly average Black Smoke and SO_2 concentrations. Black Smoke concentrations ranged from 10 to over 60 $\mu g/m^3$, SO_2 concentrations from 20 to 100 $\mu g/m^3$. Significant relationships were found between hospital admissions and daily as well as weekly Black Smoke and SO_2 concentrations in the winter period. These relationships were found to be independent of weather conditions. There was no attempt to separate effects of Black Smoke from those of SO_2.

2.1.4 Lung function and other effects

Ostro et al. studied a panel of asthmatic patients in Denver, Colorado, in the winter of 1987/1988 (16). 24-hour average concentrations of $PM_{2.5}$, a measure of respirable particulate matter, ranged from 1 - 73 $\mu g/m^3$. $PM_{2.5}$ concentrations were found to be related to asthma rating in this panel after adjustment for auto-correlation, temperature and a number of other potential confounders.

Forsberg et al. (17) studied a panel of asthmatic patients living in northern Sweden. In the area, wood is used extensively for residential heating. In the period of observation (March and April), SO_2 concentrations ranged from 1 - 13 $\mu g/m^3$, and Black Smoke from 1 - 21 $\mu g/m^3$. Daily reports of shortness of breath were related to Black Smoke after adjustment for weather variables. In one location 1 km away from the study area, 12-hour TSP samples were taken, and a maximum concentration of 101 $\mu g/m^3$ was found, suggesting that the actual particle mass concentration may have been much higher than the Black Smoke concentration in the area.

Braun-Fahrländer et al. studied daily changes in respiratory symptoms in 625 young children living in two Swiss cities (18). 24-hour average TSP levels ranged from 30 - 117 $\mu g/m^3$. The reported incidence of upper respiratory symptoms was found to be associated with TSP concentrations measured on the previous day. A graphical analysis suggested that this effect could be observed at TSP levels well below 100 $\mu g/m^3$.

Pope et al. studied daily changes in lung function and acute respiratory symptoms in a panel of subjects living in Utah Valley (Utah), where a large steel mill causes increased concentrations of PM_{10} but not of other pollutants (19). Subjects included a sample of wheezing school children and a sample of asthma patients 8 - 72 years of age. The observation period included the winter months of 1989/1990. 24-hour PM_{10} concentrations ranged from 11 - 195 $\mu g/m^3$, and on only two days, a concentration of 150 $\mu g/m^3$ was exceeded. The Peak Expiratory Flowrate (PEF) was found to be related to PM_{10} concentrations of the preceding days. Respiratory symptoms and asthma medication use increased with increasing PM_{10} concentrations in the school-based sample of children. In the asthma patients, only the use of extra asthma medications was found to be associated with PM_{10}. After excluding the two days with PM_{10} concentrations over 150 $\mu g/m^3$, the highest PM_{10} concentration was 114 $\mu g/m^3$. The relationship between PEF and PM_{10} remained unchanged after this exclusion.

Pope et al. studied panels of symptomatic and asymptomatic children in Utah Valley in the winter of 1990/1991 (20). 24-hour PM_{10} concentrations ranged from 7 - 251 $\mu g/m^3$. On 14 days during the study period, a level of 150 $\mu g/m^3$ was exceeded. PEF was decreased, and the reporting of respiratory symptoms was increased in both panels when PM_{10} concentrations increased. All observations from days with or immediately following days with PM_{10} concentrations over 150 $\mu g/m^3$ were excluded from some of the analyses. The results remained essentially unchanged. A tabular analysis further suggested that PEF was decreased, and respiratory symptoms were increased at PM_{10} concentrations exceeding 39 $\mu g/m^3$.

In another study from the Utah Valley, Ransom and Pope investigated elementary school absences in relationship to PM_{10} pollution over a period of six years, 1985 - 1990 (21). The highest PM_{10} concentration observed in this period was 365 $\mu g/m^3$, and exceeded 150 $\mu g/m^3$ on approximately 10

days each year. School absenteeism was found to be related to 4-week moving average PM_{10} concentrations, after adjustment for weather variables and a number of other potential confounders. The relationships generally remained after excluding observations obtained on days when PM_{10} had exceeded 150 $\mu g/m^3$ within the previous four weeks.

Roemer et al. studied a panel of children with chronic respiratory symptoms in The Netherlands in the winter of 1990/1991 (22). 24-hour average PM_{10} concentrations exceeded 150 $\mu g/m^3$ on one day only in the observation period, reaching 174 $\mu g/m^3$. SO_2 levels were never higher than 105 $\mu g/m^3$, and Black Smoke concentrations (24-hour averages) ranged from 2 - 120 $\mu g/m^3$. Daily changes in PEF, asthma attacks, wheeze and bronchodilator use were found to be associated with PM_{10}, Black Smoke and SO_2. A tabular analysis suggested that effects on wheeze and bronchodilator use were observable from concentrations exceeding 40 $\mu g/m^3$. SO_2, Black Smoke and PM_{10} were highly correlated in this data set, so that effects of particles and SO_2 on lung function could not be separated. Despite the high correlation, effects of PM_{10} on symptoms and medication use were more clear than those of SO_2 in a multivariate analysis.

A group of school children not participating in the above study was investigated in this period with repeated spirometry (23,24). Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV_1) were associated with 24 hour concentrations of PM_{10}, SO_2 as well as Black Smoke. There was no relationship between air pollution and acute respiratory symptoms in this panel.

Hoek and Brunekreef (25) studied panels of school children in the winters of 1988 - 1990 in The Netherlands. All children were tested repeatedly with spirometry over periods of about 10 - 15 weeks. In the observation period, 24-hour PM_{10} concentrations ranged from 14 - 126 $\mu g/m^3$, SO_2 from 0 - 94 $\mu g/m^3$ and NO_2 from 2 - 70 $\mu g/m^3$. PEF and Maximum Mid Expiratory Flow (MMEF) were found to be negatively associated with PM_{10} and NO_2 concentrations measured either on the same day or the day before the lung function tests, and after adjustment for ambient temperature.

Wjst et al. (31) studied the effect of road traffic in Munich on pulmonary function and respiratory symptoms in children. The results of the study showed an association between traffic load and reduced pulmonary function and increased respiratory symptoms in 10 year old children. In addition, one of the purposes of this evaluation was to show that the assigned traffic rates correlated with air pollution, because car traffic counts reflects more the synergistic action of all emitted substances than a single marker of air pollution.

In Japan, Nitta et al. (32) studied a panel of female residents living close to mayor roadways in Tokyo, where there is consistently heavy traffic. They examined the relationship between the prevalence of respiratory symptoms and household location with respect to distances from the roadside. The results of the study suggest that respiratory symptoms that are related to mucus hypersecretion might have an association with automobile exhaust.

2.1.5 Summary

Table 2.1 summarizes the results of the studies on particles that were discussed in this section. These studies indicate that increases in daily mortality have been found in a situation where measured PM_{10} concentrations never exceeded 100 $\mu g/m^3$ (9), in a situation where TSP concentra-

tions were censored to below 137 $\mu g/m^3$ (5), in three situations where a graphical analysis suggested that effects on mortality were present at levels below 100 $\mu g/m^3$ of either PM_{10} (6) or TSP (7, 8). A re-analysis of data from London (UK) further suggested that daily mortality was related to Black Smoke without evidence of a threshold at levels down to 20 $\mu g/m^3$ (4).

Hospital admissions for respiratory disorders were found to be related to low concentrations of particles in four recent studies. Most convincing is the study from Seattle (14) where measured PM_{10} levels never exceeded 103 $\mu g/m^3$. Studies from Barcelona (Spain) have documented effects at Black Smoke levels censored to below 150 $\mu g/m^3$ (12, 13), and a study from Germany suggested effects on hospital and paediatrician croup visits at TSP levels below 100 $\mu g/m^3$ by graphical analysis (10).

Effects of particulate pollution on acute respiratory symptoms, lung function and school absenteeism have been found in several recent studies. Some of these were conducted entirely at concentration levels: Black Smoke < 120 $\mu g/m^3$ (22-24), Black Smoke < 25 $\mu g/m^3$ (17), PM_{10} < 130 $\mu g/m^3$ (25). Other studies have employed censoring in the analysis of the data: to below 150 $\mu g/m^3$ PM_{10} (20, 21) or < 115 $\mu g/m^3$ (19). One study (18) suggested effects on acute respiratory symptoms at TSP levels below 100 $\mu g/m^3$ by graphical analysis.

The variety of particulate air pollution measures employed in these studies makes evaluation in terms of one single indicator somewhat problematic. For the US relationships between the three primary indicators PM_{10}, TSP and BS have been suggested (26) as PM_{10} is approximately equal to BS and PM_{10} TSP * 0.55. A proportionality between PM_{10} and $PM_{2.5}$ of 0.6 was suggested. However, such relationships may vary from place to place and with time, depending on the contribution of local sources. In the Netherlands, the relationships between various measures of particulate matter pollution are almost certainly different from those cited above (30). Nevertheless, on the basis of these relationships the data summarized in table 1 suggest that particulate air pollution is associated with daily mortality, hospital admissions, symptom exacerbations and lung function changes at levels not exceeding 100 $\mu g/m^3$, expressed as PM_{10} and averaged over 24 hours. Indeed, several of the graphical and tabular analyses suggest that it is difficult to establish a threshold below which such effects would not be found to be associated with particles. So far, studies have simply not been reported that have specifically analyzed associations between particles and acute health events using cut-off points below 100 $\mu g/m^3$.

Table 2.1 Summary of studies relating 24-hour average particle concentrations of less than 200 $\mu g/m^3$ (TSP or Black Smoke) or 150 $\mu g/m^3$ (PM_{10}) with specific effects on human health.

Ref.	Concentrations	Category of health effect			
		Mortality	Hospital Admissions	Symptom Exacerbations	Lung Function Changes
(4)	? (BS)	+			
(5)	< 137 (TSP)	+			
(6)	< 100 (PM_{10})	+			
(7,8)	< 100 (TSP)	+			
(9)	< 100 (PM_{10})	+			
(10)	< 100 (TSP)		+		
(11)	? (BS)		+		
(12,13)	< 150 (BS)		+		
(14)	< 105 (PM_{10})		+		
(15)	< 60 (BS, weekly)		+		
(19)	< 115 (PM_{10})			+	+
(16)	< 75 ($PM_{2.5}$)			+	
(18)	< 100 (TSP)			+	
(20)	< 150 (PM_{10})			+	+
(21)	< 150 (PM_{10})			+	
(22-24)	< 120 (BS), < 175 (PM_{10})			+	+
(17)	< 25 (BS)			+	
(25)	< 130 (PM_{10})			-	+

Most of the studies cited in this brief review have attempted to estimate the contribution of specific sources to the particulate matter exposures, or to the health effects associated with them. Virtually all studies consist of single population time series, and those that have looked at more than one population simultaneously (e.g., 9) have not looked at populations with contrasting exposures, but rather at more than one, more or less similarly exposed populations. Even though a fairly large body of evidence has accumulated in recent years associating particulate matter exposure with various health effects, the available evidence does not allow us to conclude whether such effects would be different when sources of particulate matter are different, and whether effects of particles

are different in urban areas than in rural areas.

2.2 Toxicity of ambient particulate air pollution

The data base of health effects associated with acute exposure to urban particulate air pollution is rapidly growing through the reporting of various epidemiological studies. Collectively, these recent data indicate that increases in daily mortality, hospital visits, asthma exacerbations, respiratory symptoms and lung function decline are associated with 24-hour levels of urban particulate air pollution measured as PM_{10} (see 2.1). The levels of particulate matter reported in these studies are significantly lower than those previously thought to affect human health and there appears to be no evidence for a threshold value. In addition, recent epidemiological data also indicate significant associations between long-term exposure to PM_{10} or $PM_{2.5}$ levels and excess mortality, lung function decline, and respiratory symptoms, in particular at urban areas with relatively high traffic density (18, 29, 31, 32, 34, 35).

The health risk assessment of ambient particulate air pollution is hampered by a lack of human and animal toxicity data rendering evidence for a causal exposure-effect relationships and for underlying mechanisms of action. This absence of toxicity data is partly caused by the lack of suitable exposure models and relevant, particulate air samples to perform the experiments. With regard to possible mechanisms of respiratory toxicity of particulate matter it should be noticed that, differing from effects observed during summersmog episodes (36), decrements of lung function are relatively small compared to effects on morbidity and mortality. This might indicate a special mode of action, possibly resulting in potentially serious ventilation-perfusion problems.

Inhalation studies with highly insoluble particles with an inflammatory, fibrotic, or tumorigenic potential (coal dust, TiO_2, Al_2O_3, toner, carbon black, and diesel exhaust) have pointed to the importance of particle size, as well as particle surface area and surface reactivity rather than particle mass (37). Data show that ultrafine particles (< 0.1 μm) have higher deposition chance and lower clearance rates in lower airways and have a larger pulmonary toxicity per unit mass compared to the fine- and coarse-mode particles (38, 39). Pulmonary toxicity of ultrafine particles appears to occur at a much lower lung burden than suggested for larger-sized particles. In addition, there is evidence that pulmonary toxicity, primarily tumours, is more correlated with the surface area of the particles retained in the lung rather than with particle mass, or number of particles (39, 40, 41). Collectively, these studies suggest that surface area and surface reactivity of ultrafine particles play a major role in causing effects in pulmonary tissue. The relatively high surface reactivity of the ultrafine particles is suggested to be linked with its oxidative ability, possibly through reactive organic and metal ions, resulting directly or indirectly in inflammatory cell activation and release of mediators causing structural pulmonary damage and toxicity (37, 40, 42, 43, 44). Pre-existing airway disease as a major risk factor seems to be supported by toxicity data on larger impairment of clearance rates and higher biological sensitivity compared to healthy human lungs (45, 46).

Air quality data have revealed that ambient aerosols occur with a typical trimodal distribution. The mass distribution showing peaks depending on the aerodynamic particle size (D_{ae}) occurring at

coarse (inhalable)-mode (D_{ae} approximately 10 μm), fine-mode (D_{ae} approximately 1-3 μm), and ultrafine-mode particles (46, 48). The ultrafine-mode of the particulates with a D_{ae} ranging from 0.05-0.3 μm is suggested to be primarily derived from automobile engines, however, its occurrence in ambient urban air is yet largely unknown. Furthermore, owing to their small volume/mass, their contribution to the concentration of PM_{10} is almost negligible. This may explain that the PM_{10} concentration in urban and rural areas does not differ significantly although the number of primary emitted traffic exhaust particles in the cities may be much higher than in rural areas. Indeed there are indications that during increased air pollution, the ultrafine particle phase of the ambient aerosol may increase considerably (49), and PM_{10} levels do not appear to correlate with Black Smoke and levels of polycyclic aromatic hydrocarbons (50).

Human and animal toxicity studies on ambient particulate air pollution have to focus on the causality of the exposure-effect relationship and on clarifying the relative importance of the biological potency of ultrafine particles, as from traffic exhaust, in healthy and compromised lungs, thereby adding to and supporting the biological plausibility of the epidemiological findings.

3 STATE OF AFFAIRS OF RESEARCH IN THE PROGRAMME

3.1 Introduction

In the winter of 1992/1993 studies on the health effects of short-term variations in air pollution were conducted by the Wageningen Agricultural University (WAU) and the National Institute of Public Health and Environmental Protection (RIVM). For logistic reasons both study-centres used different panels. WAU studied young (7 -12) and older (50-70) subjects with and without chronic respiratory symptoms, but the members of the panels were not necessarily diagnosed by a doctor as asthmatic or as a patient with Chronic Obstructive Pulmonary Disease (COPD). The RIVM panel consisted of out-patient asthmatic children (8-12), all diagnosed as asthmatics and using maintenance medication at the moment of incorporation in the study. Therefore, in the epidemiological design a large range of children with and without respiratory symptoms was studied: children without chronic respiratory symptoms, children with positive answers on a screening questionnaire but not necessarily diagnosed as asthmatics by a doctor, and children with a doctor diagnosed asthma.

In this chapter some preliminary results of the studies of the two centres will be presented separately. In paragraph 3.4 the results of both centres will be discussed.

3.2 Epidemiological study by WAU

3.2.1 General description of the study design

The epidemiologic 'winter smog' study was designed as a panel study to detect health effects of short-term variations in air pollution concentrations. The basic policy question is to what extent current urban air pollution levels in winter are associated with adverse health effects, and to what extent traffic exhaust may be held responsible for such effects. In order to answer these questions, subjects living in large urban areas have been followed for some months in the winters of 1992/1993 (55), 1993/1994 and will be studied in the winter of 1994/1995. Simultaneously, subjects living in rural communities are studied as controls. Young (7-12) and older (50-70) subjects are being studied, and healthy subjects as well as subjects with chronic respiratory symptoms. Target panel size is 75 subjects per panel. All panel members are being examined with skin tests, determinations of IgE, eosinophilic cells, and bronchial reactivity to methacholine. Air pollution monitoring at fixed sites is carried out in the urban as well as the control communities.

3.2.2 Population selection

The pilot phase of the study in the winter of 1992/1993 was carried out. Rotterdam was chosen as a large urban area, and Bodegraven/Reeuwijk (≈30 km to the east of Rotterdam) as control communities. Areas in the centre of Rotterdam were selected in consultation with local health and environmental officers. In the winter of 1993/1994, Amsterdam was studied as urban area, and Meppel and surrounding communities (≈100 km to the north-east of Amsterdam) as control. The reason to select a control location at further distance was that in the first winter, the contrast of

exposure to PM_{10} between Rotterdam and Bodegraven/Reeuwijk was found to be smaller than expected (see below). For the winter of 1994/1995, Amsterdam again is envisaged as the urban area to be studied. A suitable control location is currently considered.

Screening questionnaires are used to obtain information on chronic respiratory symptoms. For children, questionnaires were distributed through their schools. Children with reports of attacks of shortness of breath with wheezing, doctor diagnosed asthma, current treatment for asthma and chronic cough were classified as 'symptomatic' children. Children without any reported symptoms on the screening questionnaire were classified as 'non-symptomatic' children.

Random samples of 50-70 year old adults were drawn from the population registries of the selected communities. Subjects reporting attacks of shortness of breath in the past twelve months, asthmatic attacks, current asthma medication use, chronic cough or chronic phlegm were classified as 'symptomatic' subjects. Subjects without any respiratory symptoms were classified as controls. Target panel size in this pilot was 25 persons per panel.

3.2.3 Air quality

In the urban areas, two monitoring sites are operated for the duration of the observation periods. In Rotterdam, one site was chosen as an urban 'background' site, not directly influenced by local traffic. This was a site at least 50 m away from busy roads. Another site was located next to a busy road, to obtain information on maximum street levels of pollutants ('street' site). In the control location, one monitoring station is operated, not directly influenced by road traffic or local pollution sources.

On each site, measurements are made of PM_{10}, Black Smoke, acid gases and aerosols using an annular denuder method. In addition, data on SO_2, nitric oxide (NO), carbon monoxide (CO) and NO_2 are obtained from nearby monitoring stations of the National Monitoring Network of RIVM. All of these measurements are conducted on a continuous, daily basis throughout the observation periods. Supplementary measurements of street and indoor concentrations are being made using NO_2 diffusion badges. In selected homes, indoor PM_{10} measurements are also being conducted. In the diary (see below), limited information on time-activity patterns of the participants was collected for each day of the studyperiod.

3.2.4 Health effect assessment

Variations in health status of panel members are measured by having subjects perform peak flow measurements using hand-held mini-Wright peak flow meters three times every day during the observation periods. Measurements were made in the morning when getting up, in the afternoon and in the evening before getting to sleep. Subjects are instructed to perform the measurement before taking medication. In addition, a diary is used to collect information on acute respiratory symptoms on a daily basis. Subjects are asked to record whether they experienced cough, phlegm, a runny or stuffed nose, shortness of breath, wheeze, attacks of shortness of breath with wheezing, or whether they had woken up having difficulty breathing. Subjects were also asked to record respiratory medication use (brand name and dose) each day.

3.2.5 Subject characterization

Each subject was invited to a medical examination. The examination included a bronchial methacholine challenge and a lung function test. A blood sample was drawn for determination of serum IgE, and for making leucocyte and eosinophil counts. A skin prick test was used to assess reactivity to common allergens. On the basis of these measurements, subjects can be categorized in various ways, and the relationship between these characteristics and acute health effects of air pollution can be investigated.

3.2.6 Data analysis

The analysis of the data is focused on relationships between daily variations in air pollution and daily variations in peak flow, respiratory symptoms and medication use. For each subject, the relationship between peak flow and various measures of air pollution exposure are assessed by linear regression modelling taking into account the autoregressive structure of the residuals. Individual regression coefficients are then pooled to obtain a group estimate of the air pollution effect. For symptoms and medication use, the prevalence is first calculated for each day in the observation period. Using logistic regression, the prevalence of symptoms and medication use is then related to various measures of air pollution exposure, again adjusting for autocorrelated residuals.

In the analyses that were performed so far (winter 1992/1993 only), the following restrictions have been applied (full analysis is in progress and will be reported later):

- Peak flow — only morning and evening peak flow have been analyzed
- Symptoms — only the prevalence of two symptom combinations, symptoms of the lower airways (LRS: phlegm, wheeze, shortness of breath, attacks of wheezing with shortness of breath) and symptoms of the upper airways (runny/ stuffed nose)
- Medication use — only the prevalence of bronchodilator use
- Exposure — only the 24-hour concentrations of PM_{10}, Black Smoke, SO_2, NO and NO_2 and the sum of SO_2+PM_{10}. For PM_{10} the concentration of the same day ("lag" 0), of the day before ("lag" 1), of two days before and the weekly average are being analyzed. For other components, only the 'lags' that were found to be relevant in the PM_{10} analyses are analyzed.

- Confounders time trend, ambient temperature (24 hour average), day of week. For PEF, the first 7 days are left out of the analysis to avoid learning effects (Roemer et al., 1993). The last days of april 1993 have been omitted because of high temperatures and the possibility of ozone exposure. For the analysis of symptoms, some days in the beginning have been left out because few participants had been enrolled and were reporting at the time.

3.2.7 Air quality

Table 3.1 reports the air pollution levels as they were measured in the observation period in the winter of 1992/1993 in Rotterdam and Bodegraven/Reeuwijk.

Table 3.1 Air pollution concentrations in Rotterdam (ROT) and Bodegraven/Reeuwijk (BR) (24-hour average PM_{10}, BS, SO_2, NO, NO_2 in $\mu g/m^3$, temperature in °C. Period 23/1/93-19/4/93.

	Location	Mean	Median	Range	n
PM_{10}	ROT	52.9	46.7	0.7 - 145.6	83
	BR	48.0	37.9	5.2 - 111.2	68
BS	ROT	21.4	17.8	3.4 - 67.9	74
	BR	16.2	12.5	1.8 - 45.1	68
SO_2	ROT	25.3	23.1	1.2 - 110.0	87
	BR	9.4	8.7	1.0 - 28.0	72
NO	ROT	35.2	21.3	1.2 - 177.8	87
	BR	15.0	5.8	0.0 - 129.6	72
NO_2	ROT	53.4	53.4	12.2 - 94.8	87
	BR	36.4	33.6	5.9 - 80.2	70
Temp	ROT	6.1	6.3	-0.5 - 12.2	87
	BR	5.6	5.9	-0.6 - 10.7	73

There was little difference in mean 24-hour PM_{10} concentrations between the two locations, but the maximum concentration in Rotterdam was clearly higher than in the control town. During a short period of stagnating weather conditions in February 1993, the mean PM_{10} concentrations in Rotterdam were 118 $\mu g/m^3$ vs. 92 $\mu g/m^3$ in Bodegraven/Reeuwijk, indicating that in such periods, concentrations may increase more in a large urban area than in a much smaller control town. Mean

concentrations for Black Smoke and the gaseous components were clearly higher in Rotterdam.

3.2.8 Symptom responses

Due to the pilot phase character of the study in the winter of 1992/1993, the panel size was smaller than anticipated for the children, especially in Rotterdam. Usable data were obtained for 83 children in Rotterdam and 115 in Bodegraven/Reeuwijk. It was anticipated to enrol 50 adults (Rotterdam only) in this phase. Usable data were obtained from 44 persons. Tables 3.2 and 3.3 present some prevalences of acute symptoms and medication use in classes of increasing PM_{10} concentrations.

Table 3.2 shows the distribution of the number of days (in %) in the different PM_{10}-levels. Tables 3.3 and 3.4 show some increase in LRS in all panels of children with increasing PM_{10} concentrations. There was no such increase in the adults, but baseline prevalence was higher in the adult panel. It is currently been investigated whether the results change when severity of symptoms is taken into account. Bronchodilator use increased slightly in the symptomatic panels with increasing PM_{10} concentrations.

Table 3.2 Distribution of days (in %) over different PM_{10} levels (in $\mu g/m^3$) and number of days (n) in Rotterdam (ROT) and Bodegraven/Reeuwijk (BR).

Location	< 40	40-70	70-100	>100	n days
ROT	38	35	18	10	72
BR	52	22	21	4	68

Table 3.3 Prevalence of Lower Respiratory Symptoms (LRS) and use of bronchodilator (BRO) in children on days with different PM_{10} levels (in $\mu g/m^3$) in Rotterdam (ROT) and Bodegraven/Reeuwijk (BR).

	Panel	Location	< 40	40-70	70-100	>100
LRS	Symptomatic	ROT	35.6	35.2	38.4	43.5
		BR	32.0	28.9	30.8	39.0
LRS	Non-symptomatic	ROT	6.3	7.1	7.3	11.0
		BR	7.3	7.3	8.1	10.3
BRO		ROT	5.0	5.9	6.6	6.4
		BR	5.5	4.5	5.7	9.1

Table 3.4 Prevalence of Lower Respiratory Symptoms (LRS) and use of bronchodilator (BRO) in Rotterdam adults on days with different PM_{10} levels $\mu g/m^3$).

	Panel	< 40	40-70	70-100	> 100
LRS	Symptomatic	47.3	48.3	46.2	-
	Non-symptomatic	9.5	11.6	7.5	-
BRO		9.7	12.4	12.8	-

Tables 3.5 and 3.6 present results of logistic regression analyses on these data, taking into account temperature, time trend and auto-correlated residuals.

Table 3.5 Time series analysis of symptoms and medications use in children; Odds-ratios for a change in PM_{10} concentration of 100 $\mu g/m^3$, adjusted for time trend and ambient temperature in Rotterdam (ROT) and Bodegraven/Reeuwijk (BR).

Panel	Location	LRS	Bronchodilator
Symptomatic	ROT	1.11 (0.86-1.43)	1.14 (0.76-1.71)
	BR	0.98 (0.80-1.21)	0.99 (0.72-1.36)
Non-symptomatic	ROT	1.48 (0.98-2.23)	--
	BR	1.25 (0.87-1.79)	--

Table 3.6 Time series analysis of symptoms and medications use in adults; Odds-ratios for a change in PM_{10} concentration of 100 $\mu g/m^3$, adjusted for time trend and ambient temperature.

Location	Panel	LRS	Bronchodilator
Rotterdam	Symptomatic	0.98 (0.66-1.47)	1.45 (0.83-2.52)
	Non-symptomatic	0.70 (0.21-2.35)	--

The tables show that the odds ratios were (non-significantly) increased for use of bronchodilators in both symptomatic Rotterdam panels. Symptoms seemed to increase with PM_{10} more in Rotterdam children than in control children. These analyses need further corroboration on the basis of larger datasets.

3.2.9 Peak Flow responses.

Table 3.7 shows the relationship between peak flow and daily PM_{10} levels. Coefficients were

generally negative for symptomatic subjects living in Rotterdam. Coefficients were less negative for non-symptomatic subjects and for subjects not living in Rotterdam.

Table 3.7 Regression analysis of PEF and 24-hour PM_{10}; mean regression coefficient (s.e.) in litres per minute per $\mu g/m^3$, adjusted for time trend and ambient temperature (children) in Rotterdam (ROT) and Bodegraven/Reeuwijk (BR).

Panel	Location	n	Morning PEF	Evening PEF
Symptomatic	ROT	31	0.016 (0.025)	-0.042 (0.022)#
	BR	48	-0.002 (0.022)	-0.022 (0.020)
Non-symptomatic	ROT	52	0.003 (0.018)	0.011 (0.022)
	BR	67	0.011 (0.017)	-0.010 (0.017)

# $p < 0.10$

Table 3.8 Regression analysis of PEF and 24-hour PM_{10}; mean regression coefficient (s.e.) in litres per minute per $\mu g/m^3$, adjusted for time trend and ambient temperature (adults).

Panel	Location	n	Morning PEF	Evening PEF
Symptomatic	ROT	28	-0.056 (0.037)	-0.049 (0.045)
Non-symptomatic		16	-0.029 (0.052)	-0.035 (0.031)

3.2.10 Medical characterization

Table 3.9 shows some results of the medical characterization of the children. The data show that the children who were symptomatic on the screening questionnaire had more bronchial reactivity to methacholine, and more atopy as defined by skin prick test than the non-symptomatic children. However, there was considerable overlap between the two groups, indicating that a screening questionnaire is an insufficient instrument to define potentially 'susceptible' groups. Especially children with reported recent asthma were clearly different from the others in most respects however.

Table 3.9 Medical characteristics of study children.

	FEV_1%pred n=214	20%δ FEV_1 n=191	Atopy n=211	Eosinophilia n=190	Eosinophils GM
Symptomatic: n=96	104.8±11.4	25 (29,1%)	49 (52.1%)	27 (30.3%)	255
Non-sympt.: n=120	105.1±11.5	7 (6.7%)	38 (32.5%)	26 (25.7%)	229
Asthma ever: n=11	105.3±10.6	2 (20.0%)	6 (54.5%)	2 (20.0%)	271
Recent asthma: n=46	103.0±13.4	18 (45.0%)	31 (68.9%)	21 (46.7%)	337
Chronic cough: n=39	106.8±8.7	5 (13.9%)	12 (31.6%)	4 (11.8%)	177

Table 3.10 Relationship between some medical characteristics and peak flow response to (weekly average) PM_{10} in children (coefficients in litres/minute per $\mu g/m^3$ and standard error (SE)).

	Rotterdam	Bodegraven/Reeuwijk
	ß (SE) (n)	ß (SE) (n)
>10% decline after provocation	.01 (.12) (22)	.00 (.05) (43)
<10% decline after provocation	-.04 (.05) (38)	-.05 (.04) (55)
>20% decline after provocation (2 mg)	-.09 (.08) (9)	.00 (.09) (17)
<20% decline after provocation (2 mg)	-.01 (.06) (50)	-.03 (.03) (81)
>20% decline after provocation (0.5 mg)	-.19 (.10) (3) #	.27 (.15) (6)
atopy (skin test +)	.07 (.08) (33)	.02 (.05) (42)
no atopy	-.13 (.05) (31) *	-.04 (.03) (69)
eosinophilia	-.05 (.06) (14)	.04 (.07) (29)
no eosinophilia	-.01 (.07) (41)	-.05 (.03) (68)

* $p < 0.10$

* $p < 0.05$

Table 3.10 shows the relationship between some medical characteristics and peak flow response to 24-hour PM_{10}. The results suggest that in Rotterdam, children with a high degree of BHR experienced a larger influence of PM_{10} on peak flow, but there were only few children left in this group. Clearly, the analysis of effects in subgroups according to the results of the medical characterization requires more data.

3.3 Epidemiological study by RIVM

3.3.1 General description of the study design

The study is conducted in a population of out-patient asthmatics in the age range of 8 to 12 years in the south of Rotterdam (54). In the original study proposal a population of out-patient asthmatics in the region Reeuwijk/Bodegraven was also foreseen. Therefore several consultations with paediatricians in the hospital in Gouda took place. Ultimately this did not result in participation of the hospital in the study, however. Due to time restrictions there was no opportunity to approach another study population.

3.3.2 Population selection

The study population consists out of outpatient asthmatics in the age range of 8 - 12 years, living in Rotterdam. The children were prescribed inhalation-corticosteroids or Lomudal as a maintenance medication and additional medication (e.g. sympathicomimetica) when needed. The participants were approached through three hospitals in the south of Rotterdam, and therefore most of the children were living in the south of Rotterdam. This differs from the population selected by WAU; which was mainly living in the centre of Rotterdam. Because of this difference, differences in exposure between the populations may have occurred. However, it is expected that these differences are small.

A strict definition of the group outpatient-asthmatics in terms of degree of hyperactivity, decreased lung function, IgE, and skintest was not possible due to different protocols between the hospitals. Therefore a group of patients was chosen with relatively severe symptoms, based on the maintenance medication.

3.3.3 Air quality

Air quality data measured by the National Air Quality Monitoring Network (station 418 Rotterdam Centre, and station 437 West-Maas) of RIVM and by WAU (location in the centre of Rotterdam) were used. The measurements consisted of measurements of the air pollutants PM_{10}, Black Smoke, CO, SO_2 and NO_2 (see 3.2.3). At the measurement location in the centre of Rotterdam SO_2, CO, NO_2, and NO are measured continuously, at the location in West-Maas in addition PM_{10} and Black Smoke are measured continuously. For the components PM_{10} and Black Smoke also the data from the measurement locations of the WAU were used for the analyses.

3.3.4 Health effect assessment

The same health effects were assessed using the same method as mentioned in 3.2.4.

3.3.5 Data analysis

Data from two monitoring stations 418 (Rotterdam Centre) and 437 (West-Maas) were used for the analyses. The reason for this selection is that station 418 is situated in the centre of Rotterdam, while station 437 is located to the south of Rotterdam. Unfortunately no measurement point was

available for the south of Rotterdam. Therefore none of the stations will represent the actual exposure of the participants. At this moment the concentrations measured at these stations are considered as a "best" estimator of the true exposure.
For the data analysis on the relationships between daily variations in air pollution and daily variations in peak flow, respiratory symptoms and medication are used, see 3.2.6. For medication the results for all three categories (maintenance, bronchodilator and other) are given. In addition to the levels of PM_{10}, also the results for Black Smoke are presented.

3.3.6 Results air pollution exposure

Results of the mean, minimum and maximum daily air pollution concentrations are presented in table 3.1. In table 3.11 the correlations between the daily average air pollution levels for the measurements sites Rotterdam-Centre (418), West-Maas (437) and the site measured by WAU are given.

Table 3.11 Correlation coefficients of the linear relationship between the daily average air pollution levels for the measurement sites Rotterdam-centre (418), West Maas (437) and the site measured by WAU.

		418				437						WAU	
		NO	NO_2	SO_2	CO	NO	NO_2	SO_2	CO	PM_{10}	BS	PM_{10}	BS
418	NO					0.93	0.70	0.56	0.76	0.54	0.68	0.53	0.69
	NO_2	0.62				0.54	0.76	0.46	0.56	0.49	0.56	0.51	0.62
	SO_2	0.42	0.47			0.25	0.22	0.72	0.17	0.16	0.14	0.26	0.32
	CO	0.89	0.69	0.27		0.87	0.81	0.46	0.92	0.75	0.85	0.71	0.82
437	NO_2					0.70						0.56	0.68
	SO_2					0.43	0.50					0.31	0.38
	CO					0.84	0.77	0.33				0.74	0.80
	PM_{10}					0.64	0.63	0.29	0.80			0.83	0.74
	BS					0.78	0.74	0.32	0.91	0.90		0.81	0.85
	Temp	-0.44	-0.22	0.08	-0.42	-0.40	-0.46	-0.24	-0.39	-0.27	-0.39	-0.19	-0.28
WAU	PM_{10}												0.80

The table shows that the components PM_{10}, Black Smoke, NO en CO are highly correlated (0.7 - 0.85) while CO and NO_2 are highly correlated as well (0.7 - 0.8). SO_2 is least correlated with the other components.

3.3.7 Symptom responses

In table 3.12 the results of the logistic regression analyses on respiratory symptoms, taking into

account temperature, time trend and auto-correlated residuals are summarized.

Table 3.12 Time series analysis of LRS and upper respiratory symptoms (URS); Odds-ratios for a change in daily PM_{10} concentration of 100 $\mu g/m^3$ and in daily Black Smoke (BS) concentration of 40 $\mu g/m^3$, measured at Rotterdam (ROT) and West-Maas (437); adjusted for time trend and ambient temperature.

PARAMETER		LRS	URS
PM_{10}	(ROT)	0.98 (0.78 - 1.22)	0.96 (0.78 - 1.27)
	(437)	1.01 (0.82 - 1.26)	0.90 (0.69 - 1.16)
BS	(ROT)	1.16 (0.92 - 1.45)	1.03 (0.77 - 1.37)
	(437)	1.11 (0.87 - 1.42)	0.92 (0.67 - 1.26)

Black Smoke was positively associated with LRS, no associations between PM_{10} and respiratory symptoms were observed.

3.3.8 Association between medication use and air pollution

In table 3.13 the summary results are given of the logistic regression analyses on medication use, taking into account temperature, time trend and auto-correlated residuals.

Table 3.13 Time series analysis of medication use; Odds-ratios for a change in daily PM_{10} concentration of 100 $\mu g/m^3$ and in daily Black Smoke (BS) concentration of 40 $\mu g/m^3$, for Rotterdam (ROT) and West-Maas (437); adjusted for time trend and ambient temperature.

PARAMETER		PREVENTIVE	EXTRA BRONCMED	OTHER
PM_{10}	(ROT)	2.23 (1.18 - 4.23)	1.10 (0.89 - 1.35)	0.97 (0.79 - 1.19)
	(437)	1.01 (0.58 - 1.77)	0.95 (0.77 - 1.16)	0.97 (0.81 - 1.15)
BS	(ROT)	1.23 (0.60 - 2.52)	1.10 (0.87 - 1.38)	0.93 (0.80 - 1.08)
	(437)	1.66 (0.82 - 3.37)	1.09 (0.86 - 1.39)	1.01 (0.81 - 1.24)

In general, again a positive association between the exposure to air pollution and the use of preventive medicine or extra bronchodilators was observed. The strongest associations were found for the use of the preventive medication.

3.3.9 Peak flow responses

In table 3.14 the associations between several particulate matter related air pollution indices and the morning and evening PEF are given.

Table 3.14 Association between Peak Flow (PEF) and daily PM_{10} and Black Smoke (BS) concentration at Rotterdam (ROT) and West-Maas (437), adjusted for ambient temperature and day of study (mean, standard error and median in β in litres/minutes per $\mu g/m^3$).

PARAMETER	PEF MORNING		PEF EVENING	
	MEAN (SE)	MEDIAN	MEAN (SEE)	MEDIAN
PM_{10} (ROT)	-0.027 (0.026)	-0.003	-0.007 (0.036)	-0.014
(437)	-0.043 (0.025)	-0.002	-0.034 (0.037)	-0.022
BS (ROT)	-0.059 (0.054)	-0.088	-0.045 (0.063)	-0.054
(437)	-0.114* (0.061)	-0.069	-0.063 (0.082)	-0.028

* $p < 0.10$

Both daily PM_{10} and Black Smoke concentrations were consistently negatively associated with morning and evening PEF.

3.4 Discussion

3.4.1 Status of epidemiologic 'winter smog' study

The present study was set up to provide more insight into the effects of episodes of urban 'winter smog' on symptom and lung function responses in subjects with and without chronic respiratory symptoms. Currently, only data from the pilot phase (1992/1993) are available for analysis. In the winter of 1993/1994, Amsterdam was chosen as the urban area. Meppel, Hoogeveen and surrounding communities were chosen as controls. In this year the WAU has been successful in enroling slightly more subjects than the planned 600 subjects. Preliminary inspection of these data indicates that the quality is high. RIVM encountered problems again in finding a sufficient number of children to participate in the study. In Amsterdam only 25 children joined, while 50 participated in the control area. Combined analysis of all data obtained, will hopefully answer the questions that still remain. Analysis of the pilot phase has been briefly summarized in this report (more detailed descriptions of the pilot phase have been submitted to the Ministry of Housing, Spatial Planning and the Environment in three Interim Reports, April 1993, November 1993, March 1994).

The results of the pilot phase thus far confirm findings of earlier studies from the Netherlands and elsewhere. The levels of PM_{10} are associated with a decrease in lung function, respiratory symptoms and use of medication (cf. chapter 2). Results of the pilot phase suggest that differences in response to PM_{10} may exist between the urban and control locations: the evening peak flow response in symptomatic children was larger in Rotterdam than in Bodegraven/Reeuwijk, and there was no indication of symptoms or use of medication in response to PM_{10} in the control area whereas there was one in the urban area. If such differences would be confirmed in the remainder of this programme, it might have important implications. To improve the understanding of such

findings, WAU is currently analysing the elemental composition of the sampled particulate matter. The pilot phase has also suggested a fairly large response of the use of bronchodilators in adult symptomatic subjects to PM_{10} in the absence of a symptom response. Again, if such findings would be confirmed in the remainder of the study, this would indicate that increased use of medication use should be considered to reflect a more serious health effect than a transient decrease in lung function. The data also suggested that children with serious bronchial hyperactivity (BHR) to methacholine show a stronger peak flow response to PM_{10} than children without BHR.

3.4.2 Implications of recent findings

In 1992 WHO published a report evaluating health effects of episodes of smog (27). This report contains a table specifying which health effects are to be expected at different levels of a combination of particulate matter and SO_2. The table is reproduced below (Table 3.15). In this WHO report the literature was evaluated until 1990. The review given in chapter 1 indicates that new results have been reported since. Acute health effects have recently been reported at lower levels of particulate matter exposure than previously believed. Health effects have also been associated with particulate matter in the absence of, or after adjustment for SO_2. Therefore, the table reproduced from the WHO report is to some extent outdated.

The review indicates that moderate health effects occur at levels well below those quoted in Table 3.15. For most of the effects studied recently, it is even difficult to identify a threshold level below which such effects are not likely to occur.

The health effects associated with daily variations in the concentration of particulate matter vary from changes in daily mortality to small, reversible changes in lung function. For particles especially, the body of evidence suggests that effects on mortality, hospital admissions, exacerbation of respiratory symptoms and lung function all occur at low levels of exposure. Daily counts of mortality and hospital admissions for COPD or asthma are low, so the number of subjects affected by air pollution on any given day is low as well, compared to the size of the population. In contrast, transient effects on lung function may be observed in the majority of the population, and symptom exacerbation may be detected in asthmatics and COPD patients, comprising 5-10% of the population. The apparent paradox of effects of diverging severity occurring at similar levels of exposure can be solved by taking the frequency of occurrence into account. Small changes in lung function, or slight exacerbations of symptoms, that can easily be tolerated by healthy subjects or even mildly diseased subjects, may lead to a need for acute hospitalization among the more severely ill, and may even become life threatening among those who are in very bad health already.

Table 3.15 Levels of 24-hour average concentrations of air pollutant mixtures containing SO_2 and particulate matter above which specific acute effects on human health are expected on the basis of observations made in epidemiologic studies. (This table is to some extent outdated, at this moment we do not know whether there is a 'threshold limit' for the effects of particles (quoted from 27)).

Pollutants (combination of)			
SO_2	Particles ($\mu g/m^3$)	Health effects	Overall classification
200	200 (gravimetric)	Small, transient decrements in lung function (FVC, FEV_1) in children and adults which may last for 2-4 weeks. The magnitude of the effect is in the order of 2-4% of the group mean.	Moderate
250	250 (Black Smoke)	Increase in respiratory morbidity among susceptible adults (chronic bronchitis) and possibly children.	Moderate
400	400 (Black Smoke)	Further increase in respiratory morbidity	Severe
500	500 (Black Smoke)	Increase in mortality among elderly, chronically ill people	Severe

Of course, this raises the question how serious the observed relation between particulate air pollution and daily mortality is from a point of view of public health. The effect on mortality tends to be greater among the elderly, although it is not restricted to the oldest age categories. If daily variations of particulate matter at a low level lead to some 'harvesting' effect implying that terminally ill subjects die a few days or weeks earlier than they would have anyway, the relevance for public health is not as great as when subjects are affected in all age classes and in various states of health. Unfortunately, little is known about the subjects making up the slight excesses in daily mortality associated with air pollution. It is known that at much higher levels, such as those observed in the London smog episode of 1952, some subjects suddenly died on the streets or at work (28). There is a need to gain more insight into the number of days or years of life lost associated with air pollution by particulate matter, so implications of these associations for public health can be assessed more fully. In this respect, a recent report from the United States (29) offers intrigueing observations. In a follow-up study over a 16-year period, low levels of particulate matter pollution were found to be associated with mortality independent of smoking, occupational exposure, body mass index, age, sex and education. Yearly average inhalable particulate matter levels (measured either as PM_{15} or PM_{10} in the study) ranged from 18 to 47 $\mu g/m^3$ with a small time trend. The relative risk comparing the most polluted city with the least polluted city was 1.26. These new data suggest that the associations found in the daily time series studies may imply a significant loss of life expectancy.

Quantitatively, the relationships between daily variations in particulate matter air pollution and

mortality have been expressed in several papers as percentage increase in mortality associated with a certain increase in particle pollution. The magnitude of the increase has been estimated to range from 4 - 7% per 100 $\mu g/m^3$ TSP (5, 7, 8) to 16% per 100 $\mu g/m^3$ PM_{10} (6, 9). All of these studies are from the US. When we take into account a conversion factor for the US of 0.55 (PM_{10}/TSP), the TSP coefficients translate into estimated PM_{10} effects of 7 - 13% per 100 $\mu g/m^3$. The consistency of these effects estimates is high.

For hospital admissions, effects have been estimated at 24% increase of daily COPD admissions per 100 $\mu g/m^3$ BS in Barcelona, Spain (12, 13), and a 40% increase of asthma admissions per 100 $\mu g/m^3$ PM_{10} in Seattle, US (14). There are no data to make a reliable conversion of Black Smoke into PM_{10} for Barcelona.

Effects of PM_{10} on Peak Flow of panels of children were reported in five recent papers (19, 20, 22, 24, 25). Estimated effects ranged from -40 to -110 millilitres/second Peak Flow change per 100 $\mu g/m^3$ PM_{10} - again a remarkable consistency over five independent study populations. Such changes represent a mean change in Peak Flow in the order of 2- 4% per 100 $\mu g/m^3$ PM_{10}, which in itself is not large, but especially in panels of asthmatic children, these changes have been found to be accompanied by significant increases in acute respiratory symptoms and/or use of medication (19, 20, 22).

In conclusion, several studies are now available documenting effects of particulate air pollution on health that are independent of the level of SO_2. Effects on mortality and hospital admissions for asthma have been documented at levels not exceeding 100 $\mu g/m^3$, expressed as 24-hour average PM_{10} concentration. Effects on lung function, acute respiratory symptoms and medication use have been found at 24-hour average PM_{10}-levels not exceeding 115 $\mu g/m^3$. There were no studies available on health effects of PM_{10}, when the WHO Air Quality Guidelines and the standards for particulate matter in the US and the Netherlands were developed. In this review, nine different studies documenting health effects of measured PM_{10} at low levels of exposure have been included, indicating that there is now an entirely new epidemiologic data base to be used in the process of the revising current guidelines and standards. The low levels of exposure at which effects on health were seen emphasize the urgent need for such re-evaluations.

3.5 Air quality measurements by RIVM

3.5.1 Study objectives.

The composition of air pollution, in particular during episodes, has changed considerably during the last decade. Because of the change in mixcompounds other than the combination of SO_2 and TSP have become more relevant. In this respect special attention should be given to TSP alone. Measurements were carried out in the CHaracterization Episodical Air pollution Project (CHEAP).
Currently available information on urban air pollution during winter in Western Europe is insufficient. Given the nonspecificity of responses in epidemiological studies there is a necessity for more in-depth research on levels and sources of air pollution. It is also necessary to define and support toxicological research for the confirmation of epidemiological findings. Only occasionally data from regular monitoring network activities will be useful.
In urban areas stationary and especially mobile sources are responsible for a rise in air pollution levels. Although traffic is considered the most important source, other sources, such as heating, cannot be excluded. Information on the contributions from the various sources to the particle levels (classified in various particle sizes) is essential to evaluate the epidemiological findings. Of course such information is also needed if mechanisms are to be understood and to evaluate different control scenarios.

Consequently the following objectives were defined:

- A detailed phenomenological description of the composition and levels of urban air pollution during episodes of winter-type smog in comparison with rural background levels. With this description a better understanding of the processes leading to the observed levels will be obtained.
- Identification of an indicator for the composition and levels of air pollution during various kinds of winter-type episodes. Such new indicators might replace the former combination of SO_2 and TSP.
- Estimation of contribution of different sources, in particular from traffic, and the identification of source-related tracers.
- Identification of compounds that are relevant for epidemiological studies from a toxicological perspective. This information will be relevant for design and evaluation of toxicological experiments.

3.5.2 Study design

In the design of the study the following aspects have been considered:

- Locations

  Two types of contrasting locations were selected: rural background and city background sites. For the rural background site the monitoring station of Biddinghuizen, and for the city background a monitoring station at the border of the Vondelpark in Amsterdam were selected. Amsterdam was selected as a large city with only limited industrial activities in the vicinity.

During stagnating weather conditions the wind direction is often east or south-east. Therefore Biddinghuizen (situated east of Amsterdam) could act as a background station, measuring the concentrations in the air masses before they arrive at Amsterdam.

- Selection of air pollutants.
  It is a prerequisite to include many pollutants as potential candidates for the elucidation of health effects. Furthermore, such compounds may also act as tracers for others which are not readily measured and provide information for source apportionment. Selection of compounds selection was based on the perceived relevance from epidemiological, toxicological and/or source apportionment perspectives, and the feasibility of the required logistics. The feasibility of measuring these parameters was tested in a pilot experiment conducted during one week in February 1993 in an urban situation at Utrecht and a rural situation at Scherpenzeel. Based on the experience from this pilot the following list of compounds and other parameters was selected: carbonmonoxide, nitrogenoxides and sulfurdioxide, the acidifying compounds (ammonium-nitrate and -sulphate), polycyclic aromatic hydrocarbons (speciated and as a sum), black smoke, volatile organic compounds (including the aromatics such as benzene and halogenated compounds), a limited number of aldehydes (including formaldehyde) and a wide range of heavy metals. To describe the meteorological conditions temperature, relative humidity and the height of the mixinglayer were included. Particulate matter was characterized by measuring the particle size distribution (0.03 - 30 μm).
- Sampling and measurement strategy.
  The time scale of the variation in concentrations in Dutch cities is estimated to be one hour or less, for rural areas this is three hours. This small time scale leads to a high frequency of measurements and demands extensive automation. Hourly measurements were performed for those compounds for which automated systems were available. For the compounds for which on-site sampling had to be followed by laboratory analysis, reduced averaging periods from 3 hours to 24 hours were used. The measuring frequency was once every six days during non-episodical conditions and once every three days during episodes for a period of 3 to 24 hours. Gasses, some volatile organic compounds, PAH (as sum), black smoke and the meteorological parameters were measured continuously (hourly averaged values) throughout the project period. Particle size distribution was measured every three days during non-episodes and continuously during episodes. In Amsterdam and Biddinghuizen identical sampling and measurement regimes were to be applied.
- Data processing.
  Initially an exploratory data processing approach is applied to guarantee optimal extraction of information for the phenomenological description. For source apportionment various techniques based on principal component analysis and temporal profile analysis are used.

3.5.3 Evaluation.

During the measurement period (December 1993 to beginning of March 1994) the conditions were non-episodic except for 14 -15 February 1994, in which there was a 'mild smog' in the east of the

Netherlands.

Analysis of the sampled data is in progress. A result is the temporal profile of particulate matter in Amsterdam. During a period of three weeks (which included the episode) the particle size distribution was measured continuously. Concentrations of PM_{10} and of (ultra) fine particles (particle size distribution 0.01 - 0.8 μm) increased during the episode and a few days thereafter. During this event the relative contribution of the smaller particles to the PM_{10} increased. This preliminary result suggests that concentrations of (ultra) fine particles may increase during episodes.
Future research will also be focused on variations in the physical characterization of the particles, such as surface and number, in relation to the inhaled fraction.

3.5.4 Final Remarks

The design of CHEAP is such that insights are obtained into levels of air pollution at urban background sites as well as in rural areas. The translation of the results into levels of exposure of the urban population is currently hampered by the fact that information about the small scale variations in concentrations within cities and the indoor-outdoor ratios is lacking. The latter is not only to be considered as a function of the ventilation habits of the occupants and specifics of the buildings in question but also of the different compounds. This is illustrated by the anticipated differences between the various particle size fractions. To enable a sufficiently detailed description of levels of exposure of the population on a group and individual base, more research covering transport and sinks of contaminants is necessary.
Due to the fact that during the campaign '93/'94 only a few days occurred with mild smog a follow-up is recommended.

3.6 Literature review by the University of California at Irvine (UCI)

This paragraph is based on a preliminary draft report only. The final report is expected in the fall of 1994.

3.6.1. Contributions of mobile source emissions to winter smog health effects

This study examined the potential health consequences of emissions from diesel, gasoline and LPG-fuelled engines during winter smog conditions. These contaminants were selected because their health consequences could be significant, because strategies of emission control in relation to mobile sources are expected to profoundly alter the air pollution mix, and because enough is known about the potential health consequences of exposures to make a reasonable assessment of the impact on populations, when certain demographic, dosimetric and engine use factors are quantified.

The health consequences selected for evaluation are those related to symptom exacerbation or incidence of morbidity and mortality. There are several direct studies of the effects of diesel exhaust on health, but the effects of LPG or compressed natural gas (CNG) fuelled engine exhausts on health have not been sufficiently studied. Some components of exhaust, as nitrogen oxides, sulphur oxides and volatile organic compounds have been intensively studied. The strategy of the review is to first establish the potential health effects of these components and to establish the relative differences between exhaust characteristics of the different engine types. Such data are the first step in performing a quantitative risk assessment. The project will not lead to a final statement of risk. For such an assessment other parameters concerning demographics, ambient concentrations, personal dosimetric data, and actual estimates of the projected numbers and types of vehicles have to be assembled.

3.6.2 Acute effects of inhaled particles

The data of epidemiological studies which associate inhaled particle exposure with health effects in human populations have been extensively reviewed (see also chapter 2).

3.6.3 Acute effects of nitrogen oxides

During winter smog conditions, significant concentrations of NO and NO_2 are expected to be present, regardless of the engine types and fuels burned in mobile sources. The toxicity of NO and NO_2 are related to their ability to initiate free radical reactions and cause the release of several reactive oxygen species. These, in turn, can disrupt the structure and function of cell membranes, enzymes, DNA and various organelles. At high doses, NO_2 can cause fatal pulmonary edema; at lower doses it can cause pulmonary inflammatory responses, alter lung permeability and adversely affect the immune system. There is some evidence that NO_2 may also increase bronchial reactivity and may thus relate to exacerbation of asthma. In toxicological studies, mixtures of NO_2 and acidic particles had additive or synergistic effects.

3.6.4 Acute health effects of diesel emissions

Acute exposure to diesel exhaust in occupational exposure settings is associated with eye irritation, chest tightness, coughing and transient changes in pulmonary function. Animal exposure studies with diluted diesel exhaust show few functional changes in the lung unless exposures are continued for several months. The acute irritating effects are likely related to NO_2 concentration and to aldehydes both in the vapour phase and associated with particles and to particles per se. Acute exposure symptoms for diluted diesel exhaust are most likely to be transient in healthy people, and because diesel emissions contain higher levels of NO_x and volatile organic compounds than emissions from gasoline of LPG engines, diesel emissions represent the worst case for acute health effects.

3.6.5 Engine emission characteristics

The emissions of light duty diesel engines have been well characterized as to chemical species. They contain carbonaceous particles, high concentrations of nitrogen oxides, volatile hydrocarbons, carbon monoxide and carbon dioxide. The particulate and vapour phases contain polycyclic aromatic hydrocarbons, as well as aldehydes, ketones and other compounds classified as air toxics. Both diesel and gasoline engines emit sulphur dioxide because of sulphur contaminants in the fuels. Both engines also emit benzene, either as combustion product or because of its use as an additive in some fuels as an octane enhancer.

Gasoline engines produce smaller amounts of particles, on a g/km basis. The toxicity of the particles may or may not be comparable to that of diesel exhaust particles, on a particle mass basis. Gasoline engines produce less NO_x, less CO and less CO_2, but may release more non-methane hydrocarbons than diesels.

Liquid petroleum gas (LPG, propane) engines emit less CO and CO_2 than either diesel or gasoline engines, but may emit more NO_x. These engines have a very low tendency to form air toxics other than formaldehyde (which can be controlled with catalytic converters). The emission of particles is lower than that of either diesel of gasoline engines, and if low sulphur sources of gas are used, SO_2 emissions are negligible.

3.6.6 Biological hypothesis

No clear biological hypothesis has been proposed for the mechanism of the toxic addition of urban particles. Epidemiological data do not support any single hypothesis, unequivocally. It is proposed that urban particles produce their apparent toxicity by action with the lung. Two modes of action seem most plausible: 1) the particles act as carriers for some toxicant(s), or 2) particles initiate a cascade of events through interaction with existing biological amplification systems. In the former hypothesis, the toxicity should be proportional to the total mass or surface area of particles deposited; e.g. the particles act to adsorb some toxic vapour or gas within the particle's volume. The latter hypothesis suggests that the number of particles deposited is the critical factor in evoking the

biological effect. Experiments designed to contrast the total mass vs. the number of particles could possibly differentiate between the two hypotheses. In the former case, aldehydes, heavy metals, or PAHs are potential toxicants which can be transported via ultrafine particles generated by mobile sources. Such toxicants could react with membranes or intracellular biomolecules, resulting in toxicity. In the latter case, the physical interaction of the particles with the cell membrane could result in transduction of signals through lung cell membranes similar to, but not physiologically equivalent to, normal hormones: e.g. alterations in intracellular free calcium as in signal transduction by insulin, interferon γ and the G protein cascade. Impairment of the immune system of the lung through toxicity to pulmonary macrophages could lead to the elaboration of cytokines altering airway permeability or calibre of pulmonary capillaries. Such a particle number dependent mechanism is attractive because a biological cascade exists in the lung to amplify the signal produced by the number of very small particles associated in epidemiological studies with morbidity and mortality. The transport of chemicals such as aldehydes and PAHs seems less attractive because no amplification process is currently known for the toxicity of such chemicals.

3.6.7 Integrated research programme

A quantitative risk assessment of the alternative power sources is presently difficult to make because of identified data gaps. An integrated, directed research programme is recommended to fill the data gaps.

Investigations of the emissions of mobile sources for health effects data

Engineering data should be collected to determine the particle size distribution and chemical speciation of these particles as a function of engine operating characteristics. Data are especially needed for particles in the ultrafine (< 0.10 μm diameter) mode. Environmental data needs would include investigations into the apportionment of ambient particles, on a size and chemical species basis, among the various mobile and stationary sources. Chemical speciation and particle surface property measurements for the ultrafine fraction of PM_{10} will be required for testing specific hypotheses of the relationship between health effects and particles originating from mobile sources.

Investigations of the mechanism of action of mobile source toxicity

Present epidemiological studies have not been able to identify a plausible biological mechanism of action for urban particles. Consequently, control strategies (risk management) and mitigation, both medical and environmental, have been hampered. An integrated research programme into the mechanism of action of mobile source emissions is urgently needed.

- Winter type smog includes exposures to high NO_x which includes NO. The toxicology of NO has largely been neglected on the theory that the most toxic NO_x is NO_2. Preliminary results of experiments have shown that NO may be more toxic than previously supposed. Secondly, NO is now recognized as an intracellular hormonal messenger. A re-evaluation of NO and particularly of NO and particulate exposure appears to be warranted.

- The data base on the ultrafine mode distribution of mobile source emissions needs to be expanded. For a quantitative risk assessment, the deposition pattern of the putative toxicant in the lung is needed, to investigate the region of the lung most affected. In the case of ozone toxicity, studies of regional deposition of ozone have proven to be the key for extrapolation from animal to human toxicity. Current data on the particle size distribution of mobile source emissions does not provide the detail needed to model lung deposition using particle deposition models or to test alternative hypotheses of toxicity.

- Improved data are needed for the actual size distributions and chemical compositions of particles to which the population is being exposed. Dichotomous samplers, while a vast improvement over prior methods, do not provide a quantitative assessment of the particle in the ultrafine mode. A research program into the particle size distribution in the ultrafine mode, including chemical speciation, is needed.

- A coordinated multicentred study of human and experimental animal toxicity of ultrafine mode particles is needed. The program should be highly directed in which goals to be achieved are selected in view of the problem of the toxicity of the urban aerosol. Wherever possible equivalent studies should be undertaken in experimental animals and volunteer human subjects using equivalent and sensitive disease-related endpoints, so that extrapolation from experimental animal results to humans can be made. Because of the potential confounding effects of ethnicity, local meteorology, and history of prior exposure, results from equivalent protocols undertaken at more than one centre will be more compelling.

4. POLICY QUESTIONS AND PLAN OF ACTIVITIES

4.1 Policy questions

A number of policy questions have been raised by the Air Directorate of the Ministry of Housing, Physical Planning and the Environment. The purpose of these questions is to judge our current knowledge on 'Winter smog and Traffic'.

Question 1 What is the state of affairs of the research performed in the last two years?

Epidemiological studies including characterization of air quality and personal exposure monitoring were performed by WAU, UG and RIVM in the winters of 1992/93 and 1993/94, and are planned for 1994/95. The mean 24-hour PM_{10} concentrations in these studies (range 5 - 145 $\mu g/m^3$) are similar to those found in other epidemiological studies. In these studies associations were reported between the PM_{10} concentrations and health effects. A preliminary analysis of the Dutch results confirms this. During the winter of 94/95 the epidemiological panelstudies will be finished and emphasis will be given to characterization of personal exposure. Personal exposure of PM_{10} will be included in this last phase.
A literature review, based on existing information, will provide data on the health effects of exposure to diesel, automobile and LPG exhaust and will be completed in 1994.
During the second half of the programme toxicological studies will be performed. These will be supplemented by a more detailed description by means of a model of the exposure of the population to winter smog and the contribution of traffic.

Question 2 What are the new insights in health effects caused by winter smog and traffic emissions?

On the basis of the data summarized in table 2.1 it is suggested that particulate air pollution is associated with daily mortality, hospital admissions, symptom exacerbations and lung function changes. Recent foreign studies indicate that symptom exacerbations and lung function changes are seen in populations living near streets with heavy traffic. Some studies report differences in respiratory symptoms and lung function changes for locations within the same city. This suggests a relationship with differences in exposure of the urban population living near busy streets or near more quiet streets. Studies pointing in that direction have been performed in Germany and Japan, to some extent a few studies in The Netherlands give a similar suggestion.
The occurrence of a 'worst-case' situation, described in the report on winter smog (53), is very unlikely in the light of the current scientific knowledge. Because of successful control policies in Germany and Eastern Europe, the mean levels of SO_2 have decreased substantially. The ratio of SO_2 and PM_{10} in air has therefore changed considerably. In the light of the associations of relatively low PM_{10}-levels and health effects the concern about the health effects of particulate matter has increased in spite of the decrease in SO_2 levels.

Question 3 What is the contribution of traffic to air pollution during winter smog situations? What are the effects of limiting traffic during winter smog episodes?

The answer to this question can only be given when information is available on the composition and volume of the emission of gasses and particles by traffic. By modelling the dispersion and taking the background levels into account, urban air quality may be predicted. A combination of air quality and activity patterns can be used to model the exposure of the urban population to traffic emissions. When the chain of sources, air quality and exposures is known, the process of risk assessment may be done in reverse to assess the effect of a reduction on traffic. On a limited scale this information is available for gaseous components. For particulate matter such information is still scanty. Research is proposed in the second phase of the programme to fill this important gap.

The results of the air quality measurements in 92/93 indicate there is a small difference (up to 10%) in 24-hour PM_{10} concentrations between the urban and rural locations during 'normal' weather conditions. During episodes the difference appears to increase (30%). Further chemical analyses of the collected filters are expected to indicate a different chemical make up between the urban and rural aerosol. This difference may be expected to be more pronounced than the difference in PM_{10} mass concentrations. Such analyses are foreseen in the second phase of the research project. For gaseous components the reported differences between urban and rural concentrations are larger.

Question 4 Are health effects during winter smog situations caused by traffic emissions? What are the extent and seriousness of these effects within the whole population and the population at risk?

Winter smog is a large scale phenomenon due to special atmospheric circumstances with elevated levels of pollution to which traffic contributes considerably through primary and secondary pollutants. Traffic contributes particularly to the elevated levels of the gaseous components and to a lesser extent to the particulate matter of winter smog. The exact emission of traffic and its contribution to health effects is not yet clear. Serious health effects may be expected (see the answer on questions 2 and 3).

As an internal action RIVM has performed a preliminary quantitative risk assessment of health effects caused by PM_{10}. On the basis of existing information a first attempt has been made to estimate the health effects of particulate matter for the Dutch population.

Question 5 If traffic is totally banned are health effects exacerberated?

The influence of traffic emissions on health effects is not clear yet at this stage of the project. It is not possible to indicate whether a ban on traffic in cities will decrease the health effects.

Question 6 Is the current winter smog indicator being the sum of the daily averages of PM_{10} and SO_2, a correct indicator, and if not: is there an alternative indicator available?

The current sumparameter SO_2-PM_{10} as an indicator of the seriousness of an episode of winter smog is outdated (see answer on question 2). Recent results of foreign and Dutch epidemiological research suggest that PM_{10} may be a better indicator.

Question 7 Are the current levels of the smogindicator still useful? Is there any need to change these levels? (The current levels are linked to the seriousness of the health effects: mild, moderate, severe or very severe)

This group of experts in the programme 'Winter smog and Traffic' is of the opinion that it is necessary to change the existing smogclasses because of the recent information concerning SO_2 and PM_{10} and the expected health effects in the population. As no threshold levels can be given for the health effects, serious health effects may even arise at relatively low (non episodic) levels. A further classification of these effects in different levels of seriousness therefore does not seem an easy task.

Question 8 Is there a scientific reason to change the advice on the smogregulation for the Dutch population?

A similar answer as above can be given. It would seem more appropriate to discuss this question in the committee "Health effects of air pollution" of National Health Council.

4.2 Plan of activities

Quantitative risk assessment of health effects caused by particulate air pollution, winter smog and apportionment of this risk to different sources is necessary for an effective and efficient risk management. A combination of exposure and response data is essential for this quantitative risk assessment, as indicated in the introduction. The real exposure of the urban population to winter smog is based on knowledge of the air quality and the activity pattern of the population. When all the sources of winter smog are known, the influence of a reduction of sources can be modeled until risks are reduced to the desired level. From 1992-1994 research has been performed to quantify the health effects for healthy individuals and for those with diseases of the respiratory tract in the Netherlands, in areas with a high and a low traffic density. For the second phase of this programme research is planned to quantify the exposure of the urban population and the understanding of the mechanisms of winter smog. Such information is essential for the implementation of an adequate risk management.

Exposure

Input data are essential to develop an exposure model (what is the individual exposure, what is the inhalation during different activities):

1) Characterization of the urban air quality;
2) apportionment of air quality to urban, rural and foreign sources (especially traffic emissions);
3) modelling of exposure of the urban population with the National Exposure Model;
4) validation of the modelled exposure by measuring personal exposures.

Exposure response relationship

The second part of the epidemiological study by WAU and University of Groningen is envisaged for the winter of 1994/95.

Research on the basic toxicological mechanisms is necessary to substantiate the biological plausibility of the associations from epidemiological studies. Such information is an essential basis for an effective risk management policy.

In the second phase of the research programme the following research on exposure and exposure response is planned:

1) Continuation of epidemiological research in winter 1994/1995;
2) research on the influence of particle sizes on the health effects;
3) animal research with particles occurring in the ambient urban atmosphere. If possible this should be supplemented by research with human volunteers.

Relation with foreign research

In several countries similar epidemiological studies are performed. However, the special attention of the Dutch government for the health effects of traffic emissions is not yet shared widely.

Research with human volunteers is slowly starting. In a number of countries such research is in a preliminary stage and questions and research hypotheses are formulated. One of the central questions in such research is how small increases in particle concentrations may lead to a cascade of effects resulting in serious health impairments and accelerated mortality in the elderly with cardio-pulmonary diseases. This research has to be executed in such a way that the complex ambient urban atmosphere can be presented to animals and human volunteers. Useful results for risk management of this line of research may not be expected before the change of the century.

The advantage of doing toxicological and epidemiological research in The Netherlands is that typical national characteristics will be included. Such characteristics are: a small and heavily populated country; a specific climate; its economical infrastructure and industry. When the research would only be performed in foreign countries its results would have to be converted to the Dutch situation and , useful results may certainly not be expected within a few years. Doing research in the Netherlands will lead to quicker results. An outline on the plan of activities is given.

Outline Plan of activities 1995 Winter smog and Traffic

	Estimated cost in thousands of guilders
1. Continuation of epidemiological study 1994/1995	850
- Confirmation preliminary results of epidemiological studies in 1993 and 1994	
- 4 study populations, among which 2 target panels	
- detailed characterization of particles ('fine coarse'), in particular recognition and quantification of sources (especially traffic and import emissions) (also ad 2) for the support the modelling of the real exposure	
2. Characterization air quality in urban locations during winter smog episodes in behalf of effect and exposure studies including source recognition	550
- relationship between air quality and sources in:	
- urban locations	
- rural locations	
- foreign countries	
- relationship between particle sizes, chemical composition and sources	
- Concentration model of urban aerosols (kf 350)	
3. Development causal relationship between exposure to winter smog and (severe) health effects	300
- concentration of particles and exposure of animals and/or humans to ambient particulate matter from the centre of the city, streets and rural locations	
- research into the numbers, surface and mass of particles and their influence on health effects	
4. Application of the National Exposure Model in the exposure modelling of the inhabitants to winter smog with or without traffic emissions	150
	Total kf 1950

ABBREVIATIONS

BR	Bodegraven/Reeuwijk
BHR	Bronchial Hyperactivity
BS	Black Smoke
CHEAP	CHaracterization of Episodical Air Pollution
CNG	Compressed natural gas
COPD	Chronic Obstructive Pulmonary Disease
D_{ae}	aerodynamic diameter
DNA	desoxynucleic acid
FEV_1	Forced Expiratory Volume in one second
FVC	Forced Expiratory Vital Capacity
GM	geometric mean
IgE	Immunoglobulin E
LML	Landelijk Meetnet Luchtkwaliteit
LPG	liquid petroleum gas
LRS	Lower Respiratory Symptoms
LUW	Landbouw Universiteit Wageningen
MMEF	Maximal Midexpiratory Flow
PAH	Polycyclic Aromatic Hydrocarbons
PEF	Peak Expiratory Flow

PM	Particulate Matter
PM_{10}	Particulate Matter with a cut off diameter of 10 μm
$PM_{2.5}$	Particulate Matter with a cut off diameter of 2.5 μm
RIVM	National Institute of Public Health and Environmental Protection
ROT	Rotterdam
RUG	Rijksuniversiteit Groningen
SE	standard error
SPM	Suspended Particulate Matter
TSP	Total Suspended Particulate matter
UG	University of Groningen
UK	United Kingdom
URS	upper respiratory symptoms
US	United States of America
US EPA	United States Environmental Protection Agency
WAU	Wageningen Agricultural University
WHO	World Health Organization

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