AIR QUALITY CRITERIA FOR NITROGEN OXIDES

SUMMARY AND CONCLUSIONS

ENVIRONMENTAL PROTECTION AGENCY

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CHAPTER 11.

SUMMARY AND CONCLUSIONS

A. INTRODUCTION

This document contains a consolidation and an assessment of the current state of knowledge regarding the group of air pollutants known as the oxides of nitrogen. This chapter provides a concise presentation of that information, including reasonable conclusions for evaluating the concentrations of nitrogen oxides (NO_X) and the accompanying situations that have an effect on either health or welfare. The studies and data cited comprise the best available basis for developing specific standards for NO_X in the ambient air, aimed at protecting public health and the environment.

Although the essential role of NO_X in the production of photochemical oxidants is treated from the physical-chemical standpoint in this document, little research has been done to demonstrate the significance of the indirect effects of NO_X on health, vegetation, and materials through the photochemical reaction mechanism; thus, only the direct effects of NO_X are treated here. A P C O publication AP-63, *Air Quality Criteria for Photochemical Oxidants*, provides a comprehensive review of photochemical oxidant effects.

Units of pollution concentration used in this document are expressed as both mass per unit volume (e.g., micrograms per cubic meter, $\mu g/m^3$) and as volume-ratios (e.g., parts per million, ppm). Conversion between these units requires a knowledge of the gas density, which varies with temperature and pressure measurement. In this document 25°C (77° F) has been taken as standard temperature, and 760 mm Hg (atmospheric pressure at sea level) as standard pressure. All references to NO_X are expressed in terms of NO_2 mass per unit volume on the basis of the conversion formula: ppm x 1880 = $\mu g/m^3$ at 25° C, 760 mm Hg, unless otherwise specified. Similarly, hydrocarbons and oxidant concentrations are expressed as mass of methane and ozone per unit volume, respectively.

B. PROPERTIES OF NITROGEN OXIDES AND PHYSICAL EFFECTS ON LIGHT TRANSMISSION

Of the oxides of nitrogen known to exist, only two, nitric oxide (NO) and nitrogen dioxide (NO_2) are emitted to the atmosphere in significant quantities. Nitric oxide is formed during all atmospheric combustion processes in a spontaneous chemical reaction between the nitrogen and oxygen in the air. The amount formed depends on the combustion temperature, the concentration of both reactants and products, and the length of time favorable conditions persist for the reaction.

Both NO and NO_2 are formed when combustion temperatures exceed approximately 1093°C (2000°F), but usually less than 0.5 percent is NO_2. More NO_2 is formed when atmospheric oxygen (O_2) reacts with NO, but at the dilute concentrations of NO characteristically found in ambient atmospheres, this reaction proceeds very slowly. During the initial phases of exhaust gas dilution, however, the concentration of NO is high, and forces the reaction to proceed more rapidly until the exhaust has been sufficiently diluted (to 1 ppm or less). At that time the major process for converting NO to NO_2 reverts to the photochemical cycle.

Visibility reduction is common in polluted atmospheres. Scattering and absorption of light rays by particles and gases reduce the

brightness and contrast of distant objects. The degree of reduction depends on the concentration and properties of the pollutants. Nitrogen dioxide absorbs light energy over the entire visible spectrum, although primarily in the shorter, blue-wavelength regions; thus, NO_2 can by itself reduce visibility. At present, however, under most ambient conditions, aerosols make the major contributions to visibility reduction.

C. SOURCES AND CONTROL OF ATMOSPHERIC NITROGEN OXIDES

On a global basis, the total amount of nitrogen oxides generated by natural sources exceeds the amount from man-made, technological sources. Natural scavenging processes keep background levels in nonurban areas low, on the order of 8 $\mu g/m^3$ (4 ppb) NO_2 and 2 $\mu g/m^3$ (2 ppb) NO. In urban areas, however, where 60 percent of the technological sources are located, the levels are frequently higher because pollutants are added faster than scavenging processes control them.

Fuel combustion is the major source of technological NO_x air pollution. Chemical processing is responsible for high, but localized emissions.

Control of NO_x emissions has been directed at both combustion sources and chemical processes. For stationary combustion sources, the control principle has been based on reducing either the flame temperature or the availability of oxygen, to prevent NO formation. Similar principles of control are applicable to motor vehicles. Catalytic principles, which have been applied to reduce NO_x emissions from chemical processes, are also being investigated for possible use in control of NO_x in motor-vehicle exhaust.

D. CHEMICAL INTERACTIONS OF NITROGEN OXIDES IN THE ATMOSPHERE

The role of NO_x in the generation of photochemical oxidants is a complex function of the interaction of certain hydrocarbons (HC) with the NO_2 photolytic cycle, which is discussed here as well as in the document AP-63, *Air Quality Criteria for Photochemical Oxidants* and the document AP-64, *Air Quality Criteria for Hydrocarbons.*

In order to fully describe the HC-NO_x-OX interrelationship a comprehensive simulation model that takes into account emission rates, chemical reactions, and atmospheric dispersion factors, is required. In the absence of such an applicable model an observation-based model was developed and applied to ambient aerometric data. This latter model is restricted to defining the maximum daily oxidant that may be reached from a given early-morning precursor level and, therefore, the model results in definition of the upper-level oxidant curve, as a function of precursor concentrations. The model for the NO_x-OX relationship indicates that an NO_x 6- to 9-a.m. value of 80 $\mu g/m^3$ (0.04 ppm) is associated with the reference concentration of 200 $\mu g/m^3$ (0.1 ppm) maximum daily 1-hour-average oxidant.

The reference concentration of 200 $\mu g/m^3$ OX used here was selected on the basis of convenience and does not represent the lowest health-related value (130 $\mu g/m^3$ OX) expressed in APCO publication AP-63, *Air Quality Criteria for Photochemical Oxidants.*

Application of the observation-based model to ambient NO_x, HC, and oxidant interrelationships showed that the peak oxidant level is dependent on the concentration of both reactants. Analysis of data from three urban areas indicates that a reference concentration of 200 $\mu g/m^3$ (0.1 ppm) maximum daily 1-hour-average oxidant is associated with an HC range of 200 to 930 $\mu g/m^3$ (0.3 to 1.4 ppm C) 6- to 9-a.m. nonmethane hydrocarbon, when the 6- to 9-a.m. average NO_x, expressed as NO_2, was below 80 $\mu g/m^3$ (0.04 ppm). Similarly, observation of the 200 $\mu g/m^3$ (0.3 ppm C) nonmethane HC level showed NO_x in the range of 80 to 320 $\mu g/m^3$ (0.04 to 0.16 ppm), expressed as NO_2. These conclusions are supported by the predominance of weekend data near the low-concentration end of the upper-limit oxidant curve, which reflects the lower oxidant values from lower emissions on weekends.

E. METHODS FOR MEASURING NITROGEN OXIDES

Research is still needed to develop and thoroughly evaluate more sensitive, reliable, and practical methods for measuring ambient levels of NO, NO_2, and NO_x. All of the field techniques in use at present can measure only NO_2 directly; NO must be oxidized to NO_2, then measured. NO_x can be determined either by summing NO and NO_2 concentrations that have been measured independently or by oxidizing NO to NO_2, then measuring the total as NO_2.

Any method used for measuring NO_2 in the ambient air should be calibrated against atmospheres containing known amounts of NO_2. The use of permeation tubes to generate the test atmospheres is recommended.

Two techniques are currently used in atmospheric monitoring programs. For sampling periods of 30 minutes or less, the most suitable currently available method for measuring NO_2 is the colorimetric Griess-Saltzman method. This method can also be automated for continuous measurement. The Jacobs-Hochheiser method is the most suitable of the available methods for long-term (up to 24 hours) sampling, or for situations requiring a delay of the analysis for more than 4 hours after sampling. The Griess-Saltzman and Jacobs-Hochheiser methods are not interchangeable, can yield different results, and must be chosen carefully, according to the purposes of the sampling to be done.

When used in conjunction with an oxidizing prescrubber to convert NO to NO_2, the continuous Griess-Saltzman method can be used to measure NO in ambient air in either a series or parallel mode, with the same or separate samples of air. Problems exist in obtaining complete NO to NO_2 oxidation, and researchers disagree as to which of the two modes is more satisfactory.

F. ATMOSPHERIC LEVELS OF NITROGEN OXIDES

Continuous measurement of the oxides of nitrogen by various monitoring networks has made it possible to compile tables of mean concentrations averaged over different time periods and to relate various temporal patterns to photochemical and meteorological parameters.

Both NO and NO_2 concentrations display distinct diurnal variations dependent on both the intensity of the solar ultraviolet energy and the amount of atmospheric mixing. In many sampling areas, these variations are also associated with the traffic patterns.

Nitric oxide shows an additional seasonal variation, with higher values occurring during the late fall and winter months. Nitrogen dioxide, however, does not display any distinct seasonal patterns.

The effect of meteorological parameters on NO and NO_2 concentrations has been reasonably well documented. As might be expected, periods of stagnation and high traffic volume in urban areas have resulted in high peak levels of NO_x.

Continuous measurement has indicated that peak values of NO above 1.2 mg/m^3 (1 ppm) are widespread, but NO_2 concentrations have rarely been measured at this level. Peak concentrations of NO_2 in urban areas rarely exceed 0.94 mg/m^3 (0.5 ppm).

Considerable differences were found among NO_2 data collected at the same site, at the same time, but by different methods. The methods of NO, NO_2, and NO_x measurement are still in need of refining and must be judged accordingly.

G. EFFECTS OF NITROGEN OXIDES ON MATERIALS

Significant effects of NO_x have been observed and studied on three classes of materials: textile dyes and additives, natural and synthetic textile fibers, and metals.

The most pronounced problem is associated with textile dyes and additives. Fading of sensitive disperse dyes used on cellulose acetate fibers has been attributed to NO_2 levels below 188 mg/m^3 (<100 ppm). Loss of color, particularly in blue- and green-dyed cotton and viscose rayon, has occurred in gas dryers where NO_x concentrations range from 1.1 to 3.7 mg/m^3 (0.6 to 2 ppm). Yellow discoloration in undyed white and pastel-colored

fabrics has recently been attributed to NO_x by controlled laboratory experiments.

Laboratory and field observations have shown that cotton and Nylon textile fibers can be deteriorated by the presence of NO_x, but specific reactants and threshold levels are undetermined at this time.

Failure of nickel-brass wire springs on relays has been related to high particulate nitrate levels. This type of stress corrosion has been observed when surface concentrations of particulate nitrates have exceeded 2.4 $\mu g/cm^2$ and relative humidity was greater than 50 percent. Another type of this corrosion has been associated with annual average particulate nitrate concentrations of 3.0 and 3.4 $\mu g/m^3$ with corresponding NO_x levels of 124 and 158 $\mu g/m^3$ (0.066 and 0.084 ppm).

H. EFFECTS OF NITROGEN OXIDES ON VEGETATION

The degree of injury occurring with the lower concentrations of NO_2 present in the atmosphere remains to be determined. Exposure of many kinds of plants to concentrations of NO_2 above 47 mg/m^3 (25 ppm) for any extended period causes acute necrotic leaf injury. Such lesions are usually characteristic for each plant, but their nonspecific character in relation to other toxicants renders these symptoms of little value in diagnosing NO_2 damage in the field.

The 1-hour visible-injury-threshold value for NO_2 can be achieved by exposing plants to 18.8 to 28.2 mg/m^3 (10 to 15 ppm). Increasing the exposure time, however, obviates the threshold level; 4.3 to 6.6 mg/m^3 (2.3 to 3.5 ppm) NO_2 administered for 8 to 21 hours and 1.9 mg/m^3 (1 ppm) NO_2 for 48 hours cause equivalent leaf injury. Continuous fumigation with 940 $\mu g/m^3$ (0.5 ppm) NO_2 for 35 days resulted in leaf drop and chlorosis in citrus, but no actual necrotic lesions developed.

The effects of exposure to low levels of NO_2 for extended periods are less evident. Recently completed studies suggested that 470 $\mu g/m^3$ (0.25 ppm) or less of NO_2, supplied continuously for 8 months will cause increased leaf drop and reduced yield in navel oranges.

The mechanism(s) by which NO_x causes direct injury to plants can only be postulated at this time. Evidence of diurnal fluctuation in sensitivity to NO_2 has been presented, and could indicate that the pollutant is reacting with a particular plant metabolite, which only accumulates at certain periods during the day. The absence of a protective metabolite within the plant at certain periods would also cause a diurnal sensitivity.

Limited information regarding the effect of nitric oxide on photosynthesis indicates that NO would reduce the growth of plants if concentrations in the range of 3.8 to 7.5 mg/m^3 (2.0 to 4.0 ppm) persisted continuously.

I. TOXICOLOGICAL EFFECTS OF NITROGEN OXIDES

Both of the prominent oxides of nitrogen present in ambient air are potential health hazards. At ambient concentrations, NO presents no direct threat to general health; NO_2 does, however. Effects of NO_2 determined in extensive studies are summarized in Table 11-1.

The toxicology of nitrous oxide (N_2O) and other oxides of nitrogen does not appear to be relevant to the problems of ambient air pollution at the present time.

1. Nitric Oxide

NO is not an irritant and is not considered to have adverse health effects at concentrations found in the atmosphere. Its greatest toxic potential at ambient concentrations is related to its tendency to undergo oxidation to NO_2. A 12-minute exposure to 3,075 mg/m^3 (2,500 ppm) NO has proved lethal to mice. In addition, NO has been observed to inhibit bacterial hydrogenase activity at lower concentrations–24.6 mg/m^3 (20 ppm). This inhibition was reversible, however, until the exposure reached about 12,300 mg/m^3 (10,000 ppm).

2. Nitrogen Dioxide

NO_2 exerts its primary toxic effect on the lungs. High concentrations, greater than 188 mg/m^3 (100 ppm), are lethal to most animal

Table 11–1. SUMMARY OF REPRESENTATIVE NO_2 EFFECTS

Effect	NO_2 concentration, ppm	NO_2 concentration, $\mu g/m^3$	Duration	Comment	Reference
Lowest level associated with reference oxidant production of 200 $\mu g/m^3$ (0.1 ppm)	0.04	80	3 hr (6 to 9 a.m.)		1
Increased incidence of acute respiratory disease in families	0.062 to 0.109	117 to 205	2 to 3 yr	Chattanooga study - 6-mo mean concentration range	2
Increased incidence of acute bronchitis in infants and school children	0.063 to 0.083	118 to 156	2 to 3 yr	Chattanooga study - 6-mo mean concentration range	3
Human olfactory threshold	0.12	225	---	Immediate perception	4
Rabbits - structural changes in lung collagen	0.25	470	4 hr/day for 6 days	Still apparent 7 days after final exposure	5
Navel orange - leaf abscission; decreased yield	0.25	470	8 mo, continuously		6
Rats - morphological changes in lung mast cells characterized by degranulation	0.5	940	4 hr	Possibly precedes onset of acute inflammatory reaction	7
	1.0	1880	1 hr		
Mice - pneumonitis; alveolar distension	0.5	940	6 to 24 hr/day for 3 to 12 mo	Possibly emphysematous condition	8
Mice - increased susceptibility to respiratory infection	0.5	940	6 to 24 hr/day up to 12 mo	Based on mortality following challenge with *K. pneumoniae*	9
Navel orange - leaf abscission, chlorosis	0.5	940	35 days, continuously		6
Rats - tachypnea, terminal bronchiolar hypertrophy	0.8	1504	Lifetime, continuously		10

Table 11-1 (Continued). SUMMARY OF REPRESENTATIVE NO_2 EFFECTS

Effect	NO_2 concentration, ppm	NO_2 concentration, $\mu g/m^3$	Duration	Comment	Reference
Rats - bronchiolar epithelial changes, loss of cilia, reduced cytoplasmic blebbing, crystalloid inclusion bodies	0.8 to 2.0	1504 to 3760	Lifetime, continuously	Possibly pre-emphysematous lesion	11
Rabbits - structural changes in lung collagen	1.0	1880	1 hr	Denaturation of structural protein suggested	12
Sensitive plants - visible leaf damage	1.0	1880	21 to 48 hr		13
Rats, monkeys - polycythemia	2.0	3760	3 wk, continuously	Approximate doubling of red cell number with lesser increases in hematocrit and hemoglobin	14
Man - increase in airway resistance	5	9,400	10 min	Transient	15
Monkeys - tissue changes in lungs, heart, liver, and kidneys	15 to 50	28,200 to 94,000	2 hr	Degree of damage directly related to concentration of NO_2	16

species; 90 percent of the deaths are caused by pulmonary edema.

The concentration time product determines nonlethal morbidity effects of NO_2 exposures. At 940 $\mu g/m^3$ (0.5 ppm) for 4 hours or 1.9 mg/m^3 (1.0 ppm) for 1 hour, mast cells of rat lungs became degranulated, possibly signifying the onset of an acute inflammatory reaction. These cells returned to normal 24 hours after exposure was terminated. Lung proteins, collagen and elastin, were found to be altered structurally in rabbits exposed to 1.9 mg/m^3 (1 ppm) NO_2 for 1 to 4 hours. The condition was also reversible within 24 hours. Similar changes were observed in rabbits exposed to 470 $\mu g/m^3$ (0.25 ppm) NO_2, 4 hours a day for 6 days, except that recovery was delayed and some denaturation was still apparent 7 days after the final exposure. Denaturation of collagen and elastin associated with repeated exposure to NO_2 has been suggested as a possible factor in the pathogenesis of pulmonary emphysema.

Early pulmonary emphysema-type lesions have been observed in dogs exposed continuously to 47.0 mg/m^3 (25 ppm) for 6 months. In lung tissue from monkeys exposed to 18.8 to 94.0 mg/m^3 (10 to 50 ppm) NO_2 for 2 hours, alveoli were expanded and had thin septal walls. This response involved increasing numbers of alveoli as the NO_2 concentration was increased. Hyperplasia has been observed in respiratory bronchiolar epithelium of hamsters exposed to 94.0 mg/m^3 (50 ppm) for 10 weeks, and a similar response was noted in major bronchi and distal portions of

the respiratory tract of hamsters exposed to 18.8 mg/m^3 (100 ppm) for 6 hours.

Long-term exposures to NO_2 concentrations that do not produce acute inflammatory responses have a cumulative, sustained effect, suggestive of a pre-emphysematous condition. Examination of lung tissue from rats exposed to 3.8 mg/m^3 (2 ppm) for their natural lifetimes showed loss of cilia; decreased bronchiolar blebbing; and intercellular, crystalloid, rod-shaped, inclusion bodies. Similar effects have been seen in lungs of rats continuously exposed to 1.5 mg/m^3 (0.8 ppm). Alveoli in lungs of mice exposed to 940 μg/m^3 (0.5 ppm) for 3 to 12 months on 6-, 18-, and 24-hour daily schedules have shown increase in size from distension rather than from septal breakage. The accompanying inflammation of the bronchiolar epithelium and reduction in distal airway size suggested the development of early focal emphysema.

Rats chronically exposed to 18.8 to 47.0 mg/m^3 (10 to 25 ppm) NO_2 developed compensatory changes, such as polycythemia and thoracic kyphosis, with lateral flaring of the ribs.

Since certain pathological changes seen in animals after experimental NO_2 exposure are similar to changes that occur in the pathogenesis of chronic obstructive pulmonary disease in man, it is suggested that long-term, low-level exposures to NO_2 may play a significant role in the development of chronic lung disease.

Exposure of mice, hamsters, and squirrel monkeys to NO_2 increased susceptibility to bacterial pneumonia and influenza infection. The susceptibility has been demonstrated by a significantly increased mortality, decreased survival time, and a reduction in ability to clear infectious agents from the lungs. In mice, threshold for increased susceptibility to *Klebsiella pneumoniae* occurred after exposure to 6.6 mg/m^3 (3.5 ppm) NO_2 for 2 hours, if the infectious challenge was given within 1 hour after the NO_2 exposure. Squirrel monkeys exposed to 18.8 mg/m^3 (10 ppm) NO_2 for 2 hours and then challenged with *K. pneumonia* aerosol retained the infectious agent in their lungs for extended periods of time.

In long-term studies of mice, significantly increased susceptibility to infection occurred after continuous daily exposure to 940 μg/m^3 (0.5 ppm) NO_2 for 3 months, and after 6- and 18-hour daily exposures for 6 months. A significant increase in susceptibility to influenza virus or *K. pneumoniae* was also seen in squirrel monkeys continuously exposed to 18.8 and 9.4 mg/m^3 (10 and 5 ppm) NO_2 for 1 and 2 months, respectively. In addition, interferon formation has been impaired and resistance to viral infection has decreased following exposure of rabbits to 47.0 mg/m^3 (25 ppm) NO_2 for 3 hours. Researchers conjecture that such increased susceptibility to infection may also be significant in the pathogenesis of human lung disease.

Inhalation of NO_2 can produce other systemic effects, although these are generally secondary to the effects on the lungs. In monkeys exposed to 28.2 to 94.0 mg/m^3 (15 to 50 ppm) NO_2 for 2 hours, cellular changes appeared in heart, liver, and kidney tissue. A circulating substance, possibly a lung antibody, has been detected in the blood of guinea pigs exposed to 9.4 mg/m^3 (5.0 ppm) for 4 hours daily, 5 days per week for 5.5 months. Rats and monkeys continuously exposed to 3.8 mg/m^3 (2.0 ppm) NO_2 for 3 weeks developed marked polycythemia. Methemoglobin has been detected in the blood of several species exposed to NO_2 concentrations greater than 122 mg/m^3 (70 ppm) for 1 hour.

The small amount of information available concerning the toxicological effects of the oxides of nitrogen in man pertains to levels higher than those found in ambient air. Experimental exposure of volunteer subjects to 9.4 mg/m^3 (5 ppm) NO_2 for 10 minutes has produced a substantial, but transient, increase in airway resistance. Other data, derived from occupational exposure to high-concentration mixtures of NO and NO_2, are complicated by the presence of other pollutants.

Impaired pulmonary function, evidenced by reduced maximal breathing capacity, increased expiratory resistance, and occasional decreased vital capacity, has been observed in patients accidentally exposed to high concentrations of nitrous fumes for a few minutes. Such evidence has persisted for more than 2 years after the exposure, in some cases. In one case, occupational exposure to 169 mg/m^3 (90 ppm) NO_2 for 30 minutes produced pulmonary edema and a vital capacity 50 percent lower than expected 18 hours later. Exposure to very high concentrations for about 5 minutes has produced death within 2 days to 5 weeks.

The threshold for odor perception of NO_2 is about 225 μg/m^3 (0.12 ppm).

J. EPIDEMIOLOGICAL APPRAISAL OF NITROGEN OXIDES

Nitrogen dioxide, the only oxide of nitrogen examined in epidemiological surveys, can be significantly correlated with increased respiratory disease at mean 24-hour concentrations between 117 and 205 μg/m^3 (0.062 and 0.109 ppm).

Effects of community exposure to NO_2 were studied in four residential areas of greater Chattanooga. The ventilatory performance ($FEV_{0.75}$) of children in a high-NO_2 area was significantly reduced, when compared to the performance of children in control areas. In addition, an 18.8 percent relative excess of respiratory illness occurred among families exposed to high NO_2 concentrations. A 10.4 percent excess occurred among families in an elevated-particulate area. The increased incidence of acute respiratory disease was observed when the mean 24-hour NO_2 concentration, measured over a 6-month period, was between 117 and 205 μg/m^3 (0.062 and 0.109 ppm) and the mean suspended nitrate level was 3.8 μg/m^3 or greater.

In a retrospective study of the same Chattanooga area, exposure to intermediate and high levels of NO_2 in ambient air was associated with a significant increase in the frequency of acute bronchitis among infants exposed for 3 years and school children exposed for 2 and 3 years. When increase was observed, the mean 24-hour NO_2 concentration, measured over a 6-month period, had ranged between 118 and 156 μg/m^3 (0.063 and 0.083 ppm) and the mean suspended nitrate level had been 2.6 μg/m^3 or greater.

A report from Czechoslovakia indicates that NO_x has produced several alterations in the peripheral blood. Increased levels of methemoglobin were observed in school children residing in a town that had relatively high ambient levels of nitrogen oxides. The findings in that report require further clarifying investigation, however, before conclusions can be drawn.

The Chattanooga studies have several implications in regard to respiratory illness – implications that can be extended to other cities. Since NO_2 does not exhibit marked seasonal variations (See discussion chapter 6, Section B,2), direct comparison of the NASN yearly averages with the lower limit at which health effects were noted in the Chattanooga studies is, therefore, possible. Any site that exhibits a concentration of 113 μg/m^3 (0.06 ppm) or greater exceeds the Chattanooga health-effect-related NO_2 value. Ten percent of cities with populations of less than 50,000 show a yearly average equal to or exceeding 113 μg/m^3 (0.06 ppm). In the population range from 50,000 to 500,000, 54 percent of the cities in the United States equal or exceed a yearly average of 113 μg/m^3 (0.06 ppm) NO_2. In the over-500,000 population class, 85 percent of the cities equal or exceed 113 μg/m^3 (0.06 ppm) NO_2 on a yearly average.

K. AREAS FOR FUTURE RESEARCH

1. Environmental Aspects of Oxides of Nitrogen

The fate of as much as 50 percent of the nitrogen oxides that become incorporated into the photochemical complex is still undetermined, for many of the nitrogen oxide end products remain unidentified.

Even for the identified nitrogen oxides the relationship between emissions and air quality

needs further definition through improved instrumentation, expansion of the number of monitoring stations, and more accurate determination of the location and distribution of sources.

A model for predicting upper limits of photochemical oxidant pollutants from observed HC and NO_X levels has been presented, but needs further definition, sophistication, and revision before it can be applied on a practical basis.

2. Effects on Vegetation and Materials

a. Materials

Further research is needed to define reliable dose-response relationships for vulnerable materials. The effects of variables such as temperature, relative humidity, sunlight, and other pollutants on the damage potential of the nitrogen oxides must also be determined.

b. Vegetation

The biochemical, enzymatic, and other metabolic responses of plants to ambient levels of the nitrogen oxides are in need of research-based delineation. Evidence of diurnal variations in sensitivity suggests the existence of either extra-sensitive or protective metabolites in some plants. Evidence of synergistic effects of NO_X in mixtures containing other air pollutants should be investigated further.

3. Toxicity of Oxides of Nitrogen

In order to ascribe toxicity to a specific concentration range of NO_X, the relation of metabolic tissue changes to NO_2 concentration-time responses and the relative importance of low-concentration, long-time exposures versus short-time, peak ambient concentrations should be studied. The interactions of the oxides of nitrogen with particulate pollutants in relation to biochemical, biophysical, infectious, immunological, and ultrastructural response parameters require further research aimed at elucidating possible synergistic damage or protection. Tolerance to NO_2 in the presence of oxidant pollutants has been suggested as a result of exploratory studies, but the biologic importance of such protection needs to be defined.

Further examination of *in vivo* biochemical and biophysical effects of exposure to typical ambient concentrations of the oxides of nitrogen relative to: (1) oxidation of fatty acid double bonds in lung surfactants; and (2) denaturation or alteration of lung proteins (collagen and elastin, enzymes, and cellular membranes) is needed before optimal treatment for, or protection from exposures can be developed.

4. Epidemiology of Oxides of Nitrogen

In order to determine the effect of NO_X on the health of the general population, epidemiological research must be expanded to include: (1) studies to determine which segments of the population are most susceptible to the oxides of nitrogen; (2) studies to precisely delineate the relationship between methemoglobin levels, peripheral blood alterations, and nitrogen oxide concentrations; (3) replication of studies of the enhanced susceptibility to respiratory infection that occurs with exposure to ambient levels of NO_X; and (4) studies to determine the relationship between other pollutants and the oxides of nitrogen and their material effect on human health.

L. CONCLUSIONS

Derived from a careful evaluation of the studies cited in this document, the conclusions given below represent the best judgment of the scientific staff of the Air Pollution Control Office of EPA regarding the effects that may occur when various levels of nitrogen oxides are reached in the ambient air. More detailed information from which the conclusions were derived, and the qualifications that entered into the considerations of these data, can be found in appropriate chapters of this document.

1. Nitric Oxide

a. Effects on Humans

No evidence shows that NO produces significant adverse health effects at the ambient

atmospheric concentrations thus far measured (chapter 9, section B.).

b. Effects on Materials and Vegetation

Damaging effects to materials at ambient pollutant levels of nitrogen oxides have been observed; however, concentrations of NO producing these effects have not been precisely determined (chapter 7, sections C and D).

When beans were exposed to concentrations of 12.3 mg/m^3 (10 ppm), apparent photosynthesis was reduced 50 to 70 percent; when exposed to 4.9 mg/m^3 (4 ppm), a 10 percent reduction occurred (chapter 8, section B).

c. Effects on Laboratory Animals

A concentration of 3,075 mg/m^3 (2,500 ppm) is lethal to mice after a 12-minute exposure. Fully reversible inhibition of bacterial hydrogenase activity occurs at a concentration of 24.6 mg/m^3 (20 ppm) (chapter 9, section B).

2. Nitrogen Dioxide

a. Effects on Humans

(1) Short-Term Exposure. Limited studies show that exposure to NO_2 for less than 24 hours continuously can have several concentration-dependent effects.

1. The olfactory threshold value of NO_2 is about 225 μg/m^3 (0.12 ppm) (chapter 9, section C.2.a.1).
2. Exposure to 9.4 mg/m^3 (5 ppm) for 10 minutes has produced transient increase in airway resistance (chapter 9, section C.2.a.2).
3. Occupational exposure to 162.2 mg/m^3 (90 ppm) for 30 minutes has produced pulmonary edema 18 hours later, accompanied by an observed vital capacity that was 50 percent of the value predicted for normal function (chapter 9, section C.2.b).

(2) Long-Term Exposure. An increased incidence of acute respiratory disease was observed in family groups when the mean range of 24-hour NO_2 concentrations, measured over a 6-month period, was between 117 and 205 μg/m^3 (0.062 and 0.109 ppm) and the mean suspended nitrate level during the same period was 3.8 μg/m^3 or greater.

The frequency of acute bronchitis increased among infants and school children when the range of mean 24-hour NO_2 concentrations, measured over a 6-month period, was between 118 and 156 μg/m^3 (0.063 and 0.083 ppm) and the mean suspended nitrate level during the same period was 2.6 μg/m^3 or greater (chapter 10, section C.1).

Yearly average NO_2 concentrations exceed the Chattanooga health-effect-related value of 113 μg/m^3 (0.06 ppm) in 10 percent of cities in the United States with populations of less than 50,000, 54 percent of cities with populations between 50,000 and 500,000, and 85 percent of cities with populations over 500,000 (chapter 10, section d.).

b. Effects on Materials and Vegetation

Although damage to materials has been attributed to the oxides of nitrogen in ambient atmospheres, the precise air-concentrations producing these effects have not been determined (chapter 7, sections C and D).

Crops and ornamental plants can be classified into three groups with respect to NO_x sensitivity: sensitive, low sensitive, and resistant. Several characteristic effects have been observed among the sensitive plants studied with regard to direct NO_2 exposure.

1. Exposure to 470 μg/m^3 (0.25 ppm) of NO_2 for 8 months caused leaf abscission and decreased yield among navel oranges (chapter 8, section G).

2. Exposure to NO_2 concentrations of 940 μg/m^3 (0.5 ppm) for 35 days resulted in leaf abscission and chlorosis on citrus fruit trees (chapter 8, section G).

3. Exposure to NO_2 concentrations of 1.9 mg/m^3 (1 ppm) for 1 day can cause overt leaf injury to sensitive plants (chapter 8, section G).

c. Effects on Laboratory Animals

(1) Short-Term Exposure. Short-term effects of NO_2 on animals can be summarized by the analyses of five salient experiments.

1. Exposure of rats to either 940 $\mu g/m^3$ (0.5 ppm) for 4 hours, or 1.9 mg/m^3 (1.0 ppm) for 1 hour has produced degranulation of lung mast cells (chapter 9, section C.1.b.3).
2. Structural changes in collagen were observed in rabbits exposed to 1.9 mg/m^3 (1.0 ppm) for 1 hour (chapter 9, section C.1.b.2).
3. The threshold for increased susceptibility of mice to respiratory infection by *K. pneumoniae* is 6.6 mg/m^3 (3.5 ppm) for 2 hours (chapter 9, section C.1.d).
4. Exposure of monkeys to 28.2 to 94.0 mg/m^3 (15 to 50 ppm) for 2 hours has produced damage to their lungs, heart, liver, and kidneys and pulmonary changes that resemble those seen in human emphysema (chapter 9, sections C.1.b.3 and C.1.c.1).
5. In rabbits exposed to 47.0 mg/m^3 (25 ppm) for 3 hours interferon formation and resistance to viral infection decreased (chapter 9, section C.1.d).

(2) Long-Term Exposure. Long-term exposure to NO_2 altered several functions in animal circulatory and respiratory systems.

1. Structural changes were found in lung tissue collagen from rabbits exposed to 470 $\mu g/m^3$ (0.25 ppm) 4 hours a day for 6 days (chapter 9, section C.1.b.2).
2. Enhanced susceptibility of mice to respiratory infection by *K. pneumoniae* was observed after 3 months of continuous exposure to 940 $\mu g/m^3$ (0.5 ppm) (chapter 9, section C.1.d).
3. Polycythemia has been reported in rats and monkeys exposed continuously to 3.8 mg/m^3 (2.0 ppm) for 3 weeks (chapter 9, section C.1.c.3).
4. Changes resembling those seen in human emphysema were reported in the following: mice exposed 6 to 24 hours daily, for a period of 3 to 12 months to 940 $\mu g/m^3$ (0.5 ppm) (chapter 9, section C.1.b.3); rats continuously exposed to 18.8 to 47.0 mg/m^3 (10 to 25 ppm) for 4 to 12 months (chapter 9, section C.1.b.3); and dogs continuously exposed to 47.0 mg/m^3 (25 ppm) for 6 months (chapter 9, section C.1.b.3).

3. Other Nitrogen Oxide Effects

a. Photochemical Relationships

An observation-based model applied to ambient NO_x, HC, and oxidant interrelationships showed that peak oxidant yield was dependent on the concentration of both reactants. Analysis of data from three urban areas indicated that a reference concentration of 200 $\mu g/m^3$ (0.1 ppm) maximum daily 1-hour-average OX could be associated with a hydrocarbon range of 200 to 930 $\mu g/m^3$ (0.3 to 1.4 ppm C) 6- to 9-a.m. nonmethane hydrocarbon, expressed as methane, when the 6- to 9-a.m. average NO_x, expressed as NO_2, was below 80 $\mu g/m^3$ (0.04 ppm). A similar observation related an NO_x range of 80 to 320 $\mu g/m^3$ (0.04 to 0.16 ppm), expressed as NO_2, with 200 $\mu g/m^3$ (0.3 ppm C) nonmethane hydrocarbon.

b. Stress Corrosion

Nitrogen oxide reaction products have been associated with corrosion and failure of electrical components. In two cities where this problem has been observed, the 1965 average airborne particulate nitrate concentration were 3.0 and 3.4 $\mu g/m^3$ with associated average NO_x levels of 124 and 158 $\mu g/m^3$ (0.066 to 0.084 ppm).

M. RESUME

Adverse health effects, as evidenced by a greater incidence of acute bronchitis among infants and school children, have been observed, under the conditions prevailing in the areas where studies were conducted, when the mean 24-hour NO_2 concentration, measured by the Jacobs-Hochheiser method, over a 6-month period, varied from 118 to 156 $\mu g/m^3$ (0.063 to 0.083 ppm). On an annual basis, a maximum 24-hour average as low as 284 $\mu g/m^3$ (0.15 ppm) would be expected to be associated with a 6-month mean of 118

$\mu g/m^3$. Adverse health effects, as evidenced by an increased incidence of acute respiratory disease, have been observed in family groups when the mean 24-hour NO_2 concentration measured over a 6-month period was between 117 and 205 $\mu g/m^3$ (0.062 and 0.109 ppm) and the mean suspended nitrate level was 3.8 $\mu g/m^3$ or greater.

An analysis of 3 years of data collected in three American cities shows that on those several days a year when meteorological conditions are most conducive to the formation of photochemical oxidant, and the 6- to 9-a.m. nonmethane hydrocarbon concentration is 200 $\mu g/m^3$ (0.3 ppm C), a 6- to 9-a.m. NO_x concentration (measured by the continuous Saltzman Method and expressed as NO_2) that ranges between 80 and 320 $\mu g/m^3$ (0.04 and 0.16 ppm) would be expected to produce a 1-hour photochemical oxidant level of 200 $\mu g/m^3$ (0.1 ppm) 2 to 4 hours later. If this same functional relationship exists at the lowest levels at which photochemical oxidant has been observed to adversely affect human health, the corresponding nonmethane hydrocarbon concentration would be approximately 130 $\mu g/m^3$ (0.2 ppm C) and the 6- to 9-a.m. NO_x level would be as high as 214 $\mu g/m^3$ (0.11 ppm).

Adverse effects on vegetation such as leaf abscission and decreased yield of navel oranges have been observed during fumigation studies when the NO_2 concentration (measured by the continuous Saltzman Method) was 470 $\mu g/m^3$ (0.25 ppm) during an 8-month period.

Nitrate compounds have been identified with corrosion and failure of electrical components. In two cities where these effects were observed, the average airborne nitrate particulate concentrations were 3.0 and 3.4 $\mu g/m^3$ with associated average NO_x levels of 124 and 158 $\mu g/m^3$ (0.066 and 0.084 ppm).

It is reasonable and prudent to conclude that, when promulgating ambient air quality standards, consideration should be given to requirements for margins of safety that would take into account possible effects on health, vegetation, and materials that might occur below the lowest of the above levels.

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