Environmental Health Criteria 4

OXIDES OF NITROGEN

Please note that the layout and pagination of this web version are not identical with the printed version.

World Health Organization

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

ENVIRONMENTAL HEALTH CRITERIA 4

OXIDES OF NITROGEN

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of either the World Health Organization or the United Nations Environment Programme

Published under the joint sponsorship of the United Nations Environment Programme and the World Health Organization

WORLD HEALTH ORGANIZATION GENEVA 1977

ISBN 92 4 154064 8

CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR OXIDES OF NITROGEN

1. SUMMARY AND RECOMMENDATIONS FOR FURTHER RESEARCH

1.1 Summary
1.1.1 Chemistry and analytical methods
1.1.2 Sources of oxides of nitrogen
1.1.3 Environmental levels and exposures
1.1.4 Effects on experimental animals
1.1.5 Effects on man
1.1.5.1 Controlled exposures
1.1.5.2 Accidental and industrial exposures
1.1.5.3 Community exposures
1.1.6 Evaluation of health risks
1.2 Recommendations for further research

2. CHEMISTRY AND ANALYTICAL METHODS
2.1 Chemical and physical properties
2.2 Atmospheric chemistry
2.3 Analytical methods
2.3.1 Sampling
2.3.2 Evaluation of analytical methods
2.3.2.1 Manual methods
2.3.2.2 Automatic methods
2.3.3 Calibration procedures

3. SOURCES OF OXIDES OF NITROGEN
3.1 Natural sources
3.2 Man-made sources
3.2.1 Stationary sources
3.2.2 Mobile sources
3.2.3 Non-combustion sources
3.2.4 Other sources

4. ENVIRONMENTAL LEVELS AND EXPOSURES
4.1 Background concentrations
4.2 Urban concentrations
4.3 Indoor exposure
4.4 Smoking

5. EFFECTS ON EXPERIMENTAL ANIMALS
5.1 Local effects on the respiratory system
5.1.1 Morphological changes
5.1.2 Functional changes
5.1.3 Biochemical effects

5.2 Other effects
5.2.1 Effects on growth and body weight
5.2.2 Immunological effects
5.2.3 Haematological effects
5.2.4 Miscellaneous biochemical effects
5.2.5 Effects on reproduction
5.2.6 Effects on the central nervous system
5.2.7 Behavioural changes
5.2.8 Carcinogenicity, mutagenicity and teratogenicity
5.3 Interaction of nitrogen dioxide and infectious agents
5.4 Summary table

6. EFFECTS ON MAN
6.1 Controlled exposures
6.2 Accidental and industrial exposures
6.3 Community exposures
6.3.1 Effects on pulmonary function
6.3.2 Effects on the incidence of acute respiratory disease
6.3.3 Effects on the prevalence of chronic respiratory disease
6.4 Summary tables

7. EVALUATION OF HEALTH RISKS FROM EXPOSURE TO OXIDES OF NITROGEN

7.1 Exposure levels
7.2 Experimental animal studies
7.3 Controlled studies in man
7.4 Effects of accidental and industrial exposures
7.5 Effects of community exposures
7.6 Evaluation of health risks

REFERENCES

NOTE TO READERS OF THE CRITERIA DOCUMENTS

While every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication, mistakes might have occurred and are likely to occur in the future. In the interest of all users of the environmental health criteria documents, readers are kindly requested to communicate any errors found to the Division of Environmental Health, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda which will appear in subsequent volumes.

In addition, experts in any particular field dealt with in the criteria documents are kindly requested to make available to the WHO Secretariat any important published information that may have inadvertently been omitted and which may change the evaluation of health risks from exposure to the environmental agent under examination, so that information may be considered in the event of updating and re-evaluating the conclusions contained in the criteria documents.

WHO TASK GROUP ON ENVIRONMENTAL
HEALTH CRITERIA FOR OXIDES OF NITROGEN
Tokyo, 23-27 August 1976

Participants

Members

Dr K. Biersteker, Medical Research Division, Municipal Health Department, Rotterdam, Netherlands

Professor K. A. Bustueva, Department of Community Hygiene, Central Institute for Advanced Medical Training, Moscow, USSR

Dr R. G. Derwent, Environmental and Medical Sciences Division, Atomic Energy Research Establishment, Harwell, England

Professor L. Friberg, Department of Environmental Hygiene, The Karolinska Institute, Stockholm, Sweden *(Chairman)*

Dr D. E. Gardner, Biomedical Research Branch, Clinical Studies Division, Health Effects Research Laboratory, Environmental Protection Agency, Research Triangle Park, NC, USA *(Rapporteur)*

Dr J. Jager, Centre of General and Environmental Hygiene, Institute of Hygiene and Epidemiology, Prague, Czechoslovakia

Dr T. Nakajima, Division of Environmental Health Research, Osaka Prefectural Institute of Public Health, Osaka, Japan *(Vice-Chairman)*

Dr G. von Nieding, Laboratorium fur Atmung und Kreislauf, Krankenhaus Bethanien, Moers, Federal Republic of Germany

Mr E. A. Schuck, US Environmental Protection Agency, Environmental Monitoring and Support Laboratory, Las Vegas, NV, USA

Observers

Dr J. Kagawa, Department of Medicine, Tokai University, Kanagawa, Japan

Professor K. Maeda, Department of Medicine, Tokyo University, Tokyo, Japan

Dr T. Okita, Department of Community Environmental Sciences, The Institute of Public Health, Tokyo, Japan

Dr H. Watanabe, Hyogo Prefectural Institute of Public Health, Kobe, Japan

Professor N. Yamaki, Faculty of Engineering, Saitama University, Saitama, Japan

Dr N. Yamate, First Section of Environmental Chemistry, National Institute of Hygienic Sciences, Tokyo, Japan

Dr G. Freeman, Department of Medical Sciences, Stanford Research Institute, Menlo Park, CA, USA *(Temporary Adviser)*

Dr Y. Hasegawa, Medical Officer, Control of Environmental Pollution and Hazards, World Health Organization, Geneva, Switzerland

Mr G. Ozolins, Scientist, Control of Environmental Pollution and Hazards, World Health Organization, Geneva, Switzerland *(Secretary)*

Professor C. M. Shy, Institute for Environmental Studies and Department of Epidemiology, School of Public Health, University of North Carolina, Chapel Hill, NC, USA *(Temporary Adviser)*

Dr T. Suzuki, The Institute of Public Health, Tokyo, Japan *(Temporary Adviser)*

Professor T. Toyama, Department of Preventive Medicine, Keio University, Tokyo, Japan *(Temporary Adviser)*

ENVIRONMENTAL HEALTH CRITERIA FOR OXIDES OF NITROGEN

A WHO Task Group on Environmental Health Criteria for Oxides of Nitrogen met in Tokyo from 23 to 27 August 1976. Dr Y. Hasegawa, Medical Officer, Control of Environmental Pollution and Hazards, Division of Environmental Health, WHO, opened the meeting on behalf of the Director-General and expressed the appreciation of the Organization to the Government of Japan for kindly acting as host to the meeting. In reply the group was welcomed by Dr M. Hashimoto, Director-General of the Air Quality Bureau, Environment Agency, Japan. The Task Group reviewed and revised the second draft criteria document and made an evaluation of the health risks from exposure to oxides of nitrogen.

The first and second drafts of the criteria document were prepared by Dr G. Freeman, Director, Department of Medical Sciences, Stanford

Research Institute, Menlo Park, CA, USA. The comments on which the second draft was based were received from the national focal points for the WHO Environmental Health Criteria Programme in Bulgaria, Canada, Czechoslovakia, Federal Republic of Germany, India, Japan, New Zealand, Poland, Sweden, the USA and the USSR; and from the Food and Agriculture Organization of the United Nations (FAO), Rome, and the World Meteorological Organization (WMO), Geneva. The collaboration of these national institutions and international organizations is gratefully acknowledged.

The Secretariat also wishes to acknowledge the most valuable collaboration in the final phase of the preparation of this document, of Professor C. M. Shy, School of Public Health, University of North Carolina, NC, USA, Dr D. E. Gardner, Chief, Biomedical Research Branch, Health Effects Research Laboratory, Environmental Protection Agency, Research Triangle Park, NC, USA, and Dr R. G. Derwent, Environmental and Medical Sciences Division, Atomic Energy Research Establishment, Harwell, England.

This document is based primarily on original publications listed in the reference section. Much valuable information may also be found in other published criteria documents (North Atlantic Treaty Organization, 1973; US Department of Health, Education, and Welfare, 1976; US Environmental Protection Agency, 1971a) and in the reviews on oxides of nitrogen by Cooper & Tabershaw (1966), Morrow (1975), and Stern, ed. (1968). Details of the WHO Environmental Health Criteria Programme including some terms frequently used in the documents may be found in the general introduction to the Environmental Health Criteria Programme published together with the environmental health criteria document on mercury (Environmental Health Criteria 1, Geneva, World Health Organization, 1976).

The following conversion factors have been used in this document.[a]

nitric oxide	1 ppm = 1230 µg/m^3	carbon monoxide	1 ppm = 1150 µg/m^3
nitrogen dioxide	1 ppm = 1880 µg/m^3	ozone	1 ppm = 2000 µg/m^3
nitrous oxide	1 ppm = 1800 µg/m^3	sulfur dioxide	1 ppm = 2600 µg/m^3

[a] When converting values expressed in ppm to µg/m^3, the numbers have been rounded up to 2 or, exceptionally 3 significant figures and, in most cases, concentrations higher than 10,000 µg/m^3 have been expressed in mg/m^3.

1. SUMMARY AND RECOMMENDATIONS FOR FURTHER RESEARCH

1.1 Summary

1.1.1 Chemistry and analytical methods

In the context of this criteria document, the term oxides of nitrogen is understood to include nitric oxide (NO) and nitrogen dioxide (NO_2). Other oxides of nitrogen which exist in the atmosphere are not known to have any biological significance and have not been referred to in this document. At the point of discharge from man-made sources, the predominant oxide of nitrogen is nitric oxide which is readily converted to nitrogen dioxide by chemical reactions in the atmosphere.

Nitric oxide and nitrogen dioxide can be measured separately or collectively by manual or automated techniques. However, whereas a certain analytical method can be quite reliable for one compound ("chemiluminescence" for nitric oxide: "Saltzman method" for nitrogen dioxide), difficulties may arise in the simultaneous monitoring of both oxides. Gas-phase titration, permeation tubes, and gravimetric standards have been used for the accurate calibration of these analytical procedures.

1.1.2 Sources of oxides of nitrogen

On a global scale, quantities of nitric oxide and nitrogen dioxide produced naturally by bacterial and volcanic action and by lightning by far outweigh those generated by man's activities. However, as they are distributed over the entire earth's surface, the resulting background atmospheric concentrations are very small.

The major source of man-made emissions of oxides of nitrogen into the atmosphere is the combustion of fossil fuels in stationary sources (heating, power generation) and in motor vehicles (internal combustion engines). Other contributions to the atmosphere come from specific non-combustion industrial processes, such as the manufacture of nitric acid and explosives. Indoor sources include smoking, gas-fired appliances, and oil stoves. Differences in the nitrogen dioxide emission of various countries are mainly due to differences in fossil fuel consumption.

Worldwide emissions of oxides of nitrogen in 1970 were estimated at approximately 53 million tonnes.

1.1.3 Environmental levels and exposures

The natural background concentration of nitrogen dioxide over land areas is usually in the range of 0.4-9.4 µg/m^3 (0.0002-0.005 ppm). This concentration is 1-2 orders of magnitude lower than the concentrations normally found in urban areas. Annual mean nitrogen dioxide concentrations in urban areas throughout the world are typically in the range of 20 90 µg/m^3 (0.01-0.05 ppm), although it is exceedingly difficult to generalize.

Data for shorter averaging periods show considerable variations depending on meteorological and seasonal conditions and on the proximity and nature of local sources of pollution. Generally, the

highest monthly means of nitrogen dioxide levels in large urban areas are about 60-110 µg/m^3 (0.03 0.06 ppm), the highest daily means 136-400 µg/m^3 (0.07-0.22 ppm), and the highest hourly values 240-850 µg/m^3 (0.13-0.45 ppm).

In contrast with typical primary air pollutants, nitrogen dioxide concentrations do not show consistent seasonal behaviour throughout all urban areas of the world and are not necessarily highest during the months of maximum photochemical activity.

Exposure from indoor sources such as home appliances and smoking should not be underestimated. In the immediate proximity of domestic gas-fired appliances, nitrogen dioxide concentrations of up to 2000 µg/m^3 (1.1 ppm) have been measured. Tobacco smoke has been reported to contain nitric oxide levels of about 98-135 mg/m^3 (80-110 ppm) and nitrogen dioxide levels of about 150-226 mg/m^3 (80-120 ppm), but these levels may fluctuate considerably with the conditions of combustion.

1.1.4 Effects on experimental animals

Reversible and irreversible adverse effects may be caused by exposure to nitrogen dioxide, depending upon the concentration, length, and mode of exposure, the species of animal tested, and the presence of infectious agents.

Morphological changes reported in a number of animal species including the mouse, rat, rabbit, guineapig, and monkey, appeared to be most prominent in the terminal bronchiolar and alveolar duct epithelia. Exposure to about 470-1900 µg/m^3 (0.25-1.0 ppm) resulted in numerous pathophysiological changes including bronchitis, bronchopneumonia, atelectasis, protein leakage into the alveolar space, changes in collagen, elastin, and mast cells of the lungs, reduction or loss of cilia and adenomatous changes.

At concentrations of 3800-47 000 µg/m^3 (2.0-25 ppm) these effects became more pronounced. The more sensitive ciliated bronchiolar and type 1 alveolar lining cells were injured first and were replaced by the proliferation of more resistant nonciliated cells, and type 2 cells, respectively. Prolonged exposure resulted in a reduction in diameter of small airways by exudate, hypertrophy of the respiratory epithelium, and swelling of the basement membrane.

In studies on the effect of nitrogen dioxide on lung function, increased respiratory rates were reported in rats exposed to concentrations as low as 1500 µg/m^3 (0.8 ppm). Reductions in both