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NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SUMMARY
SCIENCE ASSESSMENT DOCUMENT

A report by the
Federal - Provincial Working Group
on Air Quality Objectives
and Guidelines

JULY 1999

Canada

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PREFACE

The Canadian Environmental Protection Act (*CEPA*), passed into law in 1988, replaces and builds upon the Clean Air Act and the Environmental Contaminants Act. The opening statement of the Act declares that "the protection of the environment is essential to the well-being of Canada". *CEPA* allows the Federal Government to assess substances and control their impact through national environmental quality objectives, guidelines, codes of practice, and/or regulations.

Provincial Governments have the primary responsibility in many areas of air pollution control, with federal actions integrated with those of the provinces. The *CEPA* Federal/Provincial Working Group on Air Quality Objectives and Guidelines (WGAQOG), consisting of representatives of federal, provincial and territorial departments of environment and health, reviews and recommends national ambient air quality objectives.

Canada's *National Ambient Air Quality Objectives(s) (NAAQOs)* prescribe targets for air quality, measured at the relevant receptor (persons, plants, animals, materials*). National Ambient Air Quality Objectives are national goals*[1] *for outdoor air quality that protect public health, the environment, or aesthetic properties of the environment*. The development of NAAQOs involves first, a scientific review of the physical and chemical properties of a substance, its sources, environmental, animal and human health effects, and an assessment of environmental and human exposure to the substance. Secondly, this information is integrated within a framework of risk assessment. The Science Assessment Document contains this critical scientific evaluation, and lays the scientific groundwork for establishing the air quality objectives. Reference Levels, levels above which there are demonstrated effects on human health and/or the environment, are identified. A document outlining the process followed in reviewing and interpreting the scientific information is published separately.[2] This document contains the scientific evaluation of Ground Level Ozone.

National Ambient Air Quality Objectives are targets for focussing air quality management strategies and plans. The derivation of these targets may consider some elements of benefit/risk analysis, reflecting a philosophy of environmental health protection and long term risk reduction while recognizing technological and economic limits. The broad range of potential responses by ecosystems, populations, and organisms in the environment are considered. Given the range of sensitivities within and among these

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[1] The Working Group develops NAAQOs for Federal/Provincial/Territorial and Municipal Governments to use as they deem appropriate. Implementation of air quality management strategies and standards is left to those agencies or to other national processes.
The definition in the text above, along with the descriptor provided above in this footnote, together comprise the new definition for NAAQOs.

[2] A Protocol for the Development of National Ambient Air Quality Objectives Part 1: Science Assessment Document and Derivation of the Reference Levels. WGAQOG, 1996.

environmental components, the resulting objectives may not protect all.

The process of establishing National Ambient Air Quality Objectives is a dynamic and continuous one. Air quality objectives are established to reflect the current state of knowledge about an air pollutant, to provide a national indicator for assessing the quality of air in all parts of Canada, and to provide guidance to governments for making risk management decisions such as planning control strategies and setting local standards.

It is recognized that not all locations in Canada will meet these air quality objectives immediately, or at all times, and that priority given to meeting these values may be based on factors such as available control technology, costs, benefits, and the degree to which the recommended objectives are exceeded. The expectation is that strategies will be implemented to facilitate the reduction of ambient air concentrations to a level at or below the air quality objective(s) as soon as practicable. The principles of continuous improvement and nondegradation of environmental quality are advocated.

NOTE: In January 1998, Canadian Environment Ministers (with the exception of Québec) signed the Canada-Wide Accord on Environmental Harmonization and its sub-agreement on Canada-Wide Standards (CWSs). The CWS process provides new tools for the management of environmental issues of national interest. Recognizing that both NAAQOs and CWSs have a role to play in the management of air quality, federal, provincial, and territorial health and environment departments have integrated the NAAQO and CWS processes. Air pollutants that have been identified by governments as needing to be managed will be targeted for either CWS or NAAQO development, not both.

In January 1998, Environment Ministers identified ozone as a priority for Canada-Wide Standards. As a result, federal, provincial, and territorial health and environment departments agreed that NAAQOs for ozone will no longer be developed. Rather, this Science Assessment Document will form the Risk Assessment report for the development of CWSs for ozone.

NOTE: This Science Assessment Document is, in general, a federal-provincial consensus document. One member of the WGAQOG, Alberta, does not, however, support some of the recommendations, including the form of the LOAEL for vegetation and the recommended Reference Levels for Human Health. This position is based on issues regarding the science and its application with respect to ozone impacts on health and the environment. Alberta nevertheless supports the publication of this document and believes that this document will make a positive contribution to the efforts of reducing ambient ozone levels in Alberta. More information on Alberta's position can be obtained from Alberta Environment, Environmental Sciences Division at (780) 427-5883 or from www.gov.ab.ca/env/protenf.html .

ACKNOWLEDGMENTS

The Science Assessment Document, upon which this Summary has been made, has been prepared primarily as a compilation of material from the NO_x/VOC Science Assessment reports by the Multistakeholder NO_x/VOC Science Program. The authors of these reports are acknowledged for their significant contributions to this report. The individual reports that have been drawn upon for this assessment are:

- Ground-level ozone and it precursors, 1980 - 1993: Report of the Ambient Data Analysis Working Group (1997)
- Ground-level ozone and precursor monitoring guidelines and implementation plan: Report of the Ambient Air Monitoring Working Group (1997)
- Report of the Health Objective Working Group (1997)
- Report of the Vegetation Objective Working Group (1997)

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SUMMARY

1. INTRODUCTION

The Canadian Environmental Protection Act (CEPA) allows the Federal Government to assess substances and control their impact through national environmental quality guidelines, codes of practice, and/or regulation. Provincial Governments have primary responsibility in many other areas of air pollution control, with Federal actions integrated with those of the Provinces. Under CEPA, the Federal / Provincial Working Group on Air Quality Objectives and Guidelines (WGAQOG), consisting of representatives of federal, provincial and territorial departments of environment and health, reviews and recommends National Ambient Air Quality Objectives.

Canada's National Ambient Air Quality Objectives (NAAQOs) are *national goals*[1] *for outdoor air quality that protect public health, the environment, or aesthetic properties of the environment.* NAAQOs are developed in two stages, the first of which is the science assessment stage, embodied within the Science Assessment Document. Reference Levels for the pollutant of concern are identified as part of the science assessment process. A Reference Level is a level above which an effect on a receptor (human or environment) has been demonstrated. Reference Levels may be proposed for one or more time periods (e.g. 24 hour, annual) and for one or more receptors (e.g. humans, vegetation). The Science Assessment Document concludes with a characterization of the risk to various receptors from exposure to ambient levels of the pollutant in the Canadian environment.

This document contains the scientific assessment of Ground Level Ozone effects on human health, vegetation, materials and animals. The document was prepared primarily as a compilation of the Canadian 1996 NO_x/VOC Science Assessment Reports[2]. Consequently, background sections of the document, included to provide contextual information for understanding the material on effects, have not been updated since publication of the NO_xVOC reports. The information on health and environmental effects was augmented by a review of the most recent peer-reviewed and publicly available literature, current to mid-1997. The issue of the human health effects of ozone is, in particular, a field of inquiry that is evolving rapidly. The document itself has been externally peer-reviewed. Although prepared in support of revisions to the current NAAQOs for ground level ozone, this document will be used as scientific support for the development of Canada Wide Standards for ground-level ozone.

[1] The Working Group develops NAAQOs for Federal/Provincial/Territorial and Municipal Governments to use as they deem appropriate. Implementation of air quality management strategies and standards is left to those agencies or to other national processes.

[2] Multistakeholder NO_x/VOC Science Program. 1997. 8 Volumes. Volume 8, Summary for Policy Makers, ISBN 1-896997-14-7E.

2. ATMOSPHERIC CHEMISTRY

Ozone is a natural constituent of both the upper atmosphere (the stratosphere) and the lower atmosphere (the troposphere). In the stratosphere, ozone (O_3) and oxygen (O_2) are part of a natural cycle of formation and destruction that is driven by energy from the sun. Most of the ozone in the stratosphere is concentrated in the middle stratosphere in a band commonly referred to as "the ozone layer". The ozone layer plays a critical function in protecting life on earth from damaging UV radiation from the sun.

At ground level, however, ozone is a pollutant. The sources of ground level ozone are: 1) direct transport from the stratosphere (a minor source), and 2) formation in the troposphere (a major source). The chemical reactions that lead to the production of ozone in the troposphere are also driven by energy from the sun; therefore ozone is a **photochemical pollutant**. In the troposphere, ozone is the product of a complex series of chemical reactions involving nitrogen oxides (NO_x = NO + NO_2) and volatile organic compounds (VOC). These primary pollutants, known as precursor gases, are produced during the combustion of fossil fuels and are thus associated with industry and the transportation sector. Some NO_x and VOC may be produced by biogenic sources, particularly in the summer when emissions from vegetation and soils are highest. Virtually none of the ozone in the troposphere is emitted directly from natural or human sources, therefore ozone is considered a **secondary pollutant**, formed in the atmosphere from chemical precursors.

While the chemistry of ozone production is complex, the main features are well established and can be summarized as follows. Nitric oxide (NO) introduced into the atmosphere reacts rapidly with O_3 to form nitrogen dioxide (NO_2, reaction R1 Box 1). NO_2 can efficiently absorb sunlight and photo-dissociate to yield oxygen atoms (O) and NO (R2). These oxygen atoms in turn will react rapidly with molecular oxygen (O_2) to reproduce O_3 (R3; M represents a third molecule such as molecular oxygen or nitrogen (N_2) that absorbs the excess energy released in this reaction, thereby stabilizing the newly formed O_3 molecule).

Box 1 Formation and Destruction of Ozone

NO	+	O_3		$\rightarrow$	NO_2	+	O_2	R1
NO_2	+	hν		$\rightarrow$	NO	+	O	R2
O_2	+	O	+ M	$\rightarrow$	O_3	+	M	R3

Reactions R1 to R3 (Box 1) describe the photostationary state between O_3, NO and NO_2. That is, in the absence of other gases in the atmosphere, an equilibrium would be established in which the amount of ozone would be controlled by the ratio of NO_2 to NO in the atmosphere and the intensity of sunlight. However, measurements of ozone in the troposphere have revealed clearly that ozone concentrations are significantly higher than would be expected under steady-state conditions. This indicates that more complex chemical reactions are occurring and indeed,

the atmosphere is never free of chemical species that can interfere with the pathway outlined in R1 - R3.

In polluted atmospheres, the presence of gaseous hydrocarbons (denoted in Box 2 as RH but also known as VOC) and NO_x are instrumental in ozone formation. The key to understanding ozone formation is to recognize that if there were reactions other than R1 that could produce NO_2 without destroying an ozone molecule, and if this were followed by reactions R2 and R3 that result in the production of another ozone molecule, then a mechanism would be established that would lead to increasing ozone levels. This is in essence what is occurring in polluted atmospheres. Under certain conditions where hydroxyl radicals ($HO^{\bullet}$) are formed photochemically, hydrocarbons (RH) are degraded to produce peroxy radicals ($HO_2^{\bullet}$ and $RO_2^{\bullet}$) that react with NO to produce NO_2. (R4 - R8 Box 2). The net result of this series of reactions is that two ozone molecules are formed for each hydrocarbon molecule degraded. In actual fact, even more complex reactions are involved than those represented by R2 - R8, and some of these also generate ozone molecules. Considerable work has been done to try to estimate the overall yield of ozone per molecule of hydrocarbon consumed but this is a complex endeavor and it varies with the type of hydrocarbon.

Box 2 The role of hydrocarbon oxidation ozone formation

$RH + HO^{\bullet}$	$\rightarrow$	$R^{\bullet} + H_2O$	R4
$R^{\bullet} + O_2 + M$	$\rightarrow$	$RO_2^{\bullet} + M$	R5
$RO_2^{\bullet} + NO$	$\rightarrow$	$RO^{\bullet} + NO_2$	R6
$RO^{\bullet} + O_2$	$\rightarrow$	$HO_2^{\bullet}$ + (RCHO and/or R_1R_2CO)	R7
$HO_2^{\bullet} + NO$	$\rightarrow$	$NO_2 + HO^{\bullet}$	R8
$2 (NO_2 + h\nu)$	$\rightarrow$	$2(NO + O)$	R2
$2(O + O_2 + M)$	$\rightarrow$	$2(O_3 + M)$	R3

Net: $RH + 4O_2 + h\nu \rightarrow 2O_3 + H_2O$ + (RCHO and/or R_1R_2CO)

Ozone is removed from the atmosphere through several processes, including both gaseous and aqueous chemical reactions, and deposition to the ground. In polluted atmospheres, during the nighttime, R2 ceases to occur since it is driven by sunlight. Consequently, R1 can dominate nighttime reactions leading to a complete removal of ozone when sufficient NO is present, as it often is in urban areas. This process is dubbed NO_x scavenging. In rural areas, NO concentrations are generally too low to scavenge ozone appreciably. NO_x scavenging can also occur during the daytime where NO concentrations are high and VOC levels are relatively low (e.g. in the early morning rush hour traffic (high NO emissions) when temperatures are still quite

low (low volatility of VOC)). Therefore, ozone levels experienced during the day depend on the relative amounts of different pollutants in the atmosphere, which in turn determines which of the myriad of chemical reactions are driving ozone chemistry at a particular time.

3. SOURCES

As ozone is a secondary pollutant, the question of sources of ground level ozone refers to sources of the gaseous precursors, NO_x and VOC. Both NO_x and VOC have anthropogenic (from human) and biogenic (from biological) sources. Anthropogenic NO_x is the product of both stationary and mobile combustion processes. Nitrogen in the fuel source combines with atmospheric oxygen at high temperature to form several NO_x species, of which NO and NO_2 are the most common. The primary anthropogenic sources of NO_x are transportation sources (i.e. vehicles), thermal electrical power plants and certain industrial processes. Emissions of NO_x from natural sources account for a small percentage of total emissions. These come from forest fires, lightening and soil microbial activity.

Many hundreds or even thousands of different organic compounds fall under the umbrella of VOC. Anthropogenic VOC are released into the atmosphere through combustion and evaporation processes. The largest sources are industrial processes (principally solvent use, petroleum refining and distribution, and chemical manufacturing of various kinds) and transportation sources. Biogenic emissions of VOC, principally from vegetation, can be substantial. Isoprenes from deciduous forests and monoterpenes from coniferous forests are the most relevant biogenic VOC involved in ozone formation.

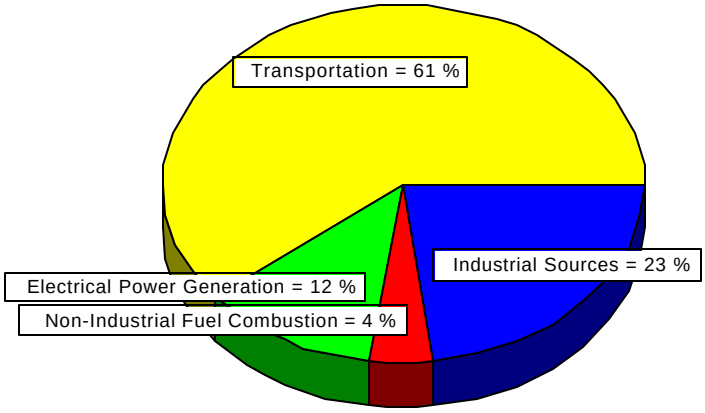
A national emissions inventory is compiled by Environment Canada, in collaboration with the provinces and territories, every 5 years. The inventory provides emission estimates for approximately 80 different sectors, within 5 major source categories: industrial, transportation, non-industrial fuel combustion, incineration and miscellaneous sources. The process of acquiring, compiling and reviewing the emissions data is a lengthy one. The 1995 Canadian Emission Inventory has only recently been finalized (see http://www.ec.gc.ca/pdb/cac/cacdoc/1995e/main95.html (for the tables in English); and http://www.ec.gc.ca/pdb/cac/cacdoc/1995f/main95f.html (for the tables in French). The results of the 1990 Emission Inventory are shown in Figures 1 and 2 (SAD Figures 4.1 and 4.2). It has been estimated that the range of uncertainty in the 1990 Inventory for NO_x emissions is about 20% and probably even higher than that for VOC emissions.

Within Canada, based on the 1990 Emission Inventory, annual NO_x emissions totaled approx. 2,060 kilotonnes, with 61% originating from the transportation sector, 23% from the industrial sector, and 12% from the electric power generating sector. VOC emissions were estimated at approx. 2,580 kilotonnes. The transportation sector produced 31% and the industrial sector 33%. Applications of surface coatings (e.g. paints), general solvent use and other miscellaneous sources accounted for 24% of VOC emissions. Biogenic emissions of VOC were estimated at 14,645 kilotonnes in 1990. Although this amount represents about 5.5 times the total anthropogenic contribution of VOC, in most urban areas of Canada, anthropogenic

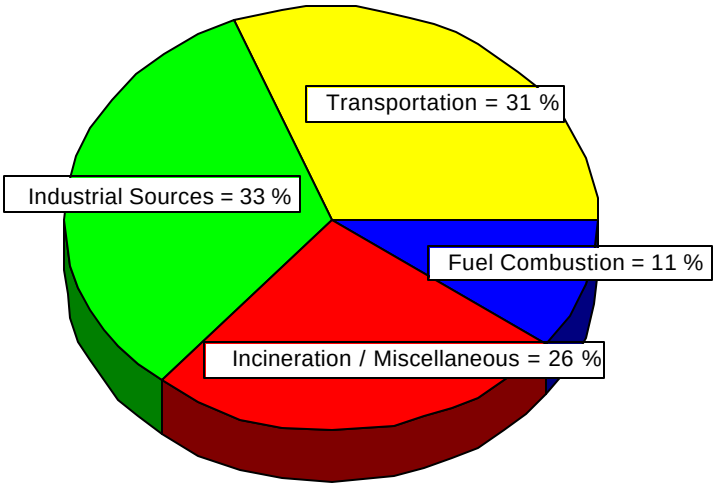
emissions exceed biogenic emissions. However, biogenic emissions of VOC undoubtedly play an important role at times in both non-urban and urban ozone levels depending on proximity to sources and the prevailing wind speed and direction.

Figure 1: 1990 Canadian NO_x emissions by sector (total = 2,060 kilotonnes)

Figure 2: 1990 Canadian VOC emissions by sector (total = 2,579 kilotonnes)



- Transportation = 1,253 ktonnes
- Electrical Power Generation = 252 ktonnes
- Non-Industrial Fuel Combustion = 73 ktonnes
- Industrial Sources = 484 ktonnes



- Transportation = 804 ktonnes
- Industrial Sources = 843 ktonnes
- Incineration / Miscellaneous = 676 ktonnes
- Fuel Combustion = 256 ktonnes

4. ENVIRONMENTAL LEVELS

4.1 Monitoring

Ozone levels in the ambient air are measured with continuous analyzers that record one minute readings, which are then averaged over one hour. With the dataset of one hour values, ozone concentrations over other averaging periods can be calculated (e.g. 6 or 8 hours). Routine monitoring of ozone in Canada uses continuous gas analyzers that operate on a UV light absorption principle. Absorption of UV light by ambient air containing ozone can be compared to that of a reference air sample that is ozone-free.

Ambient monitoring of ozone in Canada is carried out by the National Air Pollution Surveillance Network (NAPS Network), a collaboration of federal, provincial and municipal monitoring agencies. There were 153 Canadian ozone monitoring stations reporting data from 1986 – 1993. Of these sites, 112 were located in urban or suburban areas, and 41 in rural locales. In addition, short-term studies have added to the rural ozone database. There are very few long-term data sets for remote - rural locations.

4.2 Background Ozone Concentrations

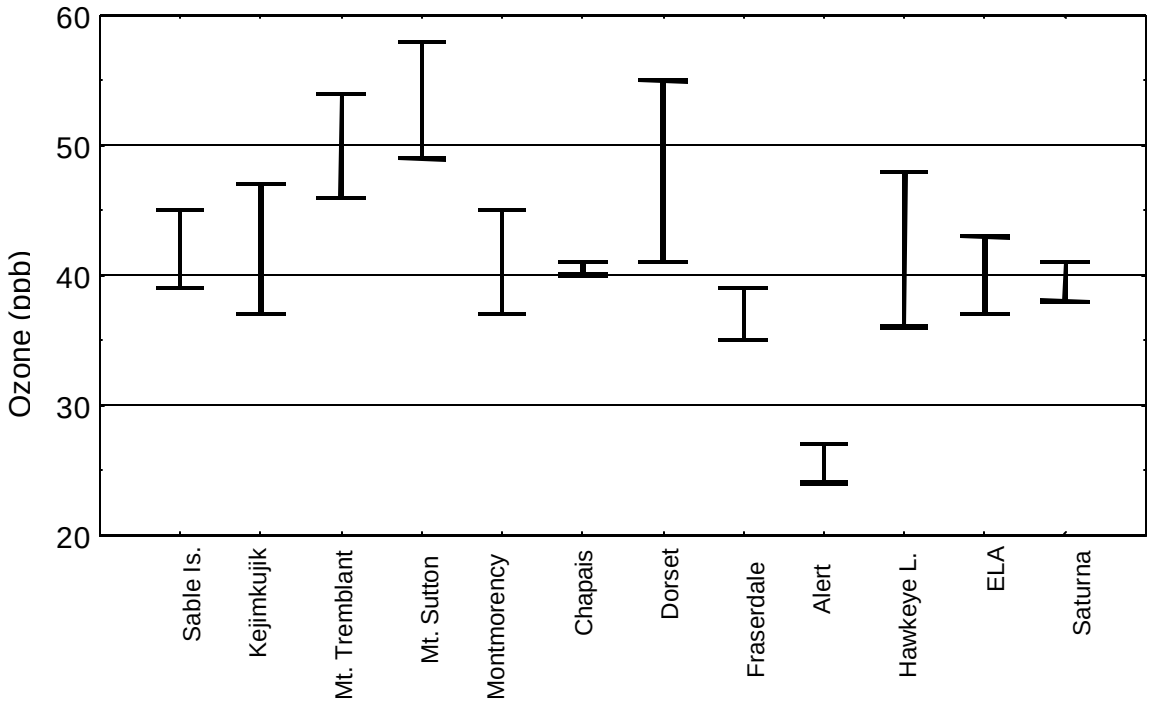
The term “background ozone” is used in different ways in different circumstances. In the truest sense, background ozone refers to the concentration of ozone in the absence of any anthropogenic input of precursor gases. Given the global transport of air pollutants though, and the almost ubiquitous presence of the precursor gases, it is not possible to identify such a level. Ozone concentrations at remote sites offer the best estimate of current background ozone levels. In these locations, ozone levels are a product of natural sources of precursors, long range transport of ozone and precursors, and contributions from stratospheric ozone. Given the limited monitoring of ozone at remote sites, “clean sites”, those distant from major urban or agricultural centres, are often used for estimates of background ozone concentrations. Ozone concentrations at remote or clean sites exhibit two general characteristics: minimal diurnal variation and seasonal peaks occurring in late winter or early spring. The peak season coincides with the time of year in northern mid-latitudes when atmospheric conditions favour the mixing of stratospheric ozone down into the lower atmosphere.

Fifteen sites in Canada are identified as being sufficiently removed from anthropogenic influence to provide reasonable estimates of background ozone concentrations. The ozone concentrations observed at these sites are similar to those reported for other locations in the Northern Hemisphere. Based on these data, reasonable estimates of background ozone for areas of Canada relatively unimpacted by anthropogenic pollution are:

Daily 1 hr. Maximum (May - Sept.)	35 - 48 ppb
Monthly 1 hr. Average (May - Sept.)	25 - 40 ppb.

When all months of the year are included, values are slightly lower. The cleanest Canadian sites experience average daily maxima concentrations even lower than those above. Alert, NWT, possibly the only truly remote monitoring site in Canada, experienced an avg. daily 1 hr. maximum of 28 ppb over the 3 year period during which concentrations were monitored. Values tend to vary from year to year as shown in Figure 3 (SAD Figure 5.2).

Figure 3: Yearly variation in mean daily maximum hourly ozone concentrations (May to September) for selected remote and rural sites.



4.3 Geographic and Meteorological Factors Affecting Ground Level Ozone

As discussed above, the concentration of ozone in the ambient air is a function of complex chemical reactions and the balance between the precursors NO_x and VOC. The formation of ozone is maximal over the summer season, when higher temperatures, more intense solar radiation and longer day lengths enhance the photochemistry. Meteorological processes and geographic / topographic features also play significant roles in determining ozone concentrations. The meteorological conditions necessary for the occurrence of high ozone concentrations are well documented; they involve slow moving, anticyclonic (high pressure) weather systems. These systems, characterized by slow wind speeds and sinking of air through the troposphere, are conducive to trapping air pollutants near ground level and preventing their dispersion and dilution. Ozone episodes are therefore generally associated with climatic and meteorological conditions that favour enhanced ozone production and limited dilution/dispersion. Geographic and/or topographic features of a region can exacerbate this situation by affecting either of these processes. For example, the Lower Fraser Valley of British

Columbia is known to be one area where the adjacent mountains act to confine air masses, contributing to episodes of high air pollution.

Ozone and its precursors can also be transported over distances that range from hundreds to a few thousand kilometers. Understanding the extent to which ambient ozone levels in an area are the result of local emissions of NO_x and VOC versus long range transport (LRT) of these gases, and of ozone, is a necessary step towards being able to control and reduce ozone concentrations. Studies have shown that the Windsor-Québec Corridor and the Southern Atlantic Region are two regions of Canada where LRT is a major contributor to episodes of high ozone concentrations.

4.4 Ozone Concentrations (1 hr.) at Canadian Sites

Ozone concentrations vary on a number of spatial and temporal scales, primarily due to meteorological variability and the impact this has on the transport of precursor gases and on photochemical processes. Ozone data from sites representative of different land uses across Canada were selected from the NAPS network and analyzed to illustrate seasonal, diurnal and day-of-the-week pattern in ozone levels. These datasets were also used for trend analysis. Much of the analysis was restricted to the period May to September in order to focus on the period of the year when photochemcial ozone production is greatest, and on the time of year when the primary “receptors” (people and vegetation) are most exposed to ambient ozone.

For the Canadian sites, mean ozone concentrations (May-Sept., 1986-1993) ranged from 6.1 ppb (Vancouver - Robson and Hornby) to 44.3 ppb (Ontario - Long Point). As shown in many studies, mean and median ozone concentrations are highest at rural sites and lowest at downtown urban sites. This pattern occurs because rural sites are affected by the transport of ozone and precursor gases from urban areas. Typically, rural areas lack the high NO_x values that prevail in downtown urban areas, which would otherwise scavenge ozone out of the air. Hourly concentrations of ozone in the 0-5 ppb range are not uncommon at urban sites in Vancouver, Toronto or Ottawa for example during the night. Maximum 1-hr. ozone values (May-Sept., 1986 -1993) varied from a minimum of 57 ppb (Vancouver - Robson and Hornby) to a maximum of 213 ppb (Vancouver – Hamilton and Paisley), with most sites recording maximum hourly ozone values over 100 ppb.

There are pronounced seasonal variations in monthly average daily means and daily maximum across Canada (Figure 4 and 5(from SAD Figures 5.3-5.6). The seasonal pattern varies slightly across the country, however, ozone concentrations are most elevated during April through September.

Figure 4: Monthly averages of daily mean and daily maximum one hour ozone (ppb) 1986 to 1993) – British Columbia, Alberta, Saskatchewan and Manitoba major urban sites.

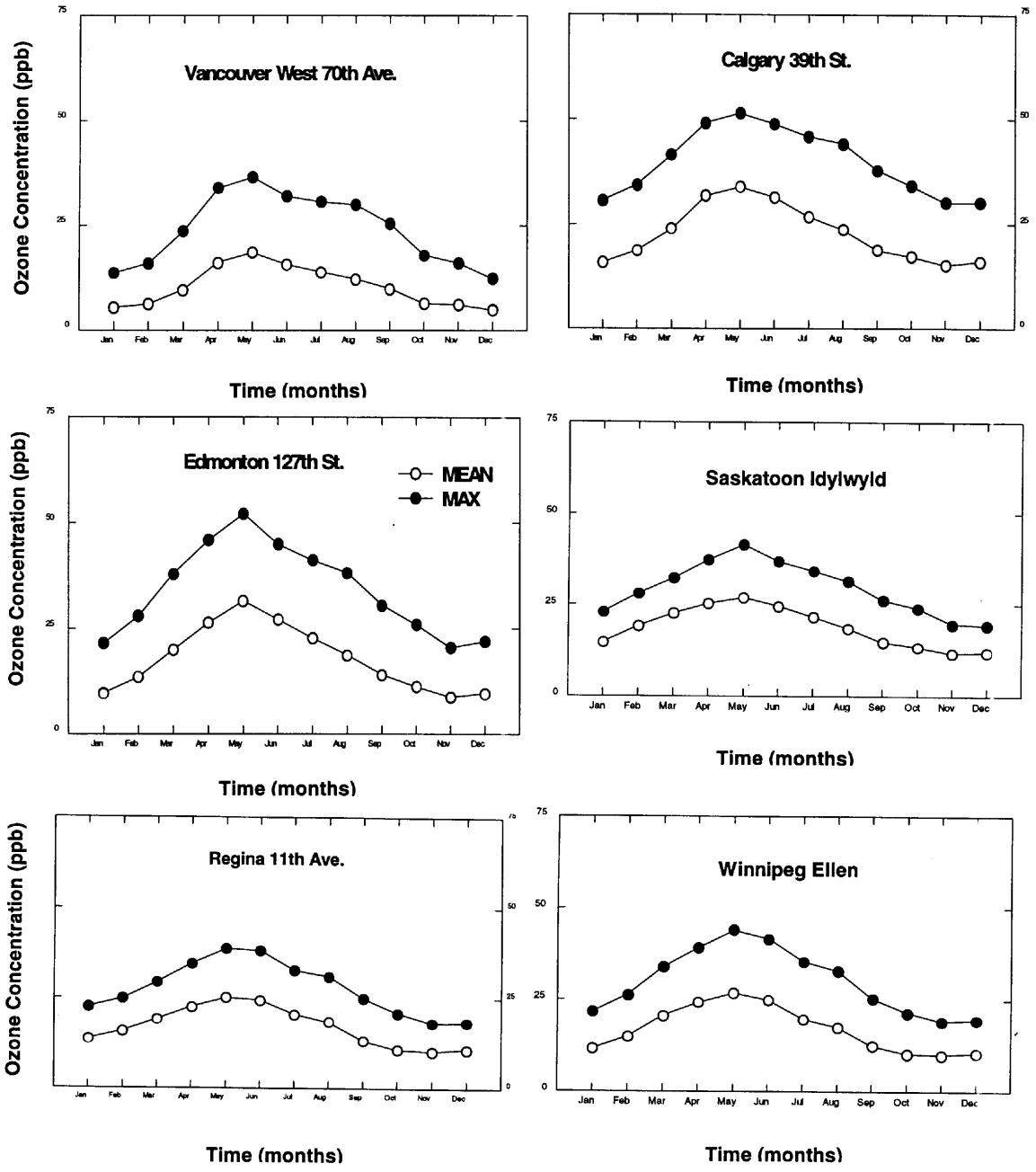
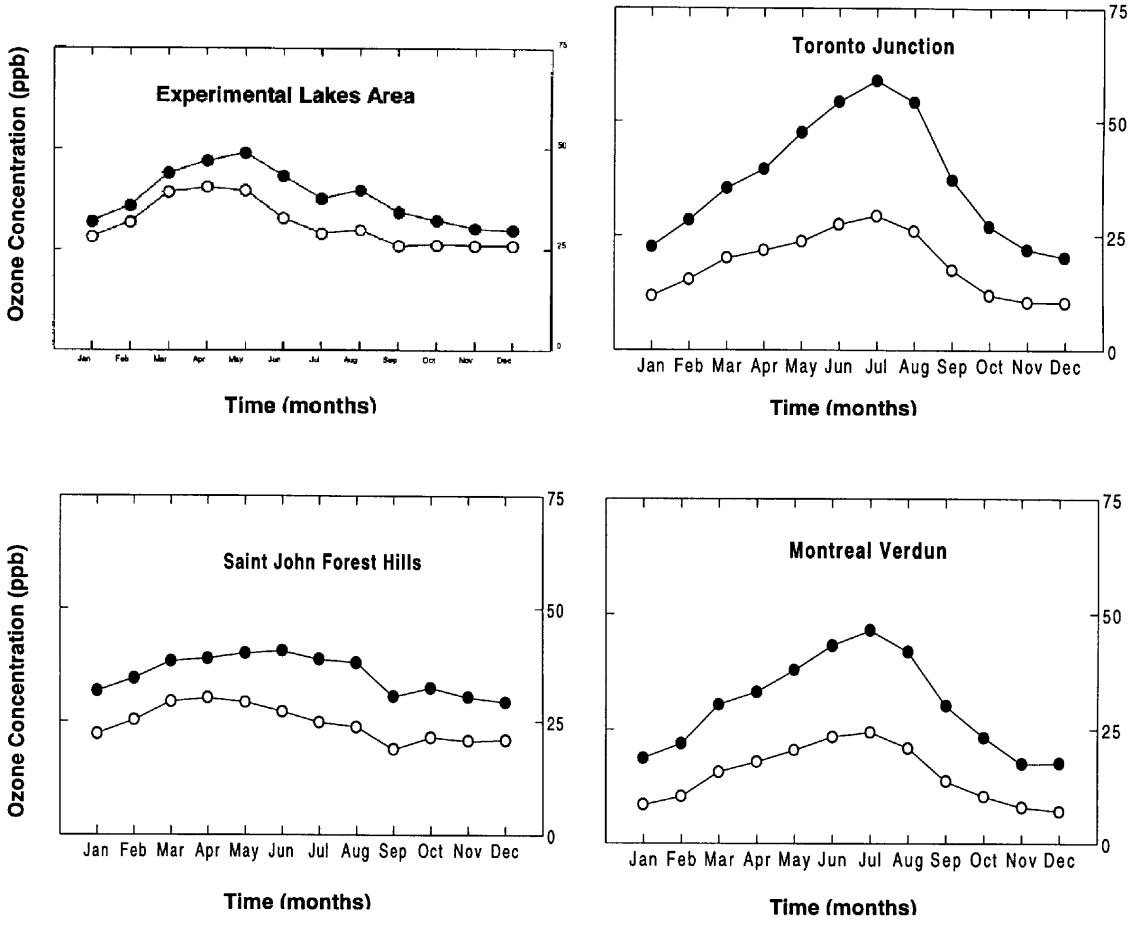


Figure 5: Monthly averages of daily mean and daily maximum one hour ozone (ppb) 1986 to 1993) – Ontario, Quebec and New Brunswick major urban sites.



Analyses of the monthly variation in ozone concentration (monthly averages of daily mean and daily maximum 1 hr. values) revealed pronounced seasonal variations in ozone concentrations at individual sites and regions across Canada, as well as variations in the time of year when maximum ozone levels are observed. Ozone concentrations exhibit a clear seasonal cycle, with concentrations rising with the onset of warmer weather in the spring and declining again as the autumn approaches. However, the “summer season” varies across the country, and ozone concentrations clearly peak much earlier in Western Canada (May) than they do in Central Canada (July). Much less seasonal variation in ozone concentrations occurs in the Atlantic Region. Higher ozone concentrations measured during the spring may reflect the impact of ozone transport from the stratosphere. In Western Canada, the tropopause (boundary between the stratosphere and the troposphere) is closest to the ground during the spring. As a result, occasional intrusion of ozone-rich air from the lower stratosphere can occur.

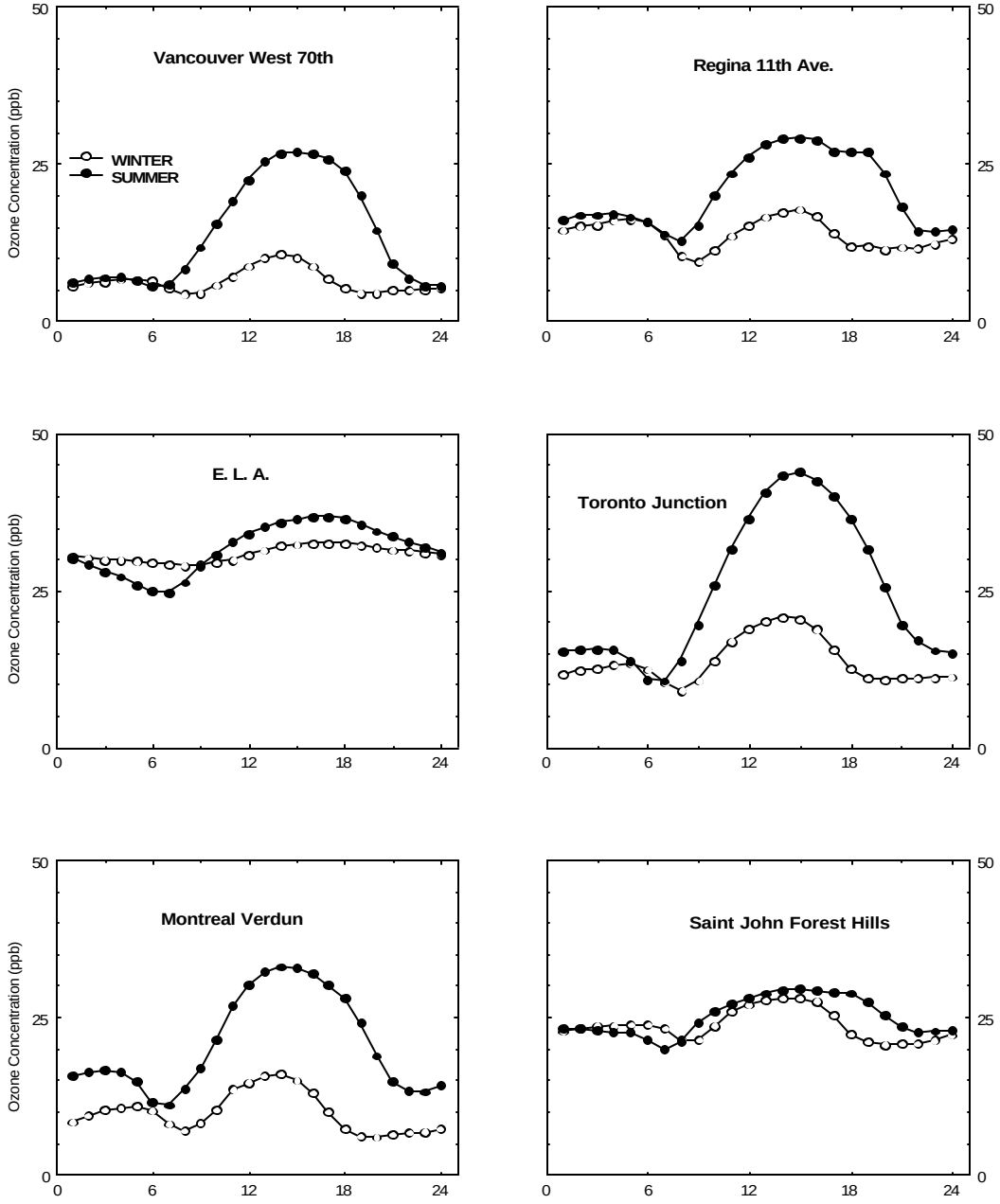
In general, the diurnal cycle of ozone concentrations can be described as unimodal, with lower nighttime concentrations and a mid-day peak. The shape and amplitude of diurnal ozone cycles

are strongly influenced by meteorological conditions, site location (relative to local pollution sources) and prevailing levels of precursors. In urban areas, the daily cycle of NO_x levels arising from vehicle emissions has a major impact on the daily cycle of ozone levels. The area within Canada with the most dynamic ozone patterns, with respect to both spatial and temporal variability, is Southwestern Ontario. This results from the combined influence of numerous sources within the region and the LRT of ozone and its precursors from the heavily industrialized Great Lakes Region of Canada and the U.S.

Analysis of summer versus winter data revealed large differences in the amplitude of the diurnal cycle between winter and summer seasons. Daytime ozone concentrations are much higher in summer than in winter. Nighttime ozone levels are comparable during both winter and summer seasons. For most sites, mean winter ozone concentrations are in the range of 15-20 ppb throughout the day. Concentrations tend to be somewhat lower at some Vancouver sites (5-10) and somewhat higher at more remote sites in Northern Ontario and in the Southern Atlantic Region (25-30 ppb) and in Montréal. There is much more variation across the country in daytime ozone concentrations during the summer (Figure 6 (from SAD Figures 5.7-5.10)).

Diurnal cycles of ozone concentrations were also examined for weekday-weekend differences. These differences are presumed to be in large part due to traffic flow patterns in urban areas, which drive prevailing NO_x levels. At many sites in major urban areas, the mean maximum 1 hr. ozone on the weekend is 10-20% - and sometimes 20-35% - higher than on weekdays. At non-urban sites that are potentially affected by transport of ozone and its precursors from nearby urban centres, there is likewise an increase, albeit smaller (4-8%), in ozone concentrations on weekends. At sites in the Atlantic and Prairie provinces, the weekend change is small. The strong weekend signal in some major urban areas may be the result of less titration (removal) of regional ozone entering the city on the weekend, rather than a function of local photochemical processes. However, it should be noted that measurements of VOC are not available on the same time scales as for ozone and NO_x. When information on VOC concentrations has been available, some investigators have been able to show that changes in VOC concentrations also influence the diurnal and weekly cycles of ozone.

Figure 6: Hourly average ozone concentrations (ppb) for summer and winter (1986-1993)

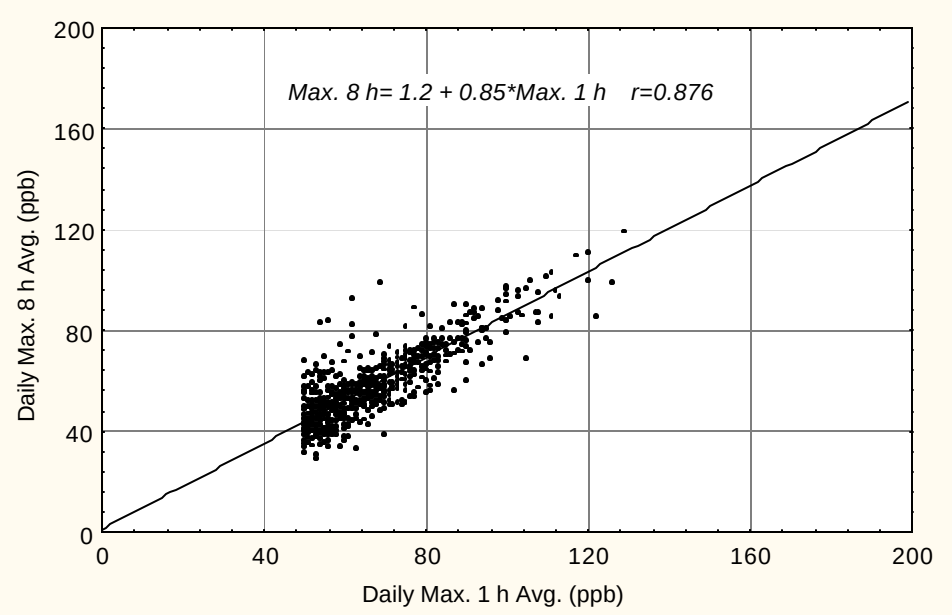


4.5 Ozone Concentrations For 8 hr Averaging Periods

An analysis of selected sites from the NAPS database was undertaken to investigate patterns in 8 hr. ozone concentrations, and the relationship between 8 hr. and 1 hr. maximum ozone concentrations. The analysis showed that for any given 8 hour daily maximum concentration, there is a very low probability that hourly maxima, 20 ppb or more greater than the 8 hr. daily maximum, will occur. Figure 7 (SAD Figure 5.24) illustrates the relationship between daily maximum 1 hr. ozone concentrations and daily maximum 8 hr. ozone concentrations using data

from 41 sites (1992). The relationship has been shown to be quite consistent over time when data from other years have been examined.

Figure 7: Relationship between daily maximum 8 hour average and daily maximum 1 hour average for 1992 (n = 1541).



4.6 Long-term Trends in Ozone Concentrations

Ozone concentrations are highly correlated with meteorological conditions (e.g. hot summers are associated with more frequent ozone episodes). Given the variation in meteorological conditions (on many time scales), and the variability this will induce in ozone concentrations, this "noise" must first be removed from the data if trends related to precursor emission controls are to be identified. A regression model which accounted for meteorological variability was applied to daily maximum 1 hr. ozone data from sites in the Lower Fraser Valley, Windsor-Québec Corridor and the Southern Atlantic Region. While the majority of sites in Ontario showed small, but statistically significant increasing trends, 3 sites showed weak declining trends and one site showed no significant trend. On average, within the whole of Ontario, ozone concentrations seemed to be increasing at a rate of approximately 1.2% per year over the period 1980-1990. For Montréal, two sites showed a statistically significant declining trend of 1.5 and 1.1% per year, while a third site showed no trend over the period 1981-1993. In Vancouver and the LFV, the majority of sites showed statistically significant increasing trends, although three sites showed declining trends. The average trend for the region was +0.45% per year over the period 1985-1992. Similar inconsistencies were noted among sites within the SAR over the period 1985-1992. These analyses illustrate the variability of ozone trends within urban areas and within geographic regions. However, the analysis is limited in that for most sites, less than 10 years of data were utilized in the trend analysis, and because most of the sites were urban. Thus the reported trends may not be indicative of rural or regional ozone behaviour.

5. MATERIAL EFFECTS

5.1 Effects Summary

Although sulphur dioxide remains the most important pollutant in the degradation of materials, other atmospheric pollutants are gaining in importance as a result of declining emissions of sulphur dioxide. Ozone is one of these. Ozone damages many different types of materials, both functionally and aesthetically, alone and in combination with other pollutants and environmental factors. Impacts of ozone alone are most significant for organic materials.

Among the stretched elastomer materials tested, natural rubber, general diene rubber, polyisoprene, polybutadiene, acrylonitrile-butadiene and styrene-butadiene were most affected by ozone. Indeed, one of the earliest techniques used to assess ambient ozone concentrations was based on the consistent and rapid cracking of stressed rubber strips when exposed to ambient air. Either the time until cracking or the depth of cracking after a specified time can be related to ambient ozone concentrations. Neoprene, silicones, ethylene, butyl rubber and propylene have not been shown to be affected by ozone. The difference in susceptibility of different elastomers is linked to their organic structure, and in particular, the relative proportion of unsaturated carbon molecules, which are most susceptible to attack by ozone. Protection of elastomers can be increased by the use of antiozonants and waxes. Degradation of elastomers also occurs as a result of exposure to natural weathering processes; in particular, to sunlight.

Ozone has the ability to damage textiles by reducing tensile and break through strength. Synthetic fibers tend to be less affected than natural fibres. Factors such as sunlight, heat, moisture and the presence of micro-organisms can also contribute to reductions in tensile strength, and may be much more important factors than exposure to ozone. However, low levels of ozone can degrade fabrics if they are sufficiently moist. Ozone also causes fading and/or discolouration of dyes. In fact, the primary causal agent of fading is ozone, although significant fading may only occur from exposure to ozone in combination with other factors (e.g. humidity). Lower molecular weight dyes appear to fade most quickly.

Ozone has the ability to embrittle and fade surface coatings by reacting with the organic binder and/or the pigment. Oil based house paints were most susceptible to ozone damage while automotive finishes and paints that contain carbonate filters were the most ozone resistant. Other factors that contribute to paint erosion are temperature, moisture, sunlight, and the presence of other ambient air pollutants. It is likely that the combined effect of these other factors will be larger than the degradation caused by ozone alone.

Damage to organic materials is caused at the molecular level by chain scissioning and cross-linking mechanisms. In some cases there is an added synergistic degradation of materials due to the presence of other ambient pollutants, specifically sulphur dioxide and nitrogen oxides, and/or high humidity levels.

The impact of ozone on metallic materials is primarily a result of synergistic effects with sulphur dioxide. In combination with sulphur dioxide, ozone accelerates the corrosive action of sulphur dioxide on metals. At typical ambient levels, the presence of ozone increases the deposition rate of sulphur dioxide to the metal surface and increases the rate of oxidation of this dioxide. Beyond this mechanism, minimal other information exists for describing potential synergistic effects. These synergistic effects have been noted for a variety of metals, such as copper, zinc, silver, aluminum, nickel and iron. Corrosion of these metals will also occur in the presence of other pollutants such as nitrogen oxides and organic acids.

Ozone on its own has little ability to affect other inorganic materials either. Corrosion of stone materials, such as marbles, sandstone, limestones, bricks, concrete, and gravel, does occur but as a result of the synergy between ozone and sulphur dioxide. Other environmental factors can also influence the effect of ozone on building materials.

5.2 Quantification of Impacts

In the majority of studies reviewed related to organic materials, effects were reported qualitatively (e.g., fading/cracking). Effect levels and corresponding exposure periods were assessed for elastomers, textiles, and dyes and surface coatings; however, no concentration-response relationships were developed. Where concentration-response relationships were identified (e.g. for paints, metals and stones), the ways in which the effects of ozone were quantified was diverse. Also, differences in mathematical expression of the relationship hampered the merging of the results into an overall concentration-response relationship for any given material.

Therefore, it is not yet possible to define concentration-response relationships or effect levels to describe the impact of ozone on materials. However, it should be recognized that chronic exposures in an ambient environment, in the order of weeks at concentrations in the range of 20 – 50 ppb, have the potential to adversely impact elastomers, textiles, paints and dyes. Erosion rates measured during field exposures for non organic materials (metals and stone) in atmospheres containing ozone in combination with sulphur dioxide, are smaller but nevertheless significant.

The most important pollutant causing material damage remains sulphur dioxide, the effects of which are well quantified. With the decline in emissions of sulphur dioxide, effects associated with exposure to nitrogen oxides and ozone are becoming more apparent. Concentrations of nitrogen oxides and ozone are highly correlated, however, and therefore their effects are not easily separated. These effects are known to be smaller than those of sulphur dioxide but beyond that, much remains to be done to characterize and quantify them.

6. VEGETATION EFFECTS

The discussion in this document on the effects of ozone on plants has been based upon the prior report of the Vegetation Objective Working Group (VOWG) of the Multistakeholder NO_X/VOC Science Program. A review of more recent literature indicated that the information base on the effects of ozone on plants had not progressed sufficiently to warrant any change to the discussion or conclusions of the report by the VOWG.

6.1 Effects Summary

Ozone injury was first observed and documented under field conditions in the Los Angeles area. The majority of research that followed through the 1950s to the 1970s was conducted with pot-grown plants under greenhouse or controlled environment conditions. It is only since the mid-1980s that research activities have attempted to mimic field conditions more closely through the use of open top chambers and fumigation systems.

Acute symptoms on broad-leaved plants consist of chlorosis, fleck, stipple and uni- or bifacial necrosis. On conifers, acute responses consist of mottle, banding and chlorosis. Chronic symptoms are related to frequent, relatively low hourly ozone concentrations, with periodic, intermittent peaks of relatively high hourly concentrations. Chronic effects can lead to changes in plant growth, productivity and quality, and these effects may occur without visible symptoms. When symptoms do develop, they can include chlorosis, delayed early season growth, premature senescence and leaf abscission. In the case of acute effects, plants can compensate for stress during respite periods; therefore, the frequency of ozone episodes and the time interval between such episodes are critical in evaluating and modeling plant response.

It is well recognized that foliage is the primary site of plant response to ozone exposure. It is also known that ozone exerts a phytotoxic effect only if a sufficient amount reaches sensitive sites within the leaf. Thus, ozone injury will not occur if the rate of uptake is low enough that the plant can detoxify the ozone or repair or compensate for the effects. Ozone can be destroyed at the leaf surface through interactions with surface waxes. Oxidation or cleavage of surface waxes can lead to changes in composition and physical properties of the leaf surface (e.g. decreased water repellence) that may subsequently affect the uptake of ozone. Once ozone enters the leaf via open stomata, it has the potential to impair cellular function. Because oxidants are also produced within the cell as a result of normal photosynthetic processes, and are injurious to cell constituents, plants have evolved enzymatic mechanisms to transform oxidants to less toxic forms. The detoxifying enzymes are saturable, however, thus cellular systems may be overwhelmed by the presence of extra oxidants from ambient ozone exposure, resulting in plant damage.

The role of exclusion or detoxifying mechanisms in determining ozone sensitivity among species or cultivars is not well understood, as there is not at present a conceptual model describing plant resistance to oxidants. Scientific understanding of resistance remains uncertain. It seems clear

that the detoxification of ozone and its products would consume energy, although whether this additional energy burden would significantly decrease plant productivity, relative to the direct effects of ozone on photosynthesis for example, is not known.

In summary, it is the integrated cellular system that confers and determines plant sensitivity to ozone. Effects at the cellular level are ultimately expressed as visible injury to the leaf or as secondary effects that can be expressed as reduced root growth, reduced yield of fruits or seeds, or both. These responses only appear after initial defence mechanisms are overrun. Biochemical and physiological changes can occur without visible injury symptoms appearing.

In Ontario, studies of the impact of ozone on crop yield have identified the following crops to be at greatest risk: dry bean, potato, onion, hay, turnip, winter wheat, soybean, spinach, green bean, flue-cured tobacco, tomato and sweet corn. Crops estimated to be marginally at risk (insufficient data did not permit more accurate quantification of loss) included cucumber, squash, pumpkin, melon, grape, burley tobacco and beet. In Alberta, the crop yield analysis consisted of a review of the available literature for ozone response based on crops grown. This information was then compared with a limited amount of urban ozone-monitoring data, and it was concluded that there were no identifiable risks to sensitive crops at that time. Other agricultural crops commonly grown in Canada but not mentioned above should not be considered resistant to the impact of ozone—their response is simply not known at this time.

Tree species common to Canada that have demonstrated ozone sensitivity with respect to a variety of endpoints (e.g. biomass, height, photosynthesis) under controlled ozone exposure conditions include: maples (sugar, silver, red), ash (white, green), spruce (white), white pine, poplar (hybrid), cottonwood, cherry, walnut, sycamore, white birch and red oak. Although ozone impacts varied significantly, and included both positive (growth stimulus) and negative (growth reduction) responses in many of the experimental studies, the response to seasonal mean exposures of 40–60 ppb for over half of the studies was reported as at least a marginal growth reduction. There is also considerable evidence that ozone can injure many annual and perennial grass species commonly used in turfgrass production in parts of Canada.

6.2 Quantification of Impacts

An absolute threshold ozone concentration above or below which vegetation injury will or will not occur has not been identified in the scientific literature. A threshold exposure level for plant biochemical response to ozone is largely conceptual in nature. Theoretically, biochemical systems could reach a saturation level above which they can no longer compensate for injury caused by ozone. A threshold dose response for ozone may exist, but the threshold may be so subtle that it cannot be detected, given current methods of investigation.

There are several endpoints that may be considered in establishing concentration-response relationships for vegetation. The two most common ones are biomass (or biomass losses) and visible foliar injury. (Note that “biomass” with respect to agricultural crops is measured as the

yield of the relevant crop part). Biomass (or yield) losses are related to chronic exposures and visible injury to acute exposures. Both biomass loss and foliar injury have been investigated in crop, ornamental and tree species.

Exposure Index

For adequately quantifying acute and chronic effects, it is necessary to identify both short- and long-term exposure indices. A number of different exposure indices were reviewed in terms of their efficacy in describing ozone exposure – plant response relationships and their suitability as management tools. This was done for both acute and chronic exposure indices. The evaluation concluded that the form of an index to protect vegetation should be cumulative (summation of hourly values) and should emphasize peak concentrations. The SUM60, the AOT40 and the W126 are three such indices. The W126 index was dismissed from consideration on the basis that it was too complex an index to administer. The review of the SUM60 and the AOT40 showed there was no compelling scientific reason to favour one or the other. Furthermore, a regression of these two indices performed using air quality data from the years 1980-1993 confirmed a high degree of similarity ($r^2 = 0.97$). Therefore, in terms of assessing the areas in Canada where vegetation is impacted by ozone, use of either the SUM60 or the AOT40 would yield similar results. Consequently, on the basis of other factors, predominantly the access to databases in the United States, where the SUM60 has been used, a decision was made to recommend use of the SUM60 in the assessment of chronic effects on vegetation in Canada. The SUM60 index was also selected for assessment of acute effects on vegetation based on studies in Ontario of white bean and radish.

The SUM60 index is the sum of hourly ozone concentrations equal to or greater than 60 ppb over the daylight period 08:00 – 19:59. The daily sums are then added over a specified time period; a 3-day SUM60 is used for the assessment of acute effects, whereas a seasonal (3-month) SUM60 is used for the assessment of chronic effects. Although the SUM60 clearly encapsulates some aspects of plant exposure that are important in the plant response (i.e. cumulative exposure over a time period and the relative importance of peak concentrations), there are other factors demonstrably important in determining plant response (e.g. phenology, time of day etc.) that are not accounted for in the SUM60 index. Furthermore, there is no biological basis for assuming that concentrations below 60 ppb ozone are not significant in the plant response. In the future it may be possible to develop a more biologically relevant index.

LOAEL Determination

In terms of quantifying the impacts on vegetation associated with exposure to ozone, this report has focused on identifying LOAELs, that is, the lowest ozone concentrations that have been shown to induce an adverse response in plants under experimental conditions. In this regard, a minimum yield loss level must be identified that can be directly attributed to ozone exposure. Losses below this amount are within the range of experimental uncertainty. Similarly, for acute effects, a trace level of foliar injury (defined as a foliar injury index score of 1-20) is the lowest

level of injury that can be reliably quantified and is therefore the recommended endpoint of assessment of acute effects on vegetation.

Given the paucity of Canadian data on ozone exposure – crop yield relationships, particularly the lack of data amenable to LOAEL determination using the SUM60 index, the U.S. NCLAN (National Crop Loss Assessment Network) database was relied upon. In order to use the data to develop LOAELs in a Canadian context, a subset of the data was analyzed by removing data for crops not grown in Canada as well as those grown in California, where growing conditions differ markedly from those in Canada. The 3 month, 12 hr. SUM60 values corresponding to 10% yield loss levels from this suite of crops are shown in Table 1 (SAD Table 8.9). From these data, turnip and wheat are identified as the most sensitive crops. Given experimental uncertainties, the limitations of the NCLAN protocol for LOAEL determination, and the amount of both inter- and intra-specific variability in the response of crops to ozone exposure, it was considered inappropriate to identify the single lowest effect level as the LOAEL. Instead, a more conservative approach was adopted, and a LOAEL range of 5900 to 7400 ppb-h was identified. This range excludes a SUM60 level of 2900 ppb-h identified for one particularly sensitive wheat cultivar.

Similarly, based upon the results of studies conducted by the U.S. EPA in the late 1980s on the impact of ozone on forest trees, a 3 month, 12 hr SUM60 LOAEL range of 4,400 to 6,600 ppb-h was identified for 10% biomass loss. This LOAEL range was based upon the response of black cherry and aspen (Table 2 (SAD Table 8.11)).

Table 1 Summary of NCLAN SUM60 index values resulting in a 10% yield loss in NCLAN studies (excluding cotton and crops assessed in California).

Crop Evaluated	Cultivar	Moisture Status	12-hour SUM60 (ppb-h)
Corn (L)	PIO		41,600
	PAG		55,800
Kidney Bean	CAL LT RED		15,200
Kidney Bean (L)	CAL LT RED		17,200
Peanut (L)	NC-6		36,200.
Potato	NORCHIP		9,900
	NORCHIP		20,300
Sorghum	DELALB		67,600
Soybean	CORSOY		15,300
	CORSOY		42,200
	AMSOY		32,800
	PELLA		18,200

	WILLIAMS		15,500
	CORSOY	Dry	71,200
	CORSOY	Wet	70,000 cont….

Table 1 cont. Summary of NCLAN SUM60 index values resulting in a 10% yield loss in NCLAN studies (excluding cotton and crops assessed in California).

Crop Evaluated	Cultivar	Moisture Status	12-hour SUM60 (ppb-h)
Soybean	RSOY	Dry	89,100
	CORSOY	Wet	62,200
	CORSOY	Dry	10,200
	CORSOY	Wet	11,800
	WILLIANS	Dry	21,100
	WILLIAMS	Wet	14,800
	HODGSON		8,400
	DAVIS		13,800
	DAVIS		23,400
	DAVIS	Dry	57,100
	DAVIS	Wet	35,200
	DAVIS	Dry	45,900
	DAVIS	Wet	24,100
	YOUNG	Dry	38,800
	YOUNG	Wet	25,000
Tobacco (L)	MCNAIR		24,400
Turnip (T)	JUST RIGHT		7,400
	PURPLE TOP		5,900
	SHOGOIN		6,600
	TOKYO CROSS		9,300
Wheat	ABE		25,100
	ARTHUR		21,300
	ROLAND		7,400
	ABE		34,800
	ARTHUR		27,700
	VONA		2,900
	VONA		7,700

Table 2: Exposure-response data for 10% level of biomass loss, for trees exposed in OTCs to ozone

Tree Species Evaluated	12-hour SUM60 (ppb-h)
Aspen – wild	19,100
	15,800
	43,700
	55,900
	55,400
	18,700
Aspen 216	14,700
Aspen 253	8,100
Aspen 259	4,700
Aspen 271	13,300
Aspen 216	9,500
Aspen 259	5,200
Aspen 271	29,600
Aspen – Wild	15,000
Douglas Fir	89,300
	250,000
	90,800
	94,400
	72,000
	70,800
	63,000
Ponderosa pine	17,900
	26,300
	18,500
	27,100
	11,300
	21,600
	19,500
	14,900
	27,900
	55,200
	43,400
Red Alder	32,100
	17,900
	79,000
	3,8008
	250,000
	21,800
Black Cherry	6,600
	4,400
Red Maple	71,700
Tulip Poplar	23,400
	19,900
	14,700
Loblolly GADR 15-91	71,000

Loblolly GAKR 15-23	212,100
Sugar Maple	25,300
	23,800
E. White Pine	21,600
	31,500
Virginia Pine	191,200

Although the history of studies on the acute phytotoxic effects of ozone on plants is a long one, there are, unfortunately, very few studies available that can be evaluated retrospectively to quantify ozone exposure – foliar injury relationships using a SUM60 exposure index. The best data available were from studies carried out in Ontario on white bean over the period 1985-1995. These studies identified a LOAEL range for trace injury in white bean of 500-700 ppb-h. Although the recommended form of the short term exposure index was based on analysis of only two crops (white bean and radish), and the LOAEL range for acute effects was derived from only the white bean studies, both these plants are known to be sensitive to foliar injury following exposure to ozone. Clearly though, there is inadequate information currently to fully characterize the risk of acute foliar injury to crops, trees and native vegetation across Canada.

6.3 Co-Occurring Pollutants

The interaction of ozone and nitrogen oxides or the three- or four-way interaction of ozone, sulphur dioxide, nitrogen oxide and acid rain has not been specifically addressed in any of the field oriented, crop yield response research to date. Although photochemical smog and other forms of atmospheric pollution involve numerous pollutants in addition to ozone, the limited amount of information available on their combined effects on vegetation precludes any specific estimate of the magnitude of these effects in relation to the effects of ozone alone. This finding should be considered in the light of observed patterns of co-occurrence of ozone, SO_2, and NO_2 in urban, rural and remote sites. In the U.S., during 1978-82, co-occurrences were found to be infrequent and of short duration. When they did occur, they were usually sequential or a combination of sequential and overlapping exposures of short duration.

Because of its phytotoxic potential, peroxyacetylnitrate (PAN) could be the most relevant co-occurring pollutant and would not be expected to exhibit short-duration type of co-occurrence. Although PAN has been documented as acting synergistically with ozone in causing increased foliar injury to some species under some conditions, this combined impact cannot yet be generalized, as considerable variability has been demonstrated in the experimental findings published to date (synergistic, antagonistic and additive responses). Given the relatively low levels of PAN reported in the Canadian atmosphere, an evaluation of combined impacts with PAN was not undertaken for this review. However, this aspect of the nature of ozone effects on vegetation also warrants further investigation.

7. BIRDS AND MAMMALS

Very little information on the effect of ozone on birds and wildlife is available. Only three studies were found that reported on effects on birds, and all of these involved domesticated birds and their response to acute exposures. Lung haemorrhage was noted in all three studies, and therefore this appears to be a consistent effect in birds in response to exposure to ozone. The absence of data on potential effects of chronic exposures is clearly a weakness of the current database.

Eleven studies on the effects of acute exposure to ozone on mammals were reviewed, all on domesticated mammals. Most of these studies were on sheep, because sheep have been proposed as a potential animal model for human effects. The most consistently observed responses include adverse effects on red blood cells and inflammatory responses. Red blood cell effects appear to be the most sensitive endpoint for assessment of effects of ozone on mammals based on the evidence presented. No studies were found that dealt with chronic exposures.

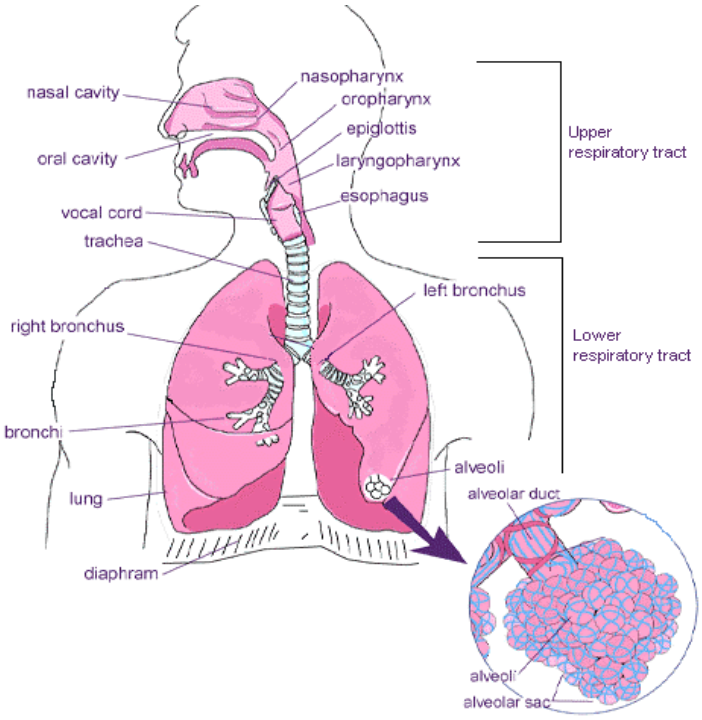
For both birds and mammals, the only significant exposure route is inhalation. Therefore, as is the case with humans, the effects of concern have to do with impacts on the respiratory system. There are notable differences, however, between the lung-air sac respiratory system of avian species and the mammalian bronchoalveolar lung. Among the most important of these are that birds have a higher mass-specific minute ventilation, higher mass specific effective ventilation of gas-exchange tissues, cross-current and counter-current gas-exchange mechanisms and a gas diffusion barrier half the thickness of that of mammals. While these differences may predispose birds to greater sensitivity to inhaled toxicants, there is insufficient information at present to make any predictions concerning relative sensitivities. There appears to be a complex relationship between a species' respiratory physiology, its pathophysiologic response to a toxic gas and other physiologic factors.

There was insufficient information to develop concentration-response relationships and very limited information on which to base effect levels for both birds and mammals. Given the paucity of experimental data and the lack of experimental exposures that reflect ambient conditions, no general conclusions can be drawn at this stage about possible effect levels in either birds or mammals.

8. HUMAN HEALTH EFFECTS

The data on health effects of ozone have been examined in human epidemiological studies, controlled human exposure studies, and animal toxicological studies. The impact of ozone on human health is mainly via the respiratory system (Figure 8). The symptoms of ozone exposure are cough, shortness of breath, decrements in spirometric values, increases in airway resistance and bronchial responsiveness to stimuli, and airway inflammation with the potential to result in Emergency Department visits or hospital admissions, or mortality.

Figure 8: Human respiratory system. The centriacinar, or central portion of the acinus (the functional respiratory unit including all structures from the respiratory bronchiole to the alveoli) is around the terminal bronchiole.



8.1 Epidemiological Studies

Types of studies

Epidemiological studies of the effects of ozone on human health explore statistical associations between changes in ambient levels of ozone and changes in the occurrence of cardiorespiratory health problems in the general population. Five basic health effect markers have been examined in epidemiological studies: mortality, hospital admissions, Emergency Department (ED) visits, field (camp and panel) studies, and chronic health effects. The latter two types of studies often

investigate respiratory symptoms, medication use, pulmonary function changes, reduced activity days, and elementary school absenteeism.

Most of the recent epidemiological studies considering acute and short-term effects (mortality, hospitalizations and ED visits) of air pollution on human health have been time-series studies. A time-series analysis is by definition longitudinal in nature. In this type of study, the timing of an adverse health event is studied relative to short-term time trends in air pollution within a defined geographic area. Major advantages of the time-series study are that it usually provides many units of observational data (typically 1000 days), and examines the temporal pattern of the event, that is, whether health effects lag peak pollution days. The time-series studies are less likely than cross-sectional studies to be biased by inter-population differences (such as age, gender, life style), since the study population does not change substantially over such a short period of time, and acts as its own 'control'.

Time-series studies are 'ecological', since they consider very large groups of people (thousands or millions) rather than individuals, and no control of the experimental conditions is possible. Usually, no individual exposure data are available due to the impracticality of obtaining information on so many people. Exposure is inferred from centrally located outdoor ambient monitoring stations, an explicit difference from the controlled human exposure (clinical) studies. The lack of a direct link between personal exposure to the toxic agent and the resulting health outcome at the individual level is a weakness of ecological studies with respect to making judgments regarding causality. In compensation for this disadvantage, the strength of the time-series study is its ability to examine the overall population responses of very large numbers of individuals to the agent under investigation and, thereby, gain an understanding of the public health impacts and risks to the population as a whole. Causality must then be judged by making use of the sum of all the information available from all epidemiological, clinical, and toxicological studies in a weight of evidence approach.

Other environmental factors and other causes of illness may confound the results and must be taken into account in the time-series as well as the cross-sectional analysis. Daily mortality and morbidity (hospitalizations, emergency department visits) are usually highly cyclic, and undergo strong seasonal fluctuations, with events such as hospitalizations highest in winter and lowest in summer in North America. Ambient ozone concentrations also are highly seasonal, with highest levels in summer and lowest levels in winter. Such seasonal trends could bias the results, and they require some means of adjustment in order to determine whether there is any association or effect of ozone on these health endpoints. Many of the most recent papers using administrative databases have made use of more sophisticated statistical techniques to correct these confounding factors. The studies that did not, are weighted more lightly in view of the strong possibility that the findings are spurious, due to confounding.

Airborne pollution always occurs as a mixture of pollutant agents. Ozone co-exposure with particulate matter (PM) has been of great concern with respect to confounding the relationship between ozone and adverse health endpoints. Some, but not all, researchers have investigated the modifying effects of one or more co-occurring pollutants, including PM [as PM_{10}, $PM_{2.5}$,

coefficient of haze (CoH), or total suspended particles (TSP)], NO_2, SO_2, or CO, on outcomes associated with ozone.

Many studies attempt to estimate the quantitative influence of ozone pollution on human health by calculating a parameter such as relative risk (RR) from the concentration-response relationships. This is presented with a measure of the uncertainty of the RR estimate, such as 95% confidence interval (95% CI). Uncertainty decreases as sample size increases, thus combining data sets is expected to yield more reliable estimates of relative risk. Combining data from several comparable studies in order to analyze them together is often referred to as meta-analysis. A meta-analysis of published peer reviewed studies is presented in this document for each category of health outcomes, based on the availability of the data, to evaluate whether they collectively indicate statistically significant associations for that outcome.

The criteria used in this assessment to select studies for inclusion in the quantitative meta-analysis, and, from within selected studies, to select from among several reported results are that the study must:

(1) measure daily mortality or hospitalization (i.e., is a time series study);
(2) report quantitative results for ozone;
(3) be an original study (rather than a review paper or an abstract) in a peer-reviewed publication;
(4) consider the entire population (rather than only a subset of the population) in the study location;
(5) adjust for effects of some measure of seasonal cycle, temperature and relative humidity;
(6) report results from a co-pollutant model, including PM or some proxy for PM in the model with ozone; PM_{10} or $PM_{2.5}$ is preferable to other measures of particulate matter, and more pollutants in the model is preferable to fewer pollutants; and
(7) consider summer results when there are results from a whole year and/or from several seasons in the same study.

Reporting a statistically significant positive result for ozone is not a criterion for study selection, nor does statistical significance or size of the relative risk estimate affect the evaluation in selecting studies. In a meta-analysis, it is reasonable that a pooled estimate, that combines estimates from all selected studies, should give more weight to those estimates from the studies with the smaller variance. This gives greater weight to those estimates with lower associated uncertainties. Variance takes into account both the consistency of data and the sample size used to obtain the estimate, two key factors that influence the reliability of results.

Acute effects: Mortality

Overall mortality studies indicate that there was a significantly positive association between ozone pollution and non-accidental mortality [Table 3 (SAD Table 12.1b)]. Seventeen of the 23 mortality studies (Table 3) reported consistent and significant associations between increases in mortality and ozone air pollution. These associations could not be explained on the basis of yearly trends, day-to-day variations, epidemics, or weather. The latter is the most important

source of variation with respect to the ozone mortality association, because ozone is often moderately correlated with temperature in summer (correlation coefficient up to 0.35), while extreme temperatures have also been associated with increased mortality. All studies took temperature into account in some way in their regressions, and also included all other cyclic factors that were shown to influence the results during preliminary analyses. These associations were found in cities across North America, in four U.S. and 13 Canadian locations, in Santiago Chile and three European cities, and in a meta-analysis including seven European cities, demonstrating consistency of results despite widely varying climatic conditions and pollutant mixtures.

The mortality association was found at mean ozone concentrations (daily one-hour maximum) between 20 and 75 ppb, below the current Canadian National Ambient Air Quality Objective for ozone of 82 ppb, across widely varying climatic conditions and pollutant mixtures in the study locations (see Table 3). A pooling of ten studies which had adjusted for seasonal cycles, weather terms and co-pollutants, reveals that the weighted estimate of risk of total non-accidental mortality is a 0.40% increase in mortality (95% CI 0.19 – 0.60%) per 10 ppb increase in ozone (daily 1-hour maximum). Several studies indicate that the ozone concentration-response relationship is approximately linear, in one case down to less than 10 ppb. In addition, these studies did not show evidence of thresholds at low concentrations. Only a few studies provided evidence of a more specific cause of death; cardiovascular deaths were associated with ozone increases in several studies while respiratory deaths were not, possibly because of proportionally fewer deaths in the latter category.

The results from the most recent reanalysis of a large Canadian database by Burnett (1998, details in Appendix A of the SAD) demonstrate a strong consistency with the previous mortality studies. This study was carried out in response to a request from the Working Group on Air Quality Objectives and Guidelines. The non-accidental mortality data from 13 cities were reviewed. The regression analysis shows that the risk for non-accidental mortality was 0.79% (95% CI: 0.59-0.99%) for every 10 ppb increase in ozone (daily 1-hour maximum). Since previous studies using similar databases have shown that CO, NO_2 and SO_2 did not confound ozone effects on mortality, it is expected that the ozone mortality impact is likely to be independent of other gaseous air pollutants. The advantage of this study is that it provided an estimate of the lowest observed adverse effect level (LOAEL) of ozone with statistical significance for mortality. The LOAEL for non-accidental mortality was 20 ppb (1-hr maximum) ($p<0.05$). The data continue to show a trend of positive association with ozone values as low as 10 ppb. There appears to be no threshold for mortality.

Six studies (7 locations) did not find any association between ozone and mortality. Some differences in the statistical treatment and/or data limitations (such as exposure data from only one monitor) were identified. These differences may explain the lack of association between ozone and mortality for these studies.

Table 3. Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models (full references in Science Assessment Document).

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis S: Significant NS: Non-significant
Detroit, MI (Schwartz 1991)	not given	no increase	----	**Results NS** Excluded, no quantitative results.
Los Angeles Co. CA (Kinney, Ozkaynak 1991)	75 $\pm$ 45	Increased, % not given	4%, O_3 and NO_2	**Results S** Excluded, no quantitative results for multi-variate model.
St. Louis MO Harriman TN (Dockery et al. 1992)	22.5 $\pm$ 18.5 (24-h mean) 23.0 $\pm$ 11.4 (24-h mean)	24-h ozone: St. Louis: 0.29% (-1.18% to 2.94%),. Harriman: -0.64% (-3.93% to 3.29%)	---	**Results NS** Excluded, no quantitative results for multi-variate model.
New York City NY (Kinney, Ozkaynak 1992)	56 (range not given)	[5.5 deaths per 10 ppb]	10%, O_3 and COH	**Results S** Excluded, no quantitative results for multi-variate model
Philadelphia PA (Li & Roth 1995)	19.8 $\pm$ 14.4 (24-h mean)	Increased for age 65y+ not increased for age <65	---	**Results S** Excluded, no quantitative results for multi-variate model
Philadelphia PA (Moolkavgar et al. 1995)	19.9 (year) (24-h mean) 35.5 (summer) (1.3-159)	Yearly data not given separately Summer: 1.5% (0.9-2.1%), 24-h ozone	Yearly: 0.62% (0.18- 1.04%) Summer: 1.5% (0.7-2.4%) +TSP, SO_2, 24-h ozone	**Results S** Included
Los Angeles CA (Kinney et al 1995)	70 $\pm$ 41 (3-201), yearly	0.2% (0% - 0.5%), yearly ozone	0% (-0.44 to 0.4%) +PM_{10}	**Results S** Included
Toronto ON (Ozkaynak et al. 1995)	36 (95th percentile 66)	(not given separately)	0.34% to 0.42% (+TSP)	**Results S** Excluded, an abstract
Sao Paulo Brazil (Saldiva et al. 1995)	38.3 + 29.7 (1-h max.), 12.5 + 11.5 (24-h mean)	For age 65+ years. 1-h: 0.4% (-0.42% to 1.03%); 24-h: -1.31% (-4.15% to 1.75%)	---	**Results NS** Excluded, no data
Philadelphia PA (Dockery et al. 1996)	not given	(not given separately)	0.9% (+$PM_{2.5}$)	**Results NS** Excluded, an abstract
Chicago IL (Ito & Thurston 1996)	38 $\pm$ 19.9, yearly, 2-d average.	1.0% (0.6-1.5%), yearly ozone, 2-d average	2-day average ozone. 0.68% (0.08-1.16%) (+PM_{10})	**Results S** Included

Table 3. Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models (full references in Science Assessment Document).

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis S: Significant NS: Non-significant
Santiago Chile (Ostro et al. 1996)	52.8 (11-264)	Yearly: OLS model: -0.57% (-0.75 to –0.38%); Poisson: 0% (-0.19% to 0.38%) Summer: OLS model: 0.20% (0-0.50%) Poisson: 0.4% (0-1.0%)	Yearly: OLS model: -0.56% (-0.92 to 0%); Poisson: -0.20% (-0.56 to 0.20) Summer: OLS model: 0.38% (-0.57 to 1.32%); Poisson: 0.4% (0-0.9%) +PM_{10}	**Results S** Included
Mexico City DF (Loomis et al. 1996)	154 (26-319) (1-h max) 62 (12-130) (24-h mean), yearly	Yearly, 1-h max. ozone: 0.24% (0.11-0.39%) Yearly, 24-h max. ozone: 0.58% (0.22-0.94%)	Yearly, 1-h max. ozone: -0.18% (-0.52 to 0.16%) (+TSP and SO_2)	**Results S** Included
London UK (Anderson et al. 1996)	Yearly: 20.6 $\pm$ 13.2 (1-h max.), 15.5 $\pm$ 10.9 (8-h mean); summer: 7-36 (8-h) 11-45 (1-h)	Yearly ozone: 1-h max: 0.83% (0.42-1.25%) 8-h mean: 1.01% (0.46-1.57%); Summer: 1-h max. 1.03%(0.53-1.53%) 8-h mean: 1.2%(0.6-1.8%)	Yearly, 8-h average ozone: 1.14% (0.59 –1.69%) with black smoke. Summer, 8-h average ozone: 1.45% (0.7-2.19%) with BS. No 1-h max. data reported.	**Results S** Included
Barcelona Spain (Sunyer et al. 1996)	28 (3.6-96) winter 44 (4.8-144) summer	Yearly: 0.96% (0.24-1.72%) Summer: 1.16% (0.34-2.02%)	---	**Results S** Excluded, no quantitative results for multi-variate model
Amsterdam NL (Verhoeff et al. 1996)	21.9 (4-41; 10-90th %), yearly	yearly ozone 0.98% (0.02-2.0%),	Yearly: 0.58% (-0.67 to1.9%) + BS 1.0% (-1.1 to 3.3%) + PM_{10}	**Results S** Included
Lyon France (Zmirou et al. 1996)	7.75 (0-72) (1-h max) 5.1 (0-40.2) (8-h mean), yearly	Increase not significant 1-h max.: 1.6% (-2.4% to 6.4%) 24-h avg.: 1.2% (-2.0% to 4.8%), yearly ozone	--- ---	**Results NS** Excluded, no quantitative results for multi-variate model
Paris France (Dab et al. 1996)	22.3 (3.1-74.8) (1-h max 14.1 (10-56) (8-h mean), yearly	Respiratory mortality only; Yearly ozone; 1-h max.: 0.8% (-1.3% to3.1%) 24-h avg.: 1.5% (-1.2% to 4.6%),	--- ---	**Results NS** Excluded, no quantitative results for multi-variate model

Table 3. Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models (full references in Science Assessment Document).

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis S: Significant NS: Non-significant
4 APHEA cities: Athens Barcelona London Paris 3 additional cities: Amsterdam Basel Zurich (Touloumi et al. 1997)	47.7 ± 21.8 (all 1-h max) 36.8 ± 17.8 21.0 ± 13.2 23.5 ± 16.7 21.9 (4-41; 10-90th %) no 1-h values given for Basle or Zurich (8-h means 12 (B) and 14 (Z)), yearly ozone	Meta-analysis pooled estimate (random effects): For a single day: 1.16% (0.40-1.96%); Average of 2-5 day cumulative ozone: 0.96% (0.48 - 1.48%) Plus 4 non-APHEA cities: 1.16% (0.40% to 1.96%) (1-h max.) All yearly ozone data,1-h max. ozone.	Meta-analysis (random effects): 1.12% (0.20-2.00%) +BS 1.28% (-0.12% to 2.72%) +NO_2 Pooled estimates with non-APHEA cities not included in bivariate analysis	**Results S** Included for 4 APHEA cities.
Philadelphia PA (Kelsall et al. 1997, Samet et al., 1997)	19.9 ± 14.6 (2-day average) 8.3-28.5 IQR (=20.2)	2-d average ozone: 1.13% (0.4% - 1.9%)	2-d average ozone: 1.01% (0.02-2.0%)+TSP 1.11% (0.38-1.84%)+SO_2 1.12% (0.73-1.84%)+NO_2 1.17% (0.40-1.94%)+CO_2 0.96% (0.33-1.59%) + all four	**Results S** Included
Zurich, Basle and Geneva, Switzerland, 1984 – 1989. (Wietlisbach et al., 1996)	Mean ± SD (presumably 24-h average): Zurich: 13.4 ± 10.5; Basle: 12.0 ± 9.7; Geneva: 0	Data are expressed as regression coefficients; no SD or confidence interval reported. No ozone data for Geneva. For total mortality, no association in Zurich or Basle. For mortality of people >65 years of age, no association in Zurich, significant association in Basle ($p<0.05$). For respiratory and cardiac mortalities, no association in any cities.	---	**Results NS** Excluded, no relative risk data reported; exposure data not detailed (1-h max. vs. 24-h average).
11 Canadian cities (Burnett et al. 1998)	16.2 (24-h mean of 11 cities) IQR 13 3-35 (5-95th centile), yearly ozone	24-h ozone: 0.86% (0.35-1.37%), yearly ozone	24-h average ozone: 1.11% (0.66-1.56%) (+NO_2. SO_2, CO) (particles contribute another 1%)	**Results S** Included
13 Canadian cities [Burnett 1998 (special analysis for WGAQOG)]	31 (1-h max) (25-38 range of means, 13 cities) 32.9 ± 16.7 (16 cities)	0.79% (0.59-0.99%), yearly ozone	---	**Results S** Excluded, no data on multi-variate analysis; not in a peer reviewed journal.
Ozone-only analyses, mean increase (%) in mortality ± SD = 0.613% ± 0.467% (n=17), per 10 ppb increase in ozone (1-h max.), 95% CI: -0.302% to 1.53%, p>0.05.				

Table 3. Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models (full references in Science Assessment Document).

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis S: Significant NS: Non-significant
Multi-pollutant analyses, mean increase (%) in mortality ± SD = 0.523% ± 0.444% (n=10), per 10 ppb increase in ozone (1-h max.), 95% CI: -0.347% to 1.39%, p>0.05. Meta-analysis of multi-pollutant studies, weighted mean increase (%) in mortality ± SD = 0.399% ± 0.105% (n=10), per 10 ppb increase in ozone (1-h max.), 95% CI: 0.193-0.604%, p<0.05.				

Acute effects: Hospitalizations

The weight of evidence is strong for an association between hospitalizations for respiratory conditions and exposure to ozone at the levels now commonly encountered in Canada [Table 4 SAD Table 12.2b)]. The weighted means of relative risk for hospitalization for respiratory illness due to 10 ppb ozone (daily 1-hour maximum) vary, according to location and illness, between 1.8% (95% CI 1.0-2.6%) for all age respiratory admissions from Canada/New York studies, 1.8% (0.7-3.0%) for all age asthma admissions in Canada/New York studies, 1.9% (1.2-2.6%) for pneumonia, COPD and total respiratory illnesses in the elderly from US Medicare studies, to 1.14% (0.43-1.84%) from APHEA (Air Pollution And Health - An European Approach) studies. These estimates of risks were obtained from meta-analyses of studies using single pollutant models. Meta-analysis of studies using multi-pollutant models reached a similar result; the weighted mean for respiratory hospitalizations per 10 ppb increase in ozone (daily 1-hour maximum) is 1.12% (95% CI 0.73-1.51%). These studies included all of Southern Ontario, 16 cities in a cross-Canada study, eight U.S. cities, and several European cities. The ozone-associated increases in respiratory hospitalization occurred in locations where the mean concentrations are well below the current Canadian National Ambient Air Quality Objective of 82 ppb (1-hr maximum). The 95th percentile for ozone in the 16 cities of the national Canadian study was 60 ppb (daily 1-hr maximum). The respiratory hospitalizations increased in an ozone concentration-dependent fashion, without showing an obvious threshold [Figure 9 (SAD Figure 12.1)].

The results from the most recent re-analysis of a large Canadian database by Burnett (1998, details in SAD Appendix A) demonstrate a strong consistency with the previous hospitalization studies. The respiratory hospitalization data were from 13 cities. The regression analysis shows that the ozone risk associated with hospitalization for respiratory diseases was 1.04% (95%CI: 0.78-1.30%) per 10 ppb increase in ozone (daily 1-hour maximum). Since previous studies using similar databases have shown that CO, NO_2, SO_2 and particulate sulphate did not confound ozone effects on respiratory hospitalization, it is reasonable to assume that the ozone effects demonstrated by Burnett (1998) are independent of other air pollutants. Further regression analysis to determine a LOAEL for respiratory hospitalization data indicates a LOAEL with statistical significance of 25 ppb (1-hr maximum) ($p<0.01$). Interestingly, in this study the relative risk shows a potential threshold between 15 and 20 ppb ozone (daily 1-hour maximum) for respiratory hospitalization, although several previous studies have shown a non-threshold response.

Table 4. Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models (full references in Science Assessment Document).

Location and reference	Ozone mean ppb (range)(1-h max., unless indicated)	Outcome	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig
Southern Ontario Bates & Sizto, '87, '89	Winter 23.34 ppb Summer 56.07 ppb	all respiratory, asthma	Significant increase in risk. Value not given.	-	**Results S** Excluded, no data from multi-variate models
NYC Buffalo Thurston et al. '92	1988 -Buffalo: 75-164 -NYC: 69-206 1989: -Buffalo: 65-128 -NYC: 53-111	all respiratory, asthma	Respiratory: NYC: 1.40% (0.60-2.20%) Buffalo: 2.50% (0.40-4.60%) Asthma: NYC: 1.67% (0.95-2.41%) Buffalo: 3.26% (1.91-4.61%)	-	**Results S** Excluded, no data from multi-variate models
Montreal, Quebec Delfino et al., 1994.	1-h max.: May-Oct. 36 (90^{th}: 59.2); July-Aug.: 41 (90^{th}: 65.8). Ozone 8-h max.: May-Oct. 30.4 (90^{th}: 51.5); July-Aug.: 35 (90^{th}: 57.3)	all respiratory admissions Asthma admissions	1-h max. ozone: not given. 8-h avg. ozone, all respiratory: 0.41% (0.073-0.737%) + temperature. 0.676% (0.416-0.936%), no temperature.	Asthma: 1-h max. ozone: 0.175% (-0.02% to 0.37%), + PM_{10} Non-asthma respiratory: 1.65% (-22.0% to 25.3%), +sulphate.	**Results S** Included
Toronto Thurston et al. '94a,b	Mean 57.5 ppb (3 years) 2 days > 120 ppb 22 days > 80 ppb	all respiratory	3.83% (2.40-5.26%)	3.64% (2.16-5.12%), + H^+ 3.68% (2.18-5.18%), +sulphate 2.93% (1.24-4.62%) ,+fine particles 2.81% (1.06-4.56%), +PM_{10} 2.61% (0.96-4.26%), +TSP	**Results S** Included, used data from ozone + fine particles
Minneapolis Schwartz '94c	24-h avg.: 26 ppb (10-90% 11-41 ppb)	Pneumonia in elderly	24-h ozone: 3.8% (0.4-8.0%)	24-h avg. ozone: 4.4% (0.4-9.4%), +temperatury, PM_{10}	**Results S** Included
Detroit Schwartz '94b	24-h avg.: 21 ppb (10-90% 7-36 ppb) 1-h max.: 53 ppb	Pneumonia and COPD in elderly	-	24-h avg. ozone: Pneumonia: 5.2% (2.6-8.0%), +PM_{10}. COPD: 5.6% (1.8-9.8%), + PM_{10} No data for 1-h. max. ozone	**Results S** Included
Birmingham, AL Schwartz '94a	O_3 24-h avg.: 25 ppb (10-90% 14-25 ppb).	Pneumonia and COPD in elderly	24-h average ozone: Pneumonia: 2.8% (-1.2% to 7.6%) COPD: 3.4% (-2.8% to 12.0%) 1-h max. ozone: pneumonia: 0.8% (-0.6% to	-	**Results NS** Excluded, no data from multi-variate models

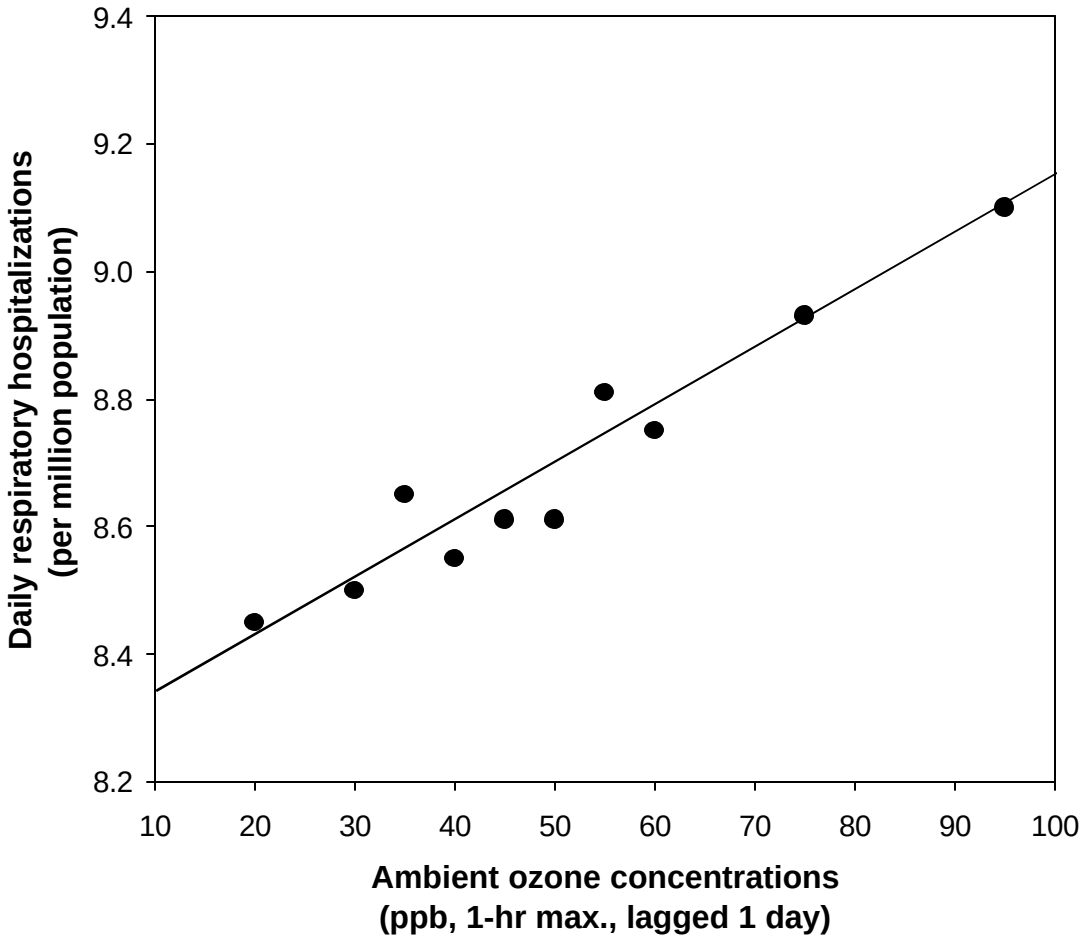
Table 4. Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models (full references in Science Assessment Document).					
Location and reference	**Ozone mean ppb (range)(1-h max., unless indicated)**	**Outcome**	**Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models**	**% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models**	**Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig**
			2.4%) COPD: 1.4% (-0.8% to 4.0%)		
Southern Ontario Burnett et al., 1994	May-Aug: 52 ppb (62-118) Other months: <40 ppb.	All respiratory	May to Aug.: 0.93% (0.75-1.11%)	May to Aug.: 0.92% (p<0.0001), + sulphate + temperature	**Results S** Excluded, no data on variances or confidence intervals.
New Haven, Conn. Tacoma, Wa. Schwartz '95	April to Oct. 24-h avg.: New Haven : 28.6 ppb (10-90%, 15.8-45.4 ppb). Tacoma: 24.5 ppb (10-90% 13.3-35.7 ppb).	all respiratory elderly (>65 y)	24-h average ozone: New Haven: 2.35% (-0.39 to 5.10%) Tacoma: 8.23% (2.35-14.9%)	24-h avg. ozone: New Haven: 2.74% (0-5.88%), +PM_{10}, 1.96% (-0.78% to 5.1%), + SO_2. Tacoma: 7.84% (2.35-14.5%) +PM_{10} 8.24% (2.35-14.5%), + SO_2.	**Results S** Included for both cities
London UK Ponce de Leon et al. '96	O_3 8-h mean: Whole year: 15.6 ppb (10-90% 3-29 ppb); summer 7-36 ppb. O_3 1-h max: 20.6 ppb (5-95% 2-46 ppb)	All respiratory	8-h average ozone, summer: 1.66% (0.85-2.50%), all age 1.01% (-0.24 to 2.32%), 0-14 y 2.59% (1.22-4.01%), 15-64 y 2.12% (0.84-3.45%), >65 y 8-h avg., whole year: 1.13% (1.43-1.83%), all age 1.03% (-0.02% to 2.12%), 0-14 y 2.06% (0.89-3.26%), 15-64 y 1.75% (0.66-2.87%), >65 y 1-h max. ozone: 0.84% (0.56-1.12%)	Whole year ozone (8-h avg.): 1.12% (0.77-1.47%), +NO_2 1.12% (0.77-1.44%), + BS 1.10% (0.75-1.45%), +SO_2	**Results S** Included
Amsterdam, Rotterdam, the Netherland. Schouten et al. '96	O_3 8-h avg.: May-Oct. (5-95%): A: 44.1 ppb (14.3-77.6); R: 42 ppb (12.8-81.1) whole year: A: 35.2 ppb (2.55-68.4 ppb); R: 32.6 ppb (3.1-71.4). O_3 1-h max.: May-Oct.: A: 49.7 ppb (21.4-88.3); R: 49.2 ppb (18.4-94.9). Whole year: A: 40.3 ppb (5.1-77.0); R: 38.8 ppb	All respiratory	1-h max. ozone, summer: A: 2.14% (-0.25% to 4.84%), >65 y -12.2% (-2.4% to 1.7%), 15-64 y R: 6.78% (2.6-11.7%), >65 y 0.51% (-1.2% to 2.4%), 15-64 y 1-h max., ozone, whole year: A: 1.39% (-0.45% to 3.4%), >65 y -0.02% (-1.8% to 1.9%), 15-64 y R:5.3% (1.7-9.5%), >65 y 0.86% (-1.0% to 2.96%), 15-64 y. 8-h avg. ozone, whole year: A: 1.18% (-0.8% to 3.4%), >65 y	-	**Results S** Excluded, no data from multi-variate models

Table 4. Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models (full references in Science Assessment Document).

Location and reference	Ozone mean ppb (range)(1-h max., unless indicated)	Outcome	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig
	(5.6- 83.7)		0.02% (-1.9% to 2.18%), 15-64y R: 4.9% (0.76-9.9%), >65 y 0.04% (-2.2% to 2.4%), 15-64 y		
Spokane, WA. Schwartz, 1996	1-h max.: 40.3 ppb (10-90% 29.6-55.6 ppb). 24-h avg.: 28.6 ppb (10-90% 20.4-37.2 ppb)	All respiratory admissions, pneumonia, and COPD, Elderly (>65 y)	all respiratory admissions: -1-h max. ozone: 9.8% (0.8-21.8%) -1-h max. ozone + tem.: 14.9% (3.5-29.4%) -24-h avg. ozone: 11.4% (-2.9% to 31.1%) Pneumonia: -1-h max. ozone: 11.6% (-2.1% to 29.1%) COPD: -1-h max. ozone: 4.9% (-9.2% to 25.7%)	-	**Results S** Excluded, no data from multi-variate models
Minneapolis-St. Paul, MN Birmingham, AL. 1986-1991 Moolgavkar et al. (1997)	24-h ozone: mean (10^{th} to 90^{th} percentile): Minn: 26.2 ppb (13.5-40.1 ppb) Birm: 25.1 (13.5-37.6 ppb)	All respiratory Pneumonia COPD Elderly (≥65 y)	Total respiratory admission: Minn: 4% (2.2-5.8%). Birm: 0.18% (–0.13% to 0.49%)	Total respiratory admission: Minn: 3.43% (1.57-5.29%) Birm: 0.18% (–0.13% to 0.49%) Pneumonia: Minn: 4.4% (2.3-6.5%) COPD: Minn: 3.0% (-0.33% to 6.3%)	**Results S** Included for both cities
Six European cities Anderson et al. 1997	O_3 1-h mean all year: A: 39.5 ppb B: 32.8 ppb L: 19.5 ppb M: - P: 18.5 ppb R: 36.4 ppb 8-h avg. all year: A: 35.2 ppb B: 28.6 ppb L: 14.3 ppb M: - P: 10.2 ppb Rotterdam: 31.1 ppb	COPD, all age	8-h avg. ozone, whole year: lag 1 d: 1.69% (0.86-2.55%) 5 cumulative days: 2.2% (1.06-3.37%) 1-h max. ozone, whole year: lag 1 d: 1.14% (0.43-1.84%) 5 cumulative days: 1.92% (0.94-2.94%) 8-h avg. ozone: cool: 1.18% (0-2.74%) warm: 1.57% (0.78-2.74%) 1-h max. ozone: cool: 0.39% (-0.78% to 1.96%) Warm: 1.18% (0.39-1.96%)	-	**Results S** Excluded, no data from multi-variate models
16 Canadian cities Burnett et al. 1997a	Spring 40 ppb Summer 38 ppb Fall 21 ppb Winter 26 ppb Whole year 31	All respiratory	All age: Winter: -0.2% (-1.2% to 0.83%); Spring: 1.4% (0.4-2.4%); Summer: 1.7% (0.87-2.47%); Fall: 0.93% (-0.07% to 1.97%)	April - Dec.: 1.43% (1.12-1.75%), +CO 1.03% (0.70-1.40%), +CO, dew point temperature 0.80% (p=0.0258), +CO, dew point temperature, PM	**Results S** Included

Table 4. Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models (full references in Science Assessment Document).					
Location and reference	**Ozone mean ppb (range)(1-h max., unless indicated)**	**Outcome**	**Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models**	**% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models**	**Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig**
	ppb (95^{th} percentile 60 ppb)		April - Dec.: 1.40% (1.14-1.66%) <65y, 1.5% (0.7-2.3%), April-Dec. >65y, 1.3% (0.33-2.4%), April-Dec.	(soiling index), in 11 cities with available PM data.	
Toronto, Ont. Burnett et al., 1997b	Daily 1-h max. 41.2 ppb (5^{th}-95^{th} percentile 22-69 ppb) used 3 day average for regressions	Total respiratory Cardiac admissions	3-d avg. ozone: non temperature: respiratory: 5.9% (4.0-7.8%) cardiac: 5.0% (2.2-7.8%) + temperature and dew point temperature: respiratory:5.6% (3.5-7.7%) cardiac: 6.4% (3.1-9.6%)	-	**Results S** Excluded, no data from multi-variate models
10 Canadian cities Burnett et al., 1997c	Daily 1-h max.: 32 ppb (5^{th} –95^{th} percentile: 10-64 ppb) 24-h avg.: 16 ppb (5^{th}-95^{th} percentile 3-35 ppb)	Congestive heart failure in elderly (>65 y)	24-h avg. ozone: not controlled for temperature 0.30% (0.03-0.57%) + temperature and dew point temperature: 0.32% (-0.025% to 0.66%)	+ temperature, DP temperature, CoH, NO_2, SO_2, and CO: 0.30% (0.006-0.594%)	Excluded, no respiratory data
Canada Burnett, 1998	O_3 1-h max: 31 ppb Range: (25-38 ppb)	All respiratory	1.04% (0.78-1.30%)	-	Excluded, no data from multi-variate models
Meta-analysis	Meta-analysis of multi-pollutant analyses, weighted mean increase (%) in respiratory hospitalizations +/- SD = 1.12% +/- 0.20% (n=8) per 10 ppb increase in ozone (1-hr max), 95% CI: 0.73 - 1.51%, p<0.05. Meta-analysis of single-pollutant analyses (Thurston and Ito, 1999), weighted mean increase (%) in respiratory hospitalizations +/- SD = 1.8% +/- 0.41% (n = 6) per 10 ppb increase in ozone (1-hr max), 95% CI: 1.0 - 2.6%, p<0.05.				

Figure 9: Association of respiratory admissions in Ontario with ozone pollution (source: Burnett et al., 1994, Environ. Res. 65: 172-179).


9.4
9.2
9.0
8.8
8.6
8.4
8.2
Daily respiratory hospitalizations
(per million population)
10
20
30
40
50
60
70
80
90
100
Ambient ozone concentrations
(ppb, 1-hr max., lagged 1 day)

Acute effects: Emergency Department (ED) visits

Hospital Emergency Department (ED) visit data generally support the findings from the respiratory hospitalization studies, i.e., increases in ambient ozone concentrations are associated with significantly increased visits to the Emergency Department [Table 5 (SAD Table 12.3b)]. The percent increase in ED visits from single-pollutant studies varies from 5.9% per 10 ppb of 1-hour maximum ozone, to 7.2% per 10 ppb of 8-hour average ozone, to 11% per 10 ppb of 24-hour average ozone, usually lagged one or two days. When adjusted for PM, temperature, and other gaseous pollutants, for a 10 ppb increase in 5-hour average ozone, the increase in respiratory ED visits is 5.6-14.2%. The mean summertime ozone levels (1-5 hour metrics) varied between 30 ppb and 90 ppb. The results are considered consistent for these studies, given that two studies looked at children, two were for all ages in general, and two for 3 or 4 individual age groups. Four studies did not show significant increases in ED visits following elevated ozone pollution. Inadequacies in statistical analyses, including lack of treatments for underlying cyclic variation in ozone, temperature, and co-pollutants likely explain these results.

Table 5. Summary of relative risk estimates for Emergency Department Visits due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models (full references listed in Science Assessment Document).

Location and reference	Ozone mean oncentrations and range	Outcome (population included)	Percent increase (95% CI) per 10 ppb ozone. Ozone only models.	Percent increase (95% CI)_ per 10 ppb ozone. Multi-variate models.
New Jersey, USA Cody et al. 1992	49 ppb (mean of 5 h from 10am-3pm) 34 days >120 ppb (1988) 8 days >120 ppb (1989)	asthma, bronchitis (all ages)	-	5-h avg. ozone: +SO_2, temperature, RH, visibility: 1988-1989 (lag 1d): 5.6% (1.7-9.5%); 1988 (lag 1d): 7.4% (2.5-12.3%); 1989 (lag 0d): 9.7% (3.2-16.2%); 1989 (lag 1d): 7.3% (1.4-13.2%)
New Jersey, USA Weisel et al. 1995	53 ppb (mean of 5 h from 10am-3pm)	asthma (all ages)	-	5-h avg. ozone: +temperature, RH, sulphate, NO_2, SO_2, visibility: 1986: 7.1% (0.04-14.2%) 1987: 7.7% (1.8-13.6%) 1988: 7.0% (1.1-12.9%) 1989: 14.2% (7.9-20.5%) 1990: 6.9% (2-11.8%)
Atlanta, Ga., USA White et al. 1994	78 ppb (mean of 1-h daily max.) (range 10-163 ppb)	asthma (children, ages 1-16 yr., mostly black, low SES)	1-h max. ozone, when >110 ppb for asthma visits: 33% (-6% to 71%) for other causes of visits: Total: 37% (2-73%) Non-upper respiratory infection: 53% (14-92%).	1-h max. ozone: + temperature, PM_{10}, day of the week: asthma visits at ozone >110 ppb: 42% (-1% to 100%, p=0.057). also corrected for autocorrelation + above factors: 43% (4-97%) + temperature, PM_{10}, day of the week, pollen: 33% (-9% to 92%). +temperature, PM_{10}, day of the week, dose-response relations: 80-90 ppb, 1% (-25% to 36%); 90-99 ppb, 24% (-7% to 65%); 100-109 ppb; 29% (-14% to 93%); 110 ppb, 50% (2-121%).
Mexico City, Mex. Romieu et al. 1995	90 $\pm$40 ppb (mean 1-h daily max) (range 10-250 ppb 28% of days >110 ppb)	asthma (children, <16 y)	-	1-h max. ozone: 8.60% (4.8-13.2%) +temperature, SO_2, day of the week; 8.6% (4.6-13.0%) +temperature, SO_2, day of the week, sex, age

Table 5. Summary of relative risk estimates for Emergency Department Visits due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models (full references listed in Science Assessment Document).				
Location and reference	**Ozone mean oncentrations and range**	**Outcome (population included)**	**Percent increase (95% CI) per 10 ppb ozone. Ozone only models.**	**Percent increase (95% CI)_ per 10 ppb ozone. Multi-variate models.**
Vancouver, BC Bates et al., 1990	1-h max., 30.4 ppb in summer; 18.8 in winter	Asthma, other respiratory and non-respiratory visits. All age, & 0-14 y, 15-60 y, 61+y	1-h max. ozone: Associated with total ED visits; not with respiratory visits. No values given.	-
Barcelona, Spain Castellsagne et al., 1995	1-h summer: 43 ppb, winter: 29 ppb	Asthma, 14-64 y.	1-h max. ozone: No association Value not given.	1-h max. ozone: +Temperature, RH, month, day of the week, soybean loading: Summer: -0.7% (-4.7% to 3.5%). Winter: 4.3% (-0.16% to 9.1%).
Melbourn, Australia Rennick & Jarman, 1992	For ozone days, average 2.7 (range 1-6) stations recorded ozone levels >120 ppb (1-h) and >50 ppb (8-h avg.).	Asthma, >2 y children	-Smog alert days not significantly related to asthma ED visits. -Ozone days not significantly related to asthma visits. Results not given.	-
Toronto, ON Kesten et al., 1995	Data not shown	Asthma visits for all ages.	-Asthma visits not assoc. with ozone on daily, weekly or monthly basis; -associated with ozone with 7 day lag, but not 1 day lag. No value given	-
Montreal, Quebec Delfino et al. 1997	8-h: 1992: 33 ppb; 1993: 36 ppb; 1-h: 1992: 29 ppb; 1993: 31 ppb	all respiratory, asthma (all ages, separated into ages <2y, 2-34y, 35-64y, 65+y)	-No assoc. in 1992, no value given. -1993, no assoc. in <2y and 2-64y, no value given -1993, significant associations in >64y. 1-h max. ozone: 5.9% (2.4-9.4%); 8-h avg. ozone: 7.2% (2.9-11.5%).	1993 data, 8-h avg. ozone: the Elderly: 5.7% (0.21-11.2%) +PM2.5
Baton Rouge, Louisiana Jones et al., 1995	69.1 ppb (mean of 1-h max) (range 25.3-165 ppb) 4 days >120 ppb. 24-h average 28.2 (9.3-57.9).	all respiratory (all ages, separated into ages 0-17 y, 18-60y, 61+y	24-h avg. ozone: Children: -7.0% (–15.4% to 1.4%) Adult: 11.1% (3.8-18.4%). Elderly: 4.5% (–1.9% to 10.9%).	24-h avg. ozone, +temperature, RH, mold, pollen: Children: -6.5% (-17.3% to 4.3%) Adults: 9.9% (0.71-19.1%) Elderly: 13.4% (–3.2% to 30.0%).

Acute effects: The field (camp and panel) studies

Camp studies have the advantage that the subjects, usually children, are active in an environment in which pollutant levels can be closely monitored. In panel studies, a group of subjects (who may be asthmatics) are selected and their medical history and activity patterns and episodes of illness are closely followed. In such studies, pollution exposure can be more accurately gauged than for the general population. Endpoints studied were primarily changes in lung function and increased symptoms.

All eight camp studies reviewed have shown that exposure of healthy or asthmatic children and adolescents to ozone under ambient conditions (daily 1-hr maximum up to 160 ppb) can result in

measurable declines in lung function and increases in respiratory symptoms. Most of the 13 panel studies reported significant decrements in pulmonary function and increases in symptoms and asthma medication use in asthmatic and healthy children and adults, in response to ozone episodes. The ozone levels ranged from low (daily 1-hour maximum below 40 ppb) to high (daily 1-hour maximum 390 ppb, in Mexico City). Outdoor workers and individuals who are exercising out of doors in summer experience measurable declines in pulmonary function, and, if exposures are repeated on consecutive days, also a systematic decline in pulmonary function. The decrements of pulmonary function were significantly associated with hourly maximum ozone (often below 80 ppb).

Chronic effects

Chronic effects have been more difficult to demonstrate at least partly because of the technical difficulty in conducting effective long term epidemiological studies and a consequent dearth of data. Most studies are cross-sectional in nature. In areas with chronically high ozone levels, a worsening of asthma symptoms, increased bronchial hyperresponsiveness and altered immunological function in children have been observed in the few studies available. Some studies have demonstrated permanent changes in lung function in the form of faster rates of lung function decline in adults living in more polluted regions, and possible lower than expected FEV_1 in children in higher ozone areas, but the effect of other co-occurring pollutants could not be evaluated. New evidence published in 1997 for persistent decrements of small airway function and new cases of asthma from chronic ozone exposure (lifelong residents of California) suggest that long term exposure to ambient ozone is of great public health and economic concern.

8.2 Controlled Human Exposure Studies

Carefully controlled, quantitative studies of exposed humans in laboratory settings offer a complementary approach to epidemiological investigations. The advantage of this type of study is the use of a highly controlled environment to identify responses to individual pollutant or pollutant mixtures to characterise exposure-response relationships where possible. In addition, such experiments provide an opportunity to examine interactions with other environmental variables, such as exercise, humidity or temperature. Potentially susceptible populations may also be directly studied, although those with more severe pre-existing disease and hence those most likely to be affected by air pollutants are naturally excluded from such studies. Clinical studies also have other limitations: for practical and ethical reasons, studies must be limited to small groups, which may not be representative of general population; exposure must also be limited to a short duration and to concentrations of pollutants that are expected to produce mild and transient responses; and exposures are often limited to a single pollutant, or to a very limited pollutant mix, which never replicates the complex mixture to which populations are actually exposed. Furthermore, transient responses in clinical studies have not been validated as predictors of more chronic and persistent effects.

Results from clinical studies

An important finding of human clinical studies is that at a given ozone concentration, the increase in ventilation results in elevated pulmonary function responses and inflammation. An increase in ventilation rate also lowers the concentration of ozone required for a given pulmonary response. Thus the concept of "effective dose" is introduced, namely, a product of the minute ventilation rate ($\underline{V}_E$), the concentration of ozone ([ozone]) and the exposure duration ($\underline{V}_E$ x [ozone] x duration). This concept provides opportunity to further develop models and to investigate the sensitivity of different ages, genders, and disease status in response to ozone exposure. This also implies that persons doing outdoor exercise during an ozone episode may be at higher risk due to their increased intake of ozone. This assumption has been confirmed by observations that exposure to ozone concentrations as low as 60 ppb for only 16 to 28 min caused a significant decrease in endurance to heavy exercise and a significant increase in respiratory symptoms.

Exposure to ozone under controlled conditions leads to the appearance of symptoms (cough, shortness of breath, etc.), decrements in spirometric values, increases in airway resistance and bronchial responsiveness to stimuli, and airway inflammation. There is a large variability in response to ozone exposure between individuals. The range of response within each individual also varies, albeit not as much as between individuals. Prolonged exposure (6.6 hours) of healthy subjects to ambient levels of ozone (as low as 80 ppb) with intermittent exercise at ventilation rate ($\underline{V}_E$) of 35 to 50 L/min has been found to cause increased bronchial responsiveness to methacholine to 33-56%, increased inflammation in deep airway (influx of polymorphonuclear neutrophils and proteins, and elevated inflammatory cytokins), and decreased FEV_1. For shorter exposure duration (1 to 4-hours) to ≤120 ppb ozone, a significant increase in bronchial responsiveness and airway inflammation has been observed, while little or no change in pulmonary function is seen.

A study using varying doses (0 to 240 ppb, back to 0 ppb) as well as a constant dose of 120 ppb over 8 hours has demonstrated that the varying doses produced FEV_1 decrements almost twice as large as the constant dose of ozone, although the total concentration was the same in the two dose regimens. These results suggest that the average dose value calculated as a mean over an 8-hour exposure may underestimate the effect of ozone on pulmonary function induced by a peak exposure.

With respect to the age difference in response to ozone, clinical studies have shown that adolescents appear to be more sensitive to ozone-induced pulmonary function decrements when compared with adults using the same dose regimen. Older adults (60 years or older) have not been shown to be more susceptible to ozone-induced pulmonary function changes than their younger counterparts when given the same dose. Of the hospitalization studies that compared the effects of ozone on different age groups, most of them did not find that elderly people (>65 years) were more at risk than younger populations (<65 years). This suggests that age itself may not be a major determinant of response to ozone exposure, and that young adults may be equally sensitive to ozone as older adults.

People with pre-existing respiratory diseases have been demonstrated to be more sensitive to ozone-induced health effects than are the healthy individuals. Patients with chronic obstructive pulmonary diseases (COPD) had significantly more loss of FEV_1 than their same age healthy counterparts (-19% versus -2%, respectively), when exposed to 240 ppb ozone for 4-hours during intermittent exercise ($\underline{V}_E$ = 20 L/min). COPD patients also show moderate increases in symptoms and decrease in blood oxygenation, conditions which were not seen in healthy subjects.

For patients with asthma, prolonged exposure (6.6 hours, to 120 to 160 ppb ozone, $\underline{V}_E$ approximately 30 L/min) has demonstrated more pronounced decrements of FEV_1 in asthmatics than in healthy subjects. Adolescent asthmatic patients appear to be more responsive to ozone-induced pulmonary function decrements. Ozone exposure at 120 - 180 ppb for 40 to 60 minutes caused significant reduction of lung function variables in adolescent asthmatics, but did not affect the lung function of adult asthmatics. Asthmatic subjects are revealed to be more sensitive toward ozone-induced airway inflammation than healthy subjects. At concentrations of 120 to 240 ppb (90 minutes at $\underline{V}_E$ - 50 L/min, and 6-hours at $\underline{V}_E$ - 25 L/min), ozone induced higher inflammatory responses in asthmatics than in healthy subjects. For patients with allergic rhinitis, data suggest that they have a greater rise in airway resistance than healthy subjects when exposed to 180 to 250 ppb ozone for 2 to 3-hours with intermittent exercise ($\underline{V}_E$ - 30 L/min). Allergen treatment exacerbated ozone-induced FEV_1 decrement in these patients.

So far no cardiac patients have been tested for their susceptibility to ozone exposure. No clinical study on tissue injury at ozone concentrations lower than 80 ppb has been conducted.

8.3 Animal Toxicological Studies

Studies on experimental animals (or on tissue samples) have many of the same advantages and disadvantages of controlled human studies. A wide range of pollutants and concentrations can be tested under controlled laboratory conditions for a dose-effect relationship, and autopsies of study animals can be performed to investigate tissue damage from exposure to pollutants. However, experimental studies very often involve well-defined pollutants that do not reflect full range of complex ambient pollutant mixtures to which humans are exposed, a problem noted above with respect to controlled human exposure studies. There is considerable uncertainty also in extrapolating results from animal inhalation studies and applying these results to humans for the purpose of risk assessment. Therefore, such studies are most appropriately used to explore mechanistic aspects of the toxicity of ozone.

Results from Animal Studies

Collectively, in the animal studies the deposition modelling of inhaled ozone indicates the terminal bronchiolar and centriacinar regions as sites of maximal tissue deposition of the gas.

For acute and short-term (<2 weeks) exposures for which adverse effects (inflammation) were observed, concentrations were as low as 100 ppb. For long-term (more than 2 weeks) studies, significant morphological changes have been observed at ozone concentrations as low as 120 ppb. The principal effects observed after acute exposures of a variety of species to ozone concentrations less than 1000 ppb are:

- effects on host defence (damaged mucociliary clearance cells, impaired alveolar macrophage phagocytotic ability, impaired bactericidal activity, reduced numbers of T- and B-lymphocytes), following acute or short-term exposures;

- lung inflammation and changes in lung permeability (increased influx of proteins and polymorphonuclear neutrophils in alveoli, airway epidelial cell necrosis, especially in centriacinar regions), after acute or long-term exposures;

- increased airway responsiveness to bronchoconstrictors (mostly acute exposures);

- impaired pulmonary function (which requires long term exposure, or acute exposure at high ozone concentrations >1000 ppb ozone), following acute or long-term exposures;

- reduction of heart rate, arterial blood pressure and core temperature, and increase in frequency of arrhythmia in rats (acute and short term exposures);

- increased mortality, at ozone concentrations as low as 300 ppb for 3 weeks, or 400 ppb for 3 hours in animals that were also challenged with *Streptococcus zooepidemicus* bacteria.

Ozone is, at most, a weak mutagen. There is not enough evidence to demonstrate that ozone is carcinogenic.

With respect to ozone interactions with other pollutants, most animal toxicological studies have been conducted with binary mixtures (predominantly with nitrogen dioxide or sulphuric acid). The effects of ozone interactions can be antagonistic, additive or synergistic, depending on the animal species, exposure regimen and endpoint studied. Therefore, the animal studies clearly demonstrate the complexities and potential importance of interactions, but do not provide a scientific basis for predicting the results of interactions under ambient exposure scenarios.

In most of the animal studies, the doses used are higher than those used for human clinical studies, as well as those seen in ambient air. However, a recent comparative dosimetric study using ^{18}O-labelled ozone on humans and rats, was able to demonstrate that the exercising humans had 4- to 5-fold higher ^{18}O concentrations in all of their bronchioalveolar lavage constituents than did the resting rats, when they were acutely exposed to the same dose of ozone (400 ppb). The humans also had significant increases in all of the airway inflammatory markers after 400 ppb ozone, whereas the rats did not. Thus, it is conceivable that the doses

used in rats (as low as 100 ppb) that produced pathological changes are relevant to the concentrations encountered by human population during ozone episodes.

Mechanisms of effects

The ozone molecule is very reactive and is not likely to penetrate through cell membranes or even the surfactant layer of the lung. Thus it has been hypothesized that a "reactive cascade", starting from interaction of ozone with the lining of the lung, forms reactive oxygen intermediates that penetrate into the cells and cause the biological effects observed. Free radicals generated from the cascade and oxygenated biomolecules that result from reaction with ozone may mediate the effects of ozone. With respect to target molecules, most of the attention has been centred on polyunsaturated fatty acids and carbon-carbon double bonds as the prime targets of ozone. Reactions with sulfhydryl, amino, and some electron-rich compounds may be equally important.

8.4 Exposure Assessment

Exposure is defined as any contact at a boundary between a person and a specific ozone concentration for a specified time interval. Exposure assessment involves estimating the intensity, frequency, and duration of human contact with ozone.

Direct personal monitoring studies have been conducted in an attempt to delineate the ozone exposure levels in the immediate microenvironment (breathing zone) of the person, as opposed to using data from a fixed ambient monitor (FAM). Personal monitoring studies in Canada and the US reveal a temporal pattern of ozone exposure levels similar to that of FAM data, although ozone levels from personal monitoring are approximately 50% lower than the concentrations from FAM. These results suggest that ozone data from FAM, often used in epidemiological studies, can be a good indicator for population exposure, especially during summer in Canada. On average, ozone concentrations obtained from personal monitoring studies are 70% higher than those in indoor air, and 50% lower than those in outdoor air. The drawback of most personal monitoring data is that they are collected over relatively long averaging times (12 hours, 24 hours or weekly). Data from health effect studies have demonstrated that acute increases in mortality and morbidity are significantly associated with daily 1-hour maximum ozone concentrations. Averaging concentrations over longer times cannot adequately assess these acute responses.

Predictive exposure assessment studies using probabilistic National (Ambient Air Quality Standard) Exposure Model (pNEM) provide estimates of the distribution of ozone exposures within a defined population for a specified exposure period. This model uses detailed information on human activity patterns, indoor-outdoor ozone concentration ratios, and air exchange rates to predict how many days a "typical person" in a sub-population cohort will be exposed above any given level during a specified exposure period.

Results from pNEM modelling using populations from Toronto, Montreal and Vancouver for 1988, 1990 and 1991 demonstrate that an average of 42% (Vancouver) to 91% (Toronto) of the population were exposed to ozone above 82 ppb (1-hour maximum; the existing Canadian National Ambient Air Quality Objective) for at least once a year. Almost 92% to 100% of the population were exposed to 50 ppb or higher level of ozone at least once a year. During the worst pollution year (1988), almost half of the Toronto population were exposed to 82 ppb ozone for more than 5 days, whereas in Vancouver only 6.4% of the population were exposed to 82 ppb ozone for more than 2 days. The pNEM data are in agreement with the results from FAM indicating that the ambient ozone concentrations and the number of episode days are significantly higher in Toronto than in Vancouver, with Montreal in the middle of the range. The pNEM data also are in line with Canadian hospitalization studies that have consistently shown a lower hospitalization risk associated with ozone in Vancouver and Montreal than in other parts of the country.

9. IDENTIFICATION OF REFERENCE LEVELS

Within the NAAQO process, *Reference Levels* are defined as a level or levels, above which there are demonstrated effects on human health and/or the environment. Conceptually, Reference Levels are LOAELS or NOAELs, where these can be defined. For non-threshold pollutants, for which LOAELs and NOAELs as traditionally conceived cannot be defined, statistical LOAELs can be used to help set the RLs. A statistical LOAEL represents the level (concentration) at which statistical significance in the concentration-response relationship is lost. Reference Levels may be identified for several receptors over specific time periods depending on the sensitivity of the target organism or material(s).

9.1 Materials, Birds and Mammals

There is insufficient information on the effects of ozone on materials or birds and mammals on which to base Reference Levels. Therefore it is recommended that no Reference Levels be developed for these receptors.

9.2 Vegetation

Form

It is recommended that the appropriate form of an index to capture chronic vegetation impacts be cumulative (i.e. hourly concentrations are summed over some period of time) and emphasize peak concentrations. The SUM60 index is such an index and is identified as being the preferred index for use in a Canadian regulatory context, for both short-term and chronic exposures. The SUM60 index is calculated by summing hourly ozone concentrations equal to and greater than 60 ppb during daylight hours (08:00 – 19:59) over a given period of time (3 days, 3 months). Adoption of the SUM60 index is recommended while a the same time it is acknowledged that there is no biological basis for inferring that hourly average concentrations below 60 ppb are not

important in affecting vegetation. Development of an exposure index for vegetation, that better reflects the many factors that influence plant response to ozone, is a key challenge for the future.

As described in Chapter 8 (Section 8.2.3), a 10 percent biomass loss level is the minimum level of yield loss that can be confidently measured and attributed to ozone exposure under experimental conditions. Loss estimates less than this can be within the range attributable to experimental error. Therefore, the 10 percent yield loss level is selected as the relevant endpoint for assessment of chronic impacts from ozone exposure.

Given the importance of protecting vegetation from both acute and chronic foliar injuries that may negatively impact crop quality and marketability, the development of a short term index was considered. Seasonal, cumulative-indices may not adequately capture the frequency and episodicity of short-term, high concentrations. Data from field studies in Ontario on two crops, radish and white bean, were available for analysis and quantification of foliar injury impacts in response to exposure to ambient ozone. The analysis consisted of testing the exisiting one-hour ozone NAAQO (82 ppb) and a cumulative one day and three day SUM60 indices. The 3-day SUM60 was identified as the best performing index overall, based upon predictions of trace foliar injury.

Level

Agricultural Crop Yield

The U.S. NCLAN database for crops, excluding crops grown in California and those not grown in Canada, was used to identify LOAELs for effects of ozone on crop yield. Given the degree of inter- and intra-species variability in crop response to ozone, it was felt that selection of a single LOAEL, from the most sensitive of all crops evaluated, as a Canadian Reference Level for effects of ozone on vegetation, would be inappropriate. Instead, a LOAEL range has been identified that represents a conservative estimate of the range of ozone concentrations above which effects are expected to occur on Canadian crops. This range is 5,900 - 7,400 ppb-h (3 month SUM60, ozone measured during the hours of 08:00 – 19:59). This range is derived from the responses of wheat and turnip (Table 1).

Tree Growth

Identification of LOAELs for effects of ozone on tree growth were based on studies conducted by the U.S. EPA in the 1980s on the impact of ozone on forest trees of the U.S. via an OTC exposure protocol similar to that of the NCLAN studies on crop yield. SUM60 values corresponding to 10 percent loss of biomass for individual tree species were presented in Table 2. As with the LOAELs for crop species, it was felt to be inappropriate to select a single LOAEL as the Canadian Reference Level, given the degree of variability within and among species. A LOAEL range is identified from the responses of black cherry and aspen (Table 2) of 4,400 – 6,600 ppb-h (3 month SUM60, with ozone measured during the hours of 08:00 – 19:59).

Foliar Injuries

Given the limited quantitative data available for foliar injury on which this LOAEL determination is based, it was felt to be inappropriate to identify a single LOAEL value. Instead a LOAEL range for trace foliar injury is identified as follows: a 3-day SUM60 during the daylight period (08:00 – 19:59) in the range of 500-700 ppb-h. Although both the form (the 3-day SUM60 index) and the range of the LOAEL for acute effects have been developed on only two crops (radish and white bean), both of these plants are known to be sensitive to foliar injury development and to be significantly impacted as a direct result of the foliar injury.

In summary, it is recommended that the cumulative SUM60 index used in the assessment of both acute and chronic effects of ozone on vegetation in Canada. The SUM60 index is the sum of hourly ozone concentrations equal to or greater than 60 ppb over the daylight period 08:00 – 19:59. The 3-day SUM60 is used for the assessment of acute effects, whereas the 3-month SUM60 is used for the assessment of chronic effects. Given experimental uncertainties, questions around how results from experimental work apply to real-world growing conditions, and the amount of both inter- and intra-specific variability in the response of plant species to ozone exposure, it was felt that identification of Canadian Reference Levels for effects on vegetation was inappropriate. Instead, LOAEL ranges have been identified for acute effects on crops and chronic effects on crops and trees. These represent conservative estimates of ozone concentrations above which effects on Canadian vegetation are expected to occur.

The LOAEL ranges for chronic effects, derived from Tables 1 and 2 of this Summary (SAD Tables 8.9 and 8.11) are as follows, based on agricultural crops and tree species:

Period of Calculation	**SUM60 range (ppb-h)**	
	crops	**Trees**
3 month daylight hours (08:00-19:59)	5,900 – 7,400	4,400 – 6,600

The LOAEL range for acute effects, derived from agricultural crops, is:

Period of Calculation	**SUM60 range (ppb-h)** **crops**
3 day daylight hours (08:00-19:59)	500 – 700

9.3 Human Health

Form

For ozone and human health effects, the Reference Levels are derived statistically from several studies and should be interpreted as a level above which there is confidence (statistical significance) in the dose-response relationship and the ability to provide some quantification of adverse endpoints. The Reference Level should therefore not be interpreted as a threshold of effects.

Based on the weight of evidence presented in Chapter 13, the strength of the epidemiological evidence for mortality and respiratory hospitalization effects at current levels of ambient ozone are significant, consistent, coherent, robust and compelling. Studies on non-accidental mortality and respiratory hospitalization provide quantitative estimates of the health risks of ozone pollution and LOAELs for these endpoints, which are the most appropriate indicators on which to base Reference Levels for ozone.

The number of studies of emergency department visits is limited (10 studies). Results from these studies were generally consistent with those from the mortality and hospitalization studies. The exposure endpoints were assessed based on 1 to 24 hour averaging times. While qualitatively sound, the quantitative aspects of these studies indicate that it would be impossible to establish a Reference Level using these data.

Measures of other respiratory health effects such as school absenteeism, days of work loss and restricted activity are usually collected through survey instruments, and thus are often subjective. Although these parameters are valid measures of respiratory health, they are not appropriate indicators for establishing a Reference Level for ozone. Small and reversible changes in lung function are measured by spirometry, which in general is a robust measure. However, clinical studies have shown that lung function changes do not correlate with tissue injury and thus lung function parameters are not suitable for deriving a Reference Level.

The acute effects are, by definition, related to peaks in ozone levels: clinical and population health studies have correlated responses with hourly or longer (up to 24 hour) exposures. A majority of North American epidemiological studies have used 1-hour daily maximum concentrations, and have found a positive association with increased mortalities, hospitalization and emergency department visits (see Chapter 12). A few European and Canadian studies have used both 1-hour and 8-hour daily maximum concentrations, and found that the results were highly consistent. Greater correlation with the health endpoints has been demonstrated for the 1-hr daily maximum average than for the 8-hr daily average, in both the Canadian epidemiological studies and those from other countries. An averaging time of 24 hours is not appropriate because of the strong diurnal pattern exhibited by ozone and the substantial year to year variation in ozone maxima at different sites across the country. Therefore, the averaging time of any target level should be 8 hours or less.

Controlled human exposure (clinical) studies have provided evidence indicating that exposure to ozone at concentrations as low as 120 ppb for 1.5 to 2 hours, or 80 ppb for 6.6 hours, caused pulmonary function decrements and airway inflammation in both asthmatic and healthy subjects. It should be noted that no clinical studies examining inflammation for 1 to 2 hours of ozone exposure at concentrations below 120 ppb have been documented.

It is noteworthy that a clinical study, that used varying doses as well as a constant dose over an 8 hour period (with the same total concentration), has demonstrated that subjects responded almost twice as markedly, in terms of pulmonary function decrements, to the varying dose regimen as the constant dose of ozone. These results suggest that the average dose value, calculated as a mean over an 8-hour exposure period, may underestimate the effect of ozone on pulmonary function induced by a peak exposure.

In view of the results from controlled human exposure and epidemiological studies, it is recommended that the ozone Reference Levels be expressed on the basis of a 1-hour daily maximum averaging time.

Level

The ozone Reference Level is defined as an estimate of the lowest ambient concentration at which statistically significant increases in health responses have been detected. In general, Reference Levels should not be interpreted as thresholds for affects. In the case of ozone, most studies indicate a continuum of effect through all ambient levels examined, and adverse effects are expected below the Reference Level. However, the analysis performed here indicates that the statistical strength of the data below the identified Reference Levels is inadequate to provide quantification of effects at lower levels.

The published literature does not provide sufficient information necessary for the derivation of Reference Levels. Instead, regression analyses were performed on mortality and respiratory hospitalization data from 13 Canadian cities over an 11-year period, and LOAELs for these two endpoints were derived (Appendix A). These LOAELs form the basis of the Reference Levels for ozone.

The Canadian data used to derive LOAELs for both total mortality and respiratory hospital admissions are consistent with the data from other published studies. These other studies were conducted in many geographic locations, including cities in North America, Europe and South America, where sources and concentrations of ozone and population composition differ from the Canadian situation. This leads to the conclusion that the data upon which Canadian studies are based are the most representative of the effects of ozone in this country while being within the range of observations across other geographical conditions, and the most appropriate for the purpose of deriving ozone Reference Levels. Furthermore, the use of raw data from 13 Canadian cities over an 11-year period (Appendix A), and the application of the same statistical treatment throughout, enhance the reliability of the results. Using the same statistical treatment

and corrections for confounding factors reduces the uncertainties around any value derived as a Reference Level.

The results of the regression analyses provide assessments for two different types of responses. The LOAEL for the total mortality rate is 20 ppb ($p \leq 0.05$), and does not represent a threshold. The respiratory hospitalization rate exhibits a threshold of effect between 15 and 20 ppb of ozone, with a LOAEL at 25 ppb ($p \leq 0.05$).

The lack of evidence of a threshold for mortality precludes the possibility that a sufficiently low level of exposure will be free of any degree of impact. Therefore, the Reference Level, a level above which there are demonstrated effects on human health, is an estimate of the lowest ambient ozone level at which statistically significant increases in health responses have been detected, and not a level below which there are no health impacts.

Recommended Reference Level

Based on the Ozone Science Assessment Document, there is sufficient evidence to conclude an association exists between ambient levels of ozone and human mortality, respiratory hospitalizations and several other health endpoints. The Working Group has developed Reference Levels for the mortality and hospitalization endpoints, as sufficient data exist for the quantification of LOAELs for these endpoints only.

The Working Group notes that this is one of the first instances in which the association between ambient ozone and mortality has been made in the context of a regulatory risk assessment. Although the 1996 US EPA Criteria Document and Staff Paper for ozone did not make a link between ozone and mortality, the subsequent "Regulatory Impact Analyses for the Particulate Matter and Ozone National Ambient Air Quality Standards and Proposed Regional Haze Rule" (July 1997) noted that the literature on this issue had been evolving rapidly. The RIA report provided an extensive review of the new literature on this subject and a quantitative analysis of the mortality risk for ozone, concluding that "this new evidence suggests that substantial additional health benefits associated with reducing ozone concentrations may exist" in addition to the benefits associated with other endpoints. The database has continued to evolve, providing even stronger evidence of an association between ambient ozone and premature mortality.

Thus, based on the analysis of Canadian mortality and respiratory hospital admission data, the following Reference Levels for ambient ozone are recommended:

Period of Calculation	**Level**	
	non-accidental mortality	**respiratory hospitalization**

Daily, 1 hour maximum	20 ppb	25 ppb

10. RISK CHARACTERIZATION

The purpose of the Risk Characterization is to evaluate the weight of evidence presented in the Science Assessment Document to determine whether or not the findings support a causal association between ground-level ozone and the noted effects. Uncertainties in the data are discussed, and the research needed to fill the gaps in scientific understanding is described. Populations that are most at risk from exposure to ozone are identified. Once a causal association is established, the next step in the Risk Characterization is to provide an estimation of population risks at current (and future) ambient ozone concentrations. This analysis will be developed in an Addendum to the Science Assessment Document.

10.1 Materials

All materials for which literature results were available experienced deleterious impacts due to ozone. Cracking, fading or erosion occurs in elastomers, textiles, textile dyes, artists' dyes, paints, metals and stone. Although the information presented is consistent in identifying the qualitative nature of the impacts, quantification of the impacts is problematic for a number of reasons, most notably the difficulty in separating the effects of ozone from those of other pollutants and/or environmental factors. Also, different methodologies employed by different investigators have complicated the task of trying to derive appropriate quantitative relationships between ozone and different materials There is no dispute, however, that ozone does impact materials in an adverse manner. There are clear causal mechanisms to account for the interaction of ozone at the molecular level with organic materials, and for the synergistic impacts of ozone and other pollutants on inorganic materials.

For regulatory purposes, what is needed is a better characterization of concentration-response relationships. To date, there have only been a few studies that have provided this type of information. Clearly this task is complicated by the synergistic nature of the reactions of ozone both with other pollutants and other environmental variables. Given the lack of relevant information for defining effect levels or concentration-response relationships, no further quantitative assessment of the impacts on materials in the Canadian environment is possible at this time.

10.2 Vegetation

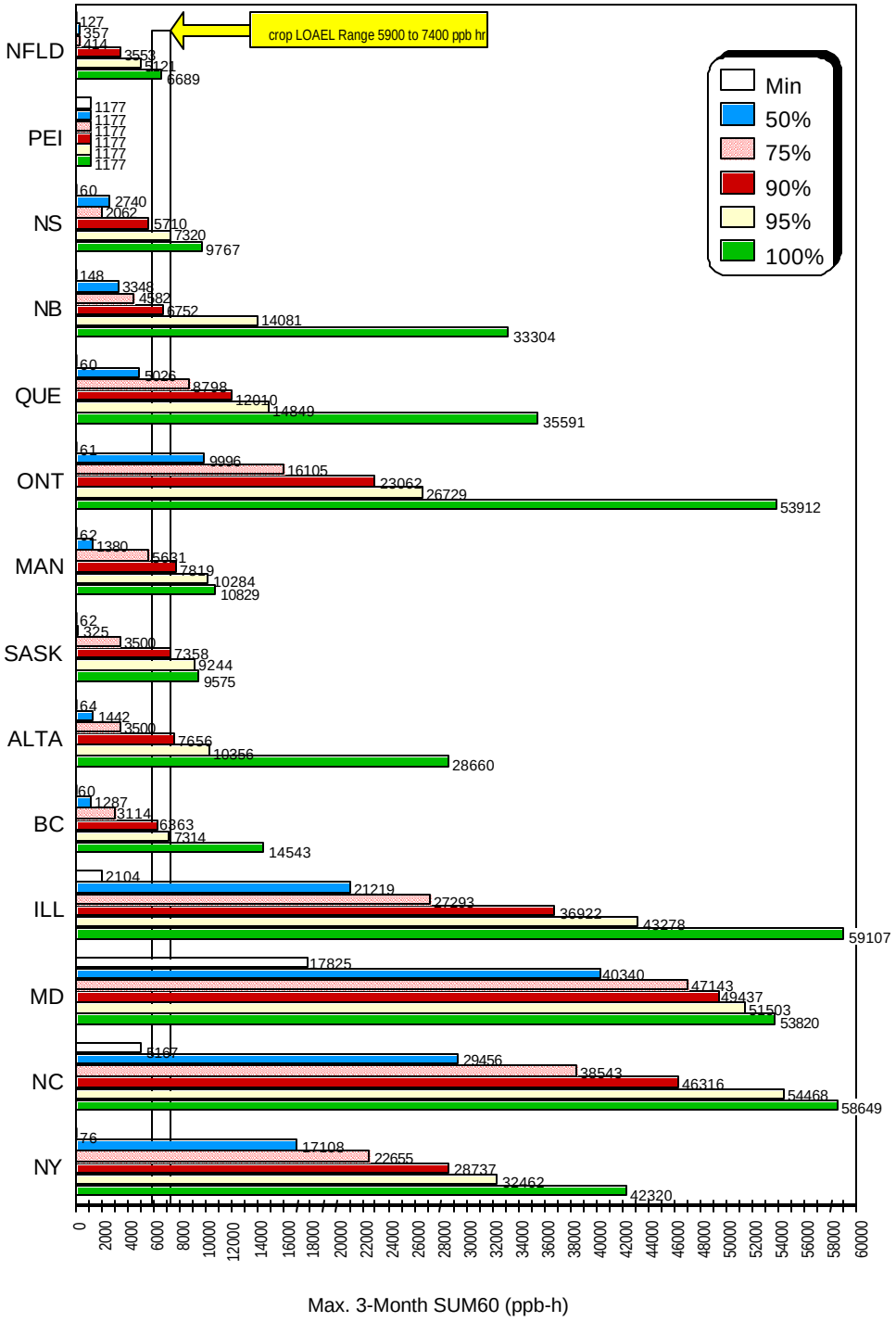
No other phytotoxic air pollutant has been studied as intensively as ozone. From the date of its first causal linkage with crop damage in the U.S. in 1958 to the present time, there have been literally thousands of concentration-response studies conducted throughout North America, Europe, Australia and numerous other countries. Based on a plethora of scientific evidence, it is now universally accepted that ozone is the most damaging of all air pollutants affecting vegetation, with many regions worldwide experiencing sufficiently high ozone levels to impair the

growth and yield of sensitive plants. Certain agricultural crop species are continually observed to be more susceptible to ozone, regardless of where they are grown. Visible foliar injury has been observed in crops grown in British Columbia, Ontario, Québec and New Brunswick, providing empirical evidence that crops are being affected at ozone concentrations currently experienced in Canada. Studies of crop yield impacts in Canada are, however, extremely limited. Potential impacts are suggested by comparing observed ambient ozone levels to the LOAELs identified for crops and trees. Data from 1980-93, from non-urban sites across Canada and in bordering U.S. states, are used here to show the distribution of maximum 3 month SUM60s. The LOAEL range for crops is presented in the Figure as a reference point; the LOAEL range for trees is slightly less than that for crops (4,400 – 6,600 vs. 5,900 – 7,400 ppb-h respectively) (Figure 10 (SAD Figure 14.1). It is apparent from this graph that:

- Ontario and, to a lesser extent, Québec and New Brunswick are the provinces most severely impacted by levels of ozone in a range where significant crop and/or tree-growth reductions are possible.

- Potentially damaging levels of ozone have been experienced periodically in several other areas of Canada: Nova Scotia, Manitoba, Saskatchewan, Alberta and British Columbia.

Figure 10: Frequency Profiles of Maximum 3-Month SUM60 Values Across Canada and the U.S. (1980-1993).



Recently, significant attention has been directed to the study and assessment of ozone impacts on vegetation with the intent of developing air quality criteria (e.g. in the U.S., Europe and Canada). Based on these activities, the following conclusions can be made concerning the weight of evidence behind the current state of knowledge.

- The toxicological evidence for ozone impacts provides a plausible mechanism for effect, though there remain areas that are poorly understood (for example, the mechanism of response of stomatal conductance to the presence of ozone, and the physiological nature of resistance to ozone). However, there is no significant debate over the general toxicological mechanisms of ozone impact.

- The research community is comfortable with the use of a cumulative exposure index to relate ambient ozone air quality to yield or biomass losses in both agricultural crops and forest species, and to acute foliar injury in crops.

- The selection of the most appropriate cumulative exposure index (e.g., SUM60, AOT40 etc.) appears to be a decision, which requires a subjective interpretation of the available science, accommodation of existing uncertainties in the experimental databases, and awareness of the forum in which such indices will be applied. In this regard, there appears to be significant comfort among expert panels in North America with selection of the SUM60 index.

Overall, the best experimental databases currently, for developing statistical relationships between agricultural crop yield losses and ambient ozone concentrations, are the open top chamber (OTC) studies from the United States and Europe. The statistical relationships observed have often been weak as a result of the limited sample sizes (number of crops and cultivars tested) and opportunities for replication. However, the yield responses have been consistent with those expected from the toxicological understanding of ozone impacts. Given that these OTC experiments restrict the composition of the input air, it is possible to screen out other potentially confounding air pollutants. Therefore, it can be stated with reasonable confidence that the observed yield losses are due to ozone impacts.

Based upon the weight of evidence discussion, it is concluded that ozone is a probable and likely cause of agricultural crop and forest impacts ranging from acute foliar injury symptoms to chronic exposures resulting in yield and biomass losses. Further, there is sufficient information available to identify LOAELs, albeit LOAEL ranges rather than unique numbers are identified for both crops and trees. That the information base is sufficient for such a conclusion is the collective opinion of vegetation effects experts. Therefore, there is a risk to vegetation (including agricultural crops, forest species and horticultural species) at ambient ozone concentrations currently experienced in Canadian urban and rural areas. Quantification of that risk through characterization of exposure – response relationships for Canadian species is currently constrained by the lack of information on exposures in non-urban areas (i.e. rural ambient ozone data).

Recommendations for improving the scientific understanding of ozone impacts on vegetation have been summarized in sections 8.4 and 14.2.7 of the Science Assessment Document. Most limiting is the dearth of information on experimental exposures of Canadian agricultural and forest species, grown under Canadian field conditions, at realistic (i.e. near ambient) ozone levels. The analyses in this assessment are to a large extent based upon experimental data collected in the United States and Europe. While the theoretical understanding of ozone vegetation impacts and ambient characteristics of ozone in Canada support the use of this information, it is important that experimental work be carried out to assess exposure – response relationships for Canadian crops and forest species under Canadian climatic and pollutant conditions. In the meantime, it is recommended that when species specific response information is required, the individual LOAELs, presented in Tables 1 and 2 (SAD Tables 8.9 and 8.11) for agricultural crops and forest species respectively, be used. For a conservative estimate of the concentration of ozone above which effects on vegetation can be expected, the LOAEL ranges of 5900-7400 ppb-h (crops) and 4,400-6,600 ppb-h (trees) (3 month SUM60 values) identified in Section 6.2 above should be used.

10.3 Birds and Mammals

The effects of concern for both birds and mammals concern impacts on the respiratory system. Though the avian lung-air sac respiratory system may predispose birds to greater sensitivity there is insufficient information at present to make any predictions concerning relative sensitivities. Also, there was insufficient information in the literature to develop concentration-response relationships and very limited information on which to base effect levels. This precludes any quantitative analysis of the risks to birds and mammals across Canada from exposure to ozone at current ambient concentrations.

10.4 Human Health

Weight of evidence for adverse health effects.7 Weight of Evidence for Ozone as a cause of adverse respiratory health effects

There are several reasons for weighting the epidemiological studies more than the controlled human exposure studies or animal toxicological studies when evaluating levels of exposure that result in adverse health effects.

(1) Epidemiological studies addressing the acute and chronic health effects in human populations involve those combinations of environmental conditions and activity levels present under real-world conditions of ozone exposure. This real-world relevance is an advantage over animal and controlled human exposure studies.
(2) Urban populations are highly heterogeneous, including individuals who encompass a large range of susceptibilities, disease status, and exposures. Their responses cannot be predicted from classical animal toxicology or even controlled human exposure (clinical) studies. Population (ecological) studies using very large administrative databases are likely

to capture a greater range of responsiveness, including those responses from the tail end of the distribution curve.

(3) Population-based epidemiological studies are predominantly time-series studies, which are longitudinal and use a single population as its own control, and thus are less vulnerable to inter-population bias.

(4) Since the purpose of such time-series epidemiological analyses is usually to help set ambient standards that will ultimately be monitored at central stations (fixed ambient monitors, FAM), the use of FAM data in the original epidemiological studies simplifies the standard-setting process (i.e., thereby avoiding any extrapolation between individual exposures measured as part of research activities and FAM concentrations employed in standards-compliance monitoring).

On the other hand, because of using FAM data, a significant drawback associated with ecological studies is the lack of knowledge about which individuals in the population are responding to a given ozone concentration, i.e., what were the ozone exposures of the individuals who were hospitalized, visited the emergency department, or died. Nevertheless, personal monitoring studies conducted in Canada and in the US have demonstrated that mean personal exposures to ozone have the same temporal trend as the FAM concentrations, suggesting that ozone data from FAM can adequately represent population exposure.

Clinical (controlled human exposure) studies provide valuable information about the threshold of a specific effect at ambient exposure concentrations of a single pollutant or of a mixture of pollutants, but not of the complex mixtures experienced in most locations. Clinical studies are valuable in providing quantitative information on the response to ozone in healthy individuals and in individuals with pre-existing respiratory disease, such as asthma and COPD. Data from controlled human exposure studies show that respiratory patients may form a prime target group for the adverse effects of ozone. Direct and conclusive information on susceptible groups cannot be obtained from the epidemiological studies based on population responses as captured in large administrative databases. Results on increased airway responsiveness, lung function changes, symptomology and airway inflammation after known doses of ozone have all been obtained from controlled human exposure studies, and provide direct evidence for the links between ozone exposure and health effects observed in the epidemiological studies. The disadvantage of the clinical studies reviewed in this document is that these studies used small sample sizes and short exposure duration, and when examining pulmonary compromised individuals, evaluated only those persons with mild conditions. The results, therefore, are not necessarily representative of the general population. No tissue injury has been tested for concentrations less than 80 ppb ozone for healthy subjects, or less than 120 ppb ozone for asthmatics. These drawbacks limit the use of clinical data for predicting the health effects in a general population and for obtaining a LOAEL or NOAEL.

Animal studies are valuable in elucidating cellular changes and mechanisms of action of ozone. They are particularly useful in studying possible effects of long-term exposures, because controlled human studies over a long time frame are impractical, and epidemiological studies on chronic endpoints are as yet too few to draw conclusions regarding chronic effects. The animal

studies were the first to demonstrate the link between ozone exposure and immunotoxicity mediated through the detrimental effect on alveolar macrophages and lymphocytes, thus impairing defense mechanisms in the lung. Acute death was seen when animals were treated with ozone (400 ppb for 3 hours) and *Streptococcus zooepidemicus* bacteria. The findings that infection-related illnesses are associated with peak ozone exposure in the epidemiological studies are thus supported as biologically plausible.

There have been difficulties in extrapolating data from animal studies to humans. Comparative dosimetric studies have provided evidence that humans receive four to five times more ozone in their lower airways than rats do when given the same dose. Following deposition in the deep airways, animals and humans have been shown to have a similar tissue dose-effect relationship (lung injury), on a per unit body weight basis. On this basis, the doses used in rats are clearly relevant to the concentrations encountered by human populations at current ambient levels of ozone. So far there has only been a limited number of comparative dosimetric studies carried out, which precludes establishing a human LOAEL or NOAEL for ozone using animal toxicological data.

In summary, the controlled exposure/clinical studies and the animal toxicity studies provide a coherent picture of ozone-induced inflammation of the respiratory tract, triggering of hyper-responsive bronchi in asthmatics and others, and destruction of cells involved in the immune defence system of the lung. It is plausible that these responses initiate a cascade of effects progressing from reduced activity, absences from work/school and physician visits, to Emergency Department visits, hospitalizations, and even death as detected in the epidemiological studies.

On causality

Epidemiological studies do not themselves provide data to elucidate biological mechanisms that would explain the observed associations. Associations found in epidemiological studies between ozone and health effects may reflect chance, bias or cause. The criteria first described by Hill (1965) and modified by succeeding epidemiologists are used in this document to assist building a case for causality.

Strength of Association

The magnitudes of associations seen in all the epidemiological studies, although seemingly small, are statistically significant in many cases, and represent large numbers of people and important impacts on public health, since most of the population is exposed.

Consistency

An association of ozone pollution with population health effects was found by many investigators in cities across North America, in Central and South America, and in Europe, with these

locations including a variety of pollutant mixes, ozone levels, weather, and socio-economic status of the populations.

Specificity

Many of the recent publications reviewed in the epidemiological sections have used some form of statistical technique to correct the cyclic impact of seasonal and weather factors on mortality, morbidity and ozone concentrations. By using regression analyses, researchers were able to differentiate the impacts of co-occurring pollutants on health endpoints. Data from the available studies demonstrate that the effects on mortality and morbidity ascribed to ozone are independent of the effects of the ambient co-pollutants.

It should be noted that some of the studies did not report the potential confounding effects of other pollutants on ozone, as these studies focused on the health risk of particulate matter. Several studies did not consider other pollutants, or considered only a limited number of co-pollutants.

Temporality

A logical temporal relationship exists, with ozone exposure followed by increased health effects. Negative lag times (health endpoints occurring before ozone changes) were investigated, and were found not to be associated with the respiratory conditions.

Concentration-response relationships

A concentration-response relationship of mortality and respiratory hospitalization was observed from very low ambient levels up to much higher concentrations in many of the studies. Dose-response relationships have been demonstrated in controlled human exposure studies for a number of spirometric variables as well as some symptoms. There have been no models established for airway inflammation.

Biological Plausibility

Ozone has been shown in animal experiments and in controlled human exposure studies to result in inflammation, epithelial cell necrosis, lowered lung function, increased airway reactivity, and increased animal mortality when the animals were subsequently challenged with a bacterial aerosol. Because of its highly reactive nature, ozone has been found to generate reactive oxygen intermediates which may cause cell membrane and macromolecule damage. In addition, asthmatics and individuals with 'hyperreactive' bronchi have been shown to be sensitive to the effects of ozone, with pain on deep inspiration, lowered lung function, increased need for medication, and asthma attacks. The experimental evidence supports the findings of the associations between ozone pollution and increased mortality and respiratory morbidity in

epidemiological studies. The progression from impaired respiratory function and tissue injury to the point where medical attention is sought is quite plausible in light of the above.

Although the doses used for animals which produce pathological changes are higher than those seen in ambient air, comparative dosimetric studies have provided evidence that humans receive four to five times more ozone in their lower airways than rats do when given the same dose. Thus, it is reasonable that the doses used in rats are relevant to concentrations currently encountered by people. Furthermore, once ozone is delivered into lower airways, the relationship between the pulmonary tissue dose (normalized to body weight) and the pulmonary injury has been predicted to be in the same linear pattern among rats, guinea pigs, rabbits and humans.

Coherence

For a given increase in ozone concentration, the percentage increase in ED visits was larger than the percentage increase in hospitalizations, and the latter larger than that of total non-accidental mortality. This difference is expected on the basis that an element of choice is involved in the decision to seek medical attention at an ED or doctor's office, while hospitalizations represent only the most serious cases as determined by a physician. In addition, compared to ED visits, the percentage increases in doctors' visits and in days with reduced activity (absences from work or school) were also greater. On balance, data from epidemiological studies provide a coherent picture of an ozone-associated progression of health effects from high numbers of incidents recorded as ED visits, compared to those who were hospitalized and died.

Susceptible Populations

Clinical studies have identified patients with asthma, COPD and allergic rhinitis to be more sensitive to ozone-induced pulmonary function decrements and airway inflammation. These patients may constitute a sub-population susceptible to ozone pollution. These observations are consistent with findings in epidemiological studies indicating that hospitalizations and ED visits due to respiratory illness, especially asthma, increased significantly following elevated ozone pollution. However, the time series studies have not provided enough data to determine if the increased respiratory illness outcomes are due to an exacerbation of existing diseases or new incidences. A few studies on chronic effects have demonstrated ozone-related increases both in cumulative asthma incidence (new cases) and in asthma severity.

Another group at high risk compared to the general population is comprised of individuals whose activities lead to elevated ventilation rates. Cyclists, joggers, walkers, outdoor workers, and children would be included in this category. For example, the lunchtime joggers would be likely to have a high ventilation rate, comparable to the heavily exercising individuals in some of the chamber studies, and be exposed at a time of day when ozone levels are at or near their daily peak in most parts of the country. Consequently, these people are more at risk than sedentary

individuals, since increased ventilation rates result in them receiving a larger ozone dose at the target tissue in the lung per unit of time, and a greater possibility of decreased FEV_1, more reporting of symptoms, and a tissue inflammatory injury.

Uncertainties

While time series studies have the advantage of being less biased by differences in indoor-outdoor concentrations within and between microenvironments, in life style, and in variability in daily time-activity patterns compared with cross-sectional studies due to the use of a single population as its own control, we do recognize that bias from exposure misclassification is a concern. This is because time series studies often rely on a single fixed ambient monitor (FAM) to characterize the pollution levels in a given community. The concentration of ozone measured at that FAM is used as a surrogate for personal/population exposure. The impact of this uncertainty is addressed in some studies by averaging the data from several FAM's on an hourly basis to better represent regional population exposure. In the province of Ontario, for example, much of the ozone is the result of broad regional air transport, and high correlations are observed between sites up to a hundred kilometres apart. Thus, studies using data from even a single FAM can provide a quantitatively sound assessment of the population impacts of ozone. Moreover, personal monitoring studies conducted in Canada and in the US have demonstrated that mean personal exposures to ozone have the same temporal trend as the FAM concentrations, which supports the use of FAM ozone data as a good indicator for population exposure.

One of the most difficult issues continues to be the role played by other pollutants (PM, SO_2, NO_2, and CO) in the health effects ascribed to ozone. Some of the available studies did not consider these co-pollutants. The fact that they may be highly correlated with ozone makes the separation of effects difficult in some instances. Nonetheless, the body of evidence amassed to date does justify the conclusion that the observed relationships can be attributed to ozone *per se.*

In some locations temperature was highly correlated with ozone ($R \geq 0.5$-0.6), making it a potential confounder since temperature is itself associated with increased respiratory distress. The method of handling temperature in the statistical analysis is therefore important, with inclusion in the regression appearing to provide the most reliable results. Removal of the temperature effect prior to running the regression with ozone carries with it the risk of removing part of the ozone effect in cases where correlation between these two factors is moderate or high.

11. Conclusions

Ground-level ozone is formed when its precursors, nitrogen oxides and volatile organic compounds, combine in the presence of sunlight. Ozone is one of several pollutants that combine to form a chemical soup that hangs in the warm, still air over many Canadian cities on

hot summer days. Scientific evidence clearly links ozone and health impacts. As a mixture, and individually, these air pollutants have the potential to cause adverse health effects.

The population-based epidemiological studies have provided a consistent and coherent evidence of an exposure-response relationship. Non-accidental mortality, hospital admissions, Emergency Department (ED) visits and reduced activity days increase monotonically as ozone concentration increases. Increased risks for non-accidental mortality, respiratory hospitalization and ED visits respectively are estimated at 0.4%, 1-2% and 6-8.6%, for every 10 ppb increase in ozone. The risks of population health effects increase monotonically, in a ozone concentration-dependent fashion. The controlled human exposure studies have identified a dose-response relationship for lung function changes, symptoms and airway inflammation, the frequency and intensity of response increasing with increases of ozone concentration, exposure duration or ventilation rate. Field (camp and panel) studies and controlled human exposure studies have identified that patients with asthma, COPD and allergic rhinitis are more susceptible to ozone-induced health effects than healthy people. Animal toxicological studies, used qualitatively, have provided evidence of mechanisms for acute and chronic effects of ozone, including mortality. Dosimetric studies of humans and animals have helped to establish a linkage for the use of animal data in predicting ozone effects on humans, and have suggested that ozone doses used to induce various tissue injuries and deaths in animals are relevant to the concentrations encountered by human populations.

Combining the information, there is convincing evidence of a significant association between ambient ozone and adverse health effects. Evidence suggests a biologically plausible mechanistic sequence(s), beginning with an inflammatory response which irritates the respiratory tract, giving rise to cough, pain which inhibits inspiration, and bronchoconstriction which reduces airflow. Ozone-induced impaired endogenous defence system (including injury of immune cells and depletion of antioxidants) would render the individual more vulnerable to viral or bacterial infections. These effects and symptoms, if severe enough, could lead to respiratory dysfunction and a requirement for medical intervention such as doctor or emergency room visits, and hospitalization. Although more data are required to fully explain the mortality associations, it is logical to expect that the biological stress related to these effects could exacerbate underlying conditions (e.g. cardiovascular problems) and lead to acute death. The inflammatory portion of the cascade of effects can be present with or without the accompaniment of pulmonary function changes depending on the sensitivity of the individual.

Results from controlled exposure studies of respiratory patients, along with the epidemiological evidence of hospitalizations, emergency room visits, and reduced activity days, suggest that people who are compromised by pre-existing respiratory diseases are more susceptible to ozone exposure.

Controlled human exposure studies indicate exercise is a potent modifying factor in the response. For a given concentration and duration of ozone exposure, the effect is strongly dependent on the level of exercise, because exercise enhances the ventilation rate and

consequently the dose delivered to the lower airways. Results from field studies using lunchtime joggers or competitive bicyclists support this finding.

Estimates of population exposure indicate that large numbers of people are exposed to low levels of ozone in Canada (below the current National Ambient Air Quality Objective). Although ambient ozone levels are higher than personal exposure data, they share the same temporal pattern, suggesting that ambient ozone data used in epidemiological studies can be an effective indicator for population exposure. It is also clear that at concentrations currently experienced in Canada, population health effects (mortality and morbidity) are occurring. The increase in unmeasured morbidity (cough, substernal soreness, increased airway reactivity, increased asthmatic attacks, increased medication use) is substantially greater than the measured outcomes from administrative databases (such as hospitalizations, Emergency Department visits).

Newly published data suggest that there likely exist health effects (pulmonary function decrements and induction of new asthma cases) from chronic exposure to ozone. Future development of air quality policy for ozone may require inclusion of an annual or seasonal objective, since this may be more important in much of Canada where chronic low exposure are more prevalent than short peaks.

The acute effects are by definition related to peaks in ozone levels, with the clinical and population health studies correlating responses with hourly or multi-hour (6 - 8 hour) exposures. Available data did not show a substantial difference in the association of health effects with 1-h maximum ozone or 8-hour average ozone levels. This is expected given the high correlation between 1-hr daily maximum and the maximum 6- or 8-hr concentrations.

An averaging time of 24 hours is not considered a best choice of metric because of the strong diurnal pattern exhibited by ozone and the substantial year to year variation in ozone maxima at different sites across the country. Therefore, the averaging time of any target level needs to be less than 12 hours. In view of the results from most Canadian studies, and from controlled human exposure studies showing effects on respiratory symptoms after an exposure (60 ppb) as short as 16-28 minutes (with continuous vigorous exercise), a slight preference is expressed for retention of an 1-hour averaging concentration.

Recommendations

The data show that there is a significant association between ambient ozone concentrations and health effects. These associations have been demonstrated in epidemiological studies, and a causal relationship has been supported through human clinical studies and animal studies. The risks associated with increases in ambient ozone concentrations and health effects such as mortality and hospitalization have been examined in a number of studies covering cities across the world. The regression analyses performed on 13 Canadian cities represent the ozone effects

across Canada. The results are similar to those observed in studies of cities across the world. Because the 13-Canadian city study (Appendix A) is, for the time being, the only study that has appropriately established LOAELs for the health effects of the Canadian population in comparison with other approaches, it is recommended that the results from these analyses be used as the basis for determining Reference Levels for ozone (Chapter 13). For risk and benefit analyses, however, it is recommended that the estimates of risk derived from meta-analyses, using studies worldwide, be used, since these studies have adjusted for possible co-pollutant effects. It must be kept in mind that adjusting for co-pollutants using multi-variate models tends to underestimate the risk attributable to ozone, as ozone and other co-pollutants are often statistically correlated.