SZW

Ministry of Social Affairs and Employment

Health-based recommended occupational exposure limit for Pyridine

Dutch expert committee on occupational standards (met Nederlandstalige samenvatting)

RA 3/93

Labour Inspectorate

Health-based recommended occupational exposure limit for Pyridine

Health-based recommended occupational exposure limit for Pyridine

Dutch expert committee on occupational standards (met Nederlandstalige samenvatting)

Sdu Uitgeverij Plantijnstraat, Den Haag 1993

CIP-gegevens Koninklijke Bibliotheek, Den Haag

Health-based

Health-based recommended occupational exposure limit for pyridine / Dutch expert committee on occupational standards. - The Hague: Directorate-General of Labour; The Hague: Sdu Uitgeverij Plantijnstraat [distr.]. - Ill. - ([Report] / Dutch expert committee for occupational standards, ISSN 0921-9641; RA 3/93)
Met samenvatting in het Nederlands.
ISBN 90 399 0518 5
Trefw.: chemische stoffen; bedrijfsgezondheidszorg.

TABLE OF CONTENTS

Nederlandstalige samenvatting

Pyridine

1. Samenvatting fysische en chemische gegevens

CAS nr: 110 - 86 - 1

Pyridine is een zeer brandgevaarlijke kleurloze tot lichtgele vloeistof met een zeer onaangename geur. Het is mengbaar met water, alkohol, ether en andere organische oplosmiddelen. Het is een goed oplosmiddel voor organische en anorganische verbindingen. Pyridine is lichter dan water en de damp is zwaarder dan lucht. Het reageert heftig met oxidatiemiddelen. Pyridine heeft een relatieve molecuulmassa van 79,1, een kookpunt van 115,3°C, een smeltpunt van -41,6°C, een relatieve dichtheid van 0,98 (water = 1), een dampspanning van 2,66 kPa (25°C) en een relatieve dampdichtheid van 2,73 (lucht = 1).
Conversiefactoren (25°C): 1 ppm = 3,23 mg/m^3; 1 mg/m^3 = 0,309 ppm

2. Monitoring

Voor de omgevingsmonitoring op de werkplek wordt verwezen naar de methode van het NIOSH (1977). Bij deze methode wordt gebruik gemaakt van persoonlijke monstername apparatuur en van een gaschromatograaf. Er is geen methode bekend voor biologische monitoring van werknemers die blootgesteld zijn aan pyridine.

3. Grenswaarden

De huidige MAC-waarde voor pyridine in Nederland is 15 mg/m^3 (5 ppm), TGG-8 uur. Deze grenswaarde geldt ook in Duitsland, het Verenigd Koninkrijk, Zweden, Frankrijk en de Verenigde Staten. Zweden adviseert ook een kort-durende grenswaarde van 35 mg/m^3 (10 ppm).

4. Toxicokinetiek

Opname kan plaatsvinden via het maagdarmkanaal, longen en huid. Na opname wordt de stof verspreid naar verschillende weefsels/organen. De hoogste concentraties na de opname worden gevonden in bloed, nieren en urine.
Er zijn weinig gegevens over het metabolisme van pyridine bij de mens. Orale toediening van een heel lage dosis pyridine bij twee proefpersonen resulteerde in het voorkomen van een aantal metabolieten in de urine. Ongeveer 30 en 10% van de toegediende dosis wordt terug gevonden in de vorm van respectievelijk pyridine N-oxide en N-methylpyridinium ion in 24-uurs urinemonsters. Uit experimenten met proefdieren blijkt dat de biotransformatie van pyridine species- en dosis-afhankelijk is. Pyridine wordt uitgescheiden via longen, huid, faeces en urine in de vorm van vrije-basen en metabolieten.

5. Effecten

Effecten bij proefdieren: Bij kortdurende blootstelling heeft pyridine een narcotische werking, tevens worden symptomen van irritatie van de slijmvliezen waargenomen. Pyridine heeft een lage acute toxiciteit

en de orale LD50 ligt hoger dan 1 g/kg bij kleine proefdieren. Effecten op de nier en lever worden gevonden na langdurende blootstelling via de voeding. Een dosis van 50 mg/kg/dag toegediend via maagsonde gedurende 90 dagen bij ratten veroorzaakt verlaging van het lichaamsgewicht en bij 70% van de dieren wordt ontsteking van de lever gevonden. Muizen die die dosis gedurende 3 maanden met drinkwater (2,0 μg/ml) kregen toegediend, vertonen toename van de vet peroxidatie in de striatum en het cerebellum deel van de hersenen. Na continue inhalatoire blootstelling van ratten aan een concentratie van 1 mg/m^3 (0,3 ppm) gedurende twee maanden werden lichte effecten gevonden op de functie van het centrale zenuwstelsel en de samenstelling van bloedeiwitten. Een samenvatting van de dosis-effect relatie bij proefdieren is beschreven in Tabel 2.

Effecten bij de mens: Een samenvatting van de dosis-effect relatie voor de mens blootgesteld aan pyridine is beschreven in Tabel 1. Volgens de OSHA ligt de dodelijke luchtconcentratie van pyridinedamp ongeveer bij 3600 ppm. Blootstelling aan gemiddeld 125 ppm in lucht, 4 uur per dag gedurende één tot twee weken, veroorzaakte lichte effecten op het centrale zenuwstelsel en het maagdarmkanaal. Zeven gevallen van chronische pyridine vergiftiging werden vermeld in een chemisch bedrijf met lucht concentraties van 20 tot 42 mg/m^3 pyridine. De symptomen zijn hoofdpijn, tijdelijke duizeligheid, overspannenheid, slapeloosheid en maagdarmklachten zoals misselijkheid en braken.

6. Evaluatie en advies

Geconcludeerd kan worden dat de kritische effecten bij kortdurende blootstelling, de prikkelende werking op de slijmvliezen van de bovenste luchtwegen en ogen zijn, en de bedwelmende werking op het centrale zenuwstelsel. Anderzijds zijn de nier en lever de kritische organen na langdurende blootstelling. Uit gegevens bij de mens blijkt dat een walgingwekkende geur voorkomt bij een concentratie van 32,3 mg/m^3 (10 ppm) pyridine in lucht. De reukgrens ligt tussen 0,04 en 2,6 mg/m^3 (0,013 - 0,82 ppm). Effecten op het centrale zenuwstelsel treden op bij concentraties tussen 19,4 en 42 mg/m^3 (6 - 13 ppm). Dit betekent dat een kortdurende advieswaarde beneden 19,4 mg/m^3 zou moeten liggen.
Voor de langdurende blootstelling aan pyridine zijn twee dierexperimentele gegevens van belang. Bij een blootstelling aan 10 of 50 ppm (32,3 of 161 mg/m^3) pyridine damp in lucht bij ratten, 5 dagen/week, gedurende 6 maanden wordt toename van het gewicht van de lever gevonden. In een andere experiment, waarbij ratten via maagsonde doseringen van 0,25, 1, 10, 25 en 50 mg/kg/dag pyridine gedurende 90 dagen kregen, werd toename van het levergewicht gevonden bij de doseringen van 10 en 25 mg/kg/d. Hieruit kan worden geconcludeerd dat de NOAEL op 1 mg/kg/d zou kunnen liggen. Extrapolatie naar de mens levert een concentratie van 7 mg/m^3 (2 ppm) pyridine damp in lucht (aangenomen dat: gemiddeld lichaamsgewicht = 70 kg, ademvolume gedurende een werkdag van 8 uur = 10 m^3 en 100% resorptie in maagdarmkanaal en longen). Ter compensatie van de onzekerheden en interspecies variaties stelt de WGD voor een veiligheidsfactor 10 te gebruiken. De gegevens over de carcinogiteit van pyridine zijn ontoereikend.

Aan de hand van de boven vermelde gegevens stelt de WGD een gezondheidskundige advieswaarde voor van 1 mg/m^3 (0,3 ppm), TGG - 8 uur en een "H" notatie.

Datum van afsluiting: juni 1993

1. INTRODUCTION

This document is a co-production of the Dutch Expert Committee on Occupational Standards (DECOS) of the Dutch Directorate-General of Labour and the Swedish Criteria Group for Occupational Standards (SCG) at the Swedish National Institute of Occupational Health. It is the product of an agreement (signed in 1988) between both groups to write joint scientific criteria documents which could be used by the national regulatory authorities both in the Netherlands and in Sweden.

The draft as prepared by dr. Margareta Warholm was first reviewed by the SCG and thereafter by the DECOS. The resulting document, as published by the Swedish National Institute of Occupational Health (Arbete och Hälsa 1991:49), is included in the present document as Annex 1.

In order to be able to serve as a basis for setting a Dutch MAC-value some extra chapters are supplemented to the Swedish version by the DECOS, resulting in the underlying document. Most important is the addition of a "Recommended Health Based Occupational Exposure Limit".

2. ANALYTICAL METHODS

2.1 ENVIRONMENTAL MONITORING

Methodology according to NIOSH (1977):

Instrumentations: Personal monitoring equipments and gas chromatography instrumentation.

Principle: A known volume of air is drawn through a charcoal tube to trap the organic vapors present. The charcoal in the tube is then transferred to a small stoppered sample container, and the analyte is desorbed with methylene chloride. An aliquot of the desorbed sample is injected into gas chromatograph. The area of the resulting peak is determined and compared with areas obtained for standards. This method is validated over the range of 7.59-30.4 mg/m^3 at an atmosphere temperature and pressure of 22 degrees Celsius and 763 mm Hg, using a 100 l sample. Under the conditions of sample size (100 l) the probable useful range of this method is 1.5 - 45 mg/m^3 at a detector sensitity that gives nearly full deflection on the stripchart recorder for a 4,5 mg sample. The method is capable of measuring much smaller amounts if the desorption efficiency is adequate. Desorption efficiency must be determined over the range used.

2.2 BIOLOGICAL MONITORING

No methods are applicable at present.

Ref: NIOSH. NIOSH manual of analytical methods. Second edition. VOL 3 (1977 PP S161-1-S161-8).

3. GUIDELINES AND STANDARDS

COUNTRY (organization)	CONCENTRATION mg/m^3	(ppm)	COMMENTS
The Netherlands 1989	15	(5)	twa - 8 hour
Sweden 1987	16	(5)	twa - 8 hour
	35	(10)	short term
United States			
ACGIH 1990 - 1991	16	(5)	twa - 8 hour
OSHA-PEL	15	(5)	twa - 8 hour
NIOSH-REL	15	(5)	twa - 8 hour
Germany 1991	15	(5)	twa - 8 hour
United Kingdom			
HSE 1991		(5)	twa - 8 hour
		(10)	short-term
France 1986		(5)	twa - 8 hour
		(10)	short - term

Ref: - Arbeidsinspectie: De nationale MAC-lijst 1992, P145
- National Swedish Board of Occupational Safety and Health. Occupational Exposure Limit Values (1987)
- American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Physical Agents and Biological Exposure Indices (1990-1991)
- ACGIH. Guide to Occupational exposure values - 1990
- Deutsche Forschungsgemeinschaft. Maximale Arbeitsplatzkonzentrationen und Biologisch Arbeitsstofftoleranzwerte 1991
- Health Safety Executive. Occupational Exposure Limits 1991
- IHRS. Values limites pour les concentrations des substances dangerouses, 1986.

4. PREVIOUS EVALUATION BY (INTER)NATIONAL BODIES

The ACGIH concluded that the TLV of 5 ppm, as a TWA, and the STEL of 10 ppm should be low enough to prevent systemic effects from exposure to pyridine, provided skin absorption is not permitted, but may not eliminate complaints about the odour.

This conclusion seems to be in contrary with the data reported beforehand in their document. It was considered that the most important effect of pyridine after exposure by inhalation was chronic poisening, the critical organs being the liver, kidney and bone marrow. Mild symptoms may be found after exposure to 10 ppm pyridine. It was also reported that long-term poisening with mild symptoms of the central nervous system occurred in workers of a plant where pyridine concentrations ranged from 6 to 12 ppm. This means that there is almost no safety margin between the TLV and the occurence of symptoms.

The DFG does not have any documentation on the MAK of pyridine.

Ref: ACGH. Documentation of the threshold limit values and biological exposure indices. Fifth edition. Cincinnati, Ohio, 1986.

5. EVALUATION OF HUMAN HEALTH RISK

5.1 Groups at extra risk

No data are available to determine specific groups at extra risk.

5.2 Assessment of health risk

In human health risk assessment due to occupational exposure to pyridine vapour, two types of exposure associated effects are of relevance. It may be summarized that the critical effects after short-term exposure is the irritation of the mucous membranes of the upper respiratory tract and eyes, and acute effects on the central nervous system. On the other hand the critical organs after long-term exposure seem to be the kidney and the liver.

Human data indicate that objectionable odour is experienced at a level of 32.3 mg/m^3 (10 ppm) pyridine. The range of odour threshold lies between 0.04 and 2.6 mg/m^3 (0.013 - 0.82 ppm) pyridine, according to Ellenhorn and Barceloux (1988). Effects on the central nervous system with symptoms of headache, nervousness, sleeplesness and occasional digestive tract problems are reported at levels of 19.4 to 42 mg/m^3 (6 - 13 ppm) pyridine in workroom air. From these events it may be concluded that the short-term occupational exposure limit should be below 19.4 mg/m^3.

Long-term exposure studies on experimental animals and human data indicate that kidney and liver are the critical organs. The human data could not be used for risk assessment because the doses used are out of proportion and the patients (epileptics) used them as drug for anticonvulsant treatment.

There are two animal experiments important for risk assessment. In one experiment with rats exposed by inhalation to levels of eighter 10 or 50 ppm (32.3 or 161.5 mg/m^3) pyridine vapour, 5d/w, 6 months, increased liver weights were found (Anonymous, 1986; Gehring 1983).

In the other study (Anderson, 1987) pyridine was administered to rats by gavage at doses of 0.25, 1.0, 10, 25 and 50 mg/kg for 90 days. At the highest dose inflammatory hepatic lesions were found as well as increased absolute and relative liver weight.

Ref: Ellenhorn, MJ and Barceloux DG Medical toxicology, diagnosis and treatment of human poisening (1988) Elsevier, New York.

Increased relative liver weights were found in female, but not in male rats, receiving 10 or 25 mg/kg pyridine. From this study it may be concluded that the NOAEL for these effects is 1 mg/kg b.w. per day. Extrapolation from rat to man means that in man (standard: 70 kg) breathing 10 m^3 volume of air in 8 hour the NOAEL should be 7 mg/m^3 (2 ppm). In this estimation the extrapolation is based on the assumption that 100% of pyridine is absorbed through the digestive tract as well as respiratory tract since the compound is completely soluble in water and penetrates very well through the skin.

In this kinetic model some assumptions have been made, e.g. the use of gavage as a method of administration, which is not the normal method of intake in real life, and the 100% absorption through the respiratory tract. The DECOS endeavors to compensate these uncertainties by using a safety factor. The data on the carcinogenic potential of pyridine are too meagre to be of use in the risk assessment. The DECOS proposes to use a safety factor of 10 and an upward roundoff to arrive at a health-based recommended occupational exposure limit of 1 mg/m^3 (0.3 ppm) t.w.a. 8 - hour pyridine vapour with a skin notation.

5.3 Health-based Recommended Occupational Exposure Limit

1 mg/m^3 (0.3 ppm) pyridine, time weighted average 8 hours, with a skin-notation.

6. RECOMMENDATION FOR RESEARCH

1. Epidemiological studies are required on groups of workers with long-term exposure to pyridine vapour.

2. Studies on the kinetic of pyridine in humans.

3. Development of biological monitoring methods.

Members of the Dutch Expert Committee on Occupational Standards (DECOS)

V.J. Feron (Chairman)

P.C. Noordam / C. Hoeksema (Scientific secretariat)

R.B. Beems

J.S.M. Boleij

G. de Jong

G. de Mik

H. Roelfzema

T. Smid

G.M.H. Swaen

H.G. Verschuuren

A.A.E. Wibowo

F. de Wit

R.L. Zielhuis

Address of the secretariat of the DECOS:

Directoraat-Generaal van de Arbeid (Directorate-General of Labour)
Directie Gezondheid (Department of Health)
P.O. Box 90804
2509 LV DEN HAAG

Tel. 070 - 3334444 / 3335312 / 3335300
Fax 070 - 3334023

ANNEX 1

ARBETE OCH HÄLSA

VETENSKAPLIG SKRIFTSERIE

1991:49

DEC and SCG Basis for an Occupational Health Standard

PYRIDINE

Margareta Warholm

ARBETS MILJÖ INSTITUTET
NATIONAL INSTITUTE FOR OCCUPATIONAL HEALTH

1990:

36. **Anders Kjellberg:**
Inte bara hörselskador. Psykologiska effekter av buller i arbetsmiljön.
37. **Agneta Löf, Christina Brohede, Elisabeth Gullstrand, Karin Lindström, Jan Sollenberg, Kent Wrangskog, Mats Hagberg och Birgitta Kolmodin-Hedman:**
Andningsskyddens effektivitet vid styrenexponering på en plastbåtsindustri.
38. **Gun-Britt Berglund, Lennart Lundgren, Lizbet Skare och Gunnel Sundström:**
Analys av kvarts i lungvävnad.
39. **Carola Lidén:**
Yrkeshudsjukdomar av filmkemikalier. Särskilt kontaktallergi och lichenoid reaktion av färgframkallningsämnen.
40. **Jan-Olof Levin (ed):**
Principer och metoder för provtagning och analys av ämnen upptagna på listan över hygieniska gränsvärden.
41. **Ulf Landström:**
Vakenhet, sömnighet och insomningsrisker under fordonskörning.
42. **Tom Hagström:**
Ungdomars livsstilar och förhållningssätt till arbete.
43. **Anders Jansson:**
Local exhaust ventilation and aerosol behaviour in industrial workplace air.
44. **Ingvar Lundberg, Annika Gustavsson, Margareta Högberg och Gun Nise:**
Alkoholdiagnoser och andra neuropsykiatriska diagnoser hos byggnadsmålare jämfört med byggnadssnickare.
45. **Anton A. E. Wibowo:**
DEC and SCG Basis for an Occupational Health Standard. Talc dusts.
46. **Bodil Persson:**
NIOH and NIOSH Basis for an Occupational Health Standard. Chlorocresol.
47. **Kristina Kemmlert, Margareta Dallner Örelius, Åsa Kilbom och Francesco Gamberale:**
Treårsuppföljning av 195 arbetsskadeanmälningar av belastningskaraktär.
48. **Helena Keskinen:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 92. Organiska syraanhydrider.
49. **Harri Vainio:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 93. Styren.

1991:

1. **S Krantz, J W Cherrie, T Schneider, I Öhberg and O Kamstrup:**
Modelling of past exposure to MMMF in the European rock/slag wool industry.
2. **Brita Beije and Per Lundberg (Eds):**
Criteria Documents from the Nordic Expert Group 1990.
3. **Tomas Lindh och Lars-Inge Andersson:**
Elektriska och magnetiska fält i elkraftindustri.
4. **Marianne Byström, Ulf Landström och Anders Kjellberg:**
Effekterna av ljudets frekvens och arbetets karaktär på störningsgraden under bullerexponering – studier av rena toner.
5. **Göran M Hägg:**
Zero crossing rate as an index of electromyographic spectral alterations and its applications to ergonomics.
6. **Jan Ahlin och Gunnela Westlander:**
Kontorslokaler och kontorsarbete – två perspektiv på kontoret som arbetsplats.
7. **Ed. Per Lundberg:**
Vetenskapligt Underlag för Hygieniska Gränsvärden 11.
8. **Ed. Per Lundberg:**
Scientific Basis for Swedish Occupational Standards XI.
9. **Göran Pershagen och Marie Vahter:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 94. Oorganisk arsenik.
10. **Gunh Mellström:**
Protective gloves of polymeric materials. Experimental permeation testing and clinical study of side effects.
11. **Ulf Landström, Anders Kjellberg, Per Löfstedt och Lena Söderberg:**
Ventilationsbuller på kontor. Ljudkaraktäristik, exponeringsnivåer och besvärsupplevelser.
12. **Ewa Menckel:**
Olycksfall. Om forskning och forskningsförmedling vid Arbetsmiljöinstitutet 1987–1990.
13. **Åsa Kilbom och Clas-Håkan Nygård (Eds):**
Arbetsmiljö för äldre
14. **Brita Beije och Per Lundberg:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 95. Isoforon.
15. **Tom Hagström:**
Ungdomars livsstilar – arbetslivets krav. En forskningsöversikt.
16. **Bo Holmberg och Christer Hogstedt:**
Cancer och genetiska skador. Verksamhetsöversikt 1987–1990.
17. **Ragnar Andersson:**
The Role of Accidentology in Occupational Injury Research.
18. **Johnny Hedendahl:**
Hygienisk bedömning av icke önskvärt ljud.
19. **Bengt Knave, Gunnela Westlander och Ulf Bergqvist:**
Datorn som hjälpmedel.
20. **Anne Renström, Per Malmberg, Per Larsson, Katrin Karlsson, Björn Sannagård och S G O Johansson:**
Bestämning av halter av musallergen i luftprover från djurhus.

ARBETE OCH HÄLSA

Redaktör: Irma Åstrand
Redaktionskommitté: Anders Kjellberg, Åsa Kilbom, Nils Stjernberg, Staffan Krantz och Olof Vesterberg.

Arbetsmiljöinstitutet, 171 84 Solna

Arbete och Hälsa 1991 : 49

DEC and SCG Basis for an Occupational Health Standard

PYRIDINE

Margareta Warholm

ARBETS MILJÖ INSTITUTET
NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH

The Swedish National Institute of Occupational Health employs over 300 scientists in research on the work environment. The research is led by 30 professors. The Institute does mostly applied research, but some question also require basic research.

The scientific competence of the Institute is concentrated in six areas: Physiology, Chemistry, Medicine, Psychology, Technology and Toxicology. This wide competence provides solid support for the Institute's cross-disciplinary approach.

The Institute is responsible for training safety engineers, physical therapists and psychologists, as well as doctors and nurses for the industrial health services.

Another of the Institute's responsibilities is disseminating information on occupational health research.

ISBN 91-7045-151-6

ISSN 0346-7821

PREFACE

An agreement has been signed by the Dutch Expert Committee for Occupational Standards (DEC) of the Dutch Directorate-General of Labour and the Swedish Criteria Group at the Swedish National Institute of Occupational Health (SCG). The purpose of the agreement is to write joint scientific criteria documents for occupational exposure limits. These limits will be developed separately by the two countries according to their different national policies.

This document on health effects of pyridine is a product of the agreement. The document was written by Dr. M. Warholm from the National Institute of Occupational Health in Solna, Sweden, and was reviewed by the Dutch Expert Committee as well as by the Swedish Criteria Group.

J. J. Kolk
Chairman
Dutch Expert Committee

B. Holmberg
Chairman
Swedish Criteria Group

Contents

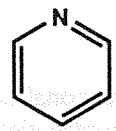
Physical and chemical properties

CAS nr: 110-86-1

Synonyms: azabenzene, azine

Molecular formula: C_5H_5N

Structural formula:



Molecular weight: 79.1

Melting point: -41.6 °C

Boiling point: 115.3 °C

Relative density: 0.98

Vapor pressure: 2.66 kPa at 25 °C

Vapor density: 2.73

Flash point: 20 °C

Solubility: completely soluble in water, alcohol, ether, acetone and benzene.

pKa: 5.19

pH value: 8.5 (0.2 M solution in water)

Conversion factors: 1 ppm=3.23 mg/m^3; 1 mg/m^3=0.309 ppm at 25 °C

Pyridine is a highly flammable, colourless (when pure) or slightly yellow liquid with a characteristic disagreeable odor and a burning taste. It is miscible with water, alcohol, ether, oils, and many other organic compounds, and is slightly alkaline in reaction. It is a good solvent for both inorganic and organic compounds. Pyridine is lighter than water and its vapors are heavier than air. Pyridine forms an azeotropic mixture with three moles of water (59 vol %-41 vol % water), which boils at 92-93° C. Contact of pyridine with strong oxidizers may cause fires and explosions. Contact with strong acids will cause violent splattering. Toxic gases and vapors (such as oxides of nitrogen and carbon monoxide) may be released in a fire involving pyridine.

In humans, the air odor threshold for pyridine in most individuals is less than 0.2 ppm (3, 4, 14), but olfactory fatigue occurs quickly (6). Pyridine becomes objectionable to unacclimatized individuals at 10 ppm (60). The irritation threshold for pyridine is 700 ppm (4, 65). This value is defined as the lowest concentration that could be distinguished from pure air by a general anosmic, i.e. by a person who has no olfactory nerve sensation, but whose trigeminal nerve sensitivity is intact. The pungency thresholds for pyridine in three anosmics described in (18) are of similar magnitude.

Production and uses

Pyridine is produced synthetically or by fractional distillation of coal tar residues.

Pyridine is used as a solvent in e.g. pharmaceutical and polycarbonate resin industries. It is particularly useful as a solvent in processes where HCl is evolved (it forms stable salts with strong acids). A main use of pyridine is in the production of agricultural chemicals, such as the herbicides paraquat and diquat, and the insecticide chlorpyrifos. Other uses include the production of piperidine, the manufacture of pharmaceuticals, and in dyeing of textiles. Minor quantities are used for the denaturation of alcohol and antifreeze mixtures, and as a flavoring agent (33, 59, 60).

Occurrence

Pyridine is found in tobacco smoke and roasted coffee, as well as in the leaves and roots of *Atropa belladonna*. It is also found in coal tar, wood oil and as a component of creosote oil (59).

In the U.S.A. in 1978, air concentrations of pyridine in work places where pyridine was manufactured or used as an intermediate ranged from 0.008 to 1 ppm. Monitoring of technicians working with pyridine in quality control and research and development laboratories of one of the pyridine manufacturers showed that the highest TWA concentration measured over a 6-hour period was 0.09 ppm (61).

Toxicokinetic data

Absorption

Pyridine is absorbed from the gastrointestinal tract, intraperitoneal cavity, and lungs. It is also rapidly absorbed through intact skin (60). Based on its aqueous and lipid solubility, the absorption of pyridine is expected to be rapid (61). In rats, uptake by tissues following i.p. administration increased with dosage (72).

Distribution

Pyridine gains access into all tissues, but the largest concentrations are found in the blood, kidney and urine (66). Based on the acute toxic effects of pyridine it can be assumed that pyridine is distributed to the central nervous system, liver and kidneys (61).

Biotransformation

Pyridine has been shown to be oxidized to several metabolites *in vivo* and *in vitro*. These include pyridine N-oxide, 3-hydroxypyridine, 2-pyridone, and 4-pyridone; an N-methylpyridinium ion metabolite is also formed (64).

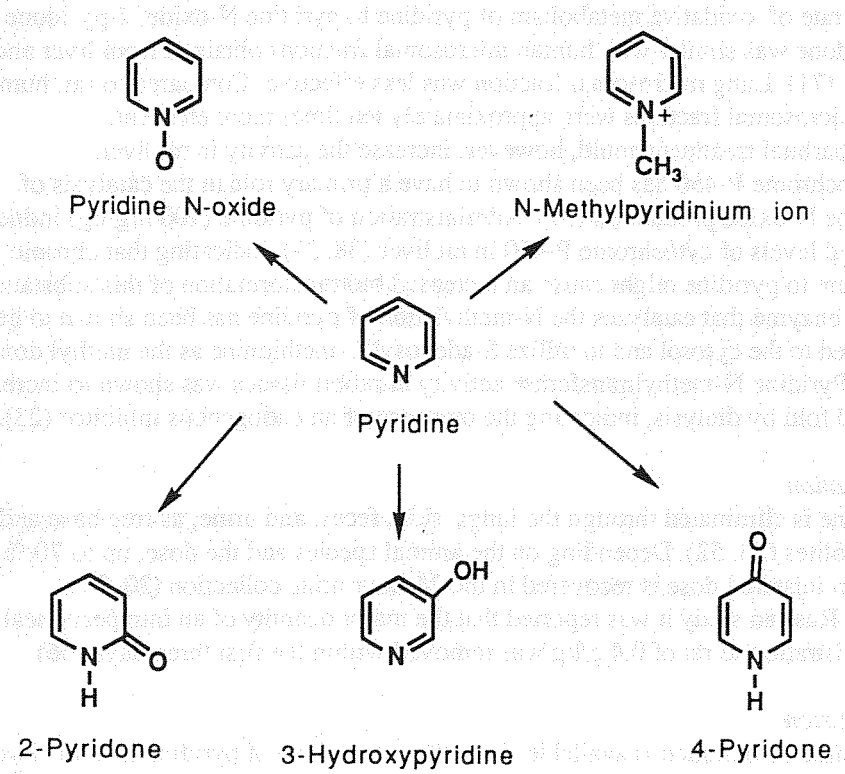


Figure 1. Structure of pyridine and some of its mammalian urinary metabolites.

Damani and co-workers investigated urinary metabolites of ^{14}C-pyridine in eight different species, including man (21). The total amount of ^{14}C excreted in the 24-h urine samples ranged from about 50% to 80% of the administered dose, which was 7 mg/kg i.p., except for the two male volunteers, who received approximately 50 µg/kg p.o. A distinct species difference in the metabolism of ^{14}C-pyridine was noted. For example, in cat and rabbit 15% to 25% of the administered dose was recovered as unchanged pyridine, whereas only minor amounts of unmetabolized substance was found in hamster, gerbil, rat, and mouse. 4-Pyridone seems to be a major metabolite in rabbit and guinea pig, whereas the most common metabolite in hamster is pyridine N-oxide. In some species a large portion of urinary metabolites is unidentified. In man, N-oxidation and N-methylation appeared to be important routes of metabolism.

In rat and guinea pig, the urinary excretion of pyridine is clearly dose-dependent (20). Thus, in the rat, the percentage of 24-h urinary metabolites dropped from 70% at an administered dose of 1 mg/kg to only 6% at a dose of 500 mg/kg. There was also a decline in the proportion of the dose excreted as N-methylpyridinium. In contrast, N-oxidation assumes greater importance as a route of metabolism at higher doses of pyridine (21, 22).

The rate of oxidative metabolism of pyridine to pyridine N-oxide, 2-pyridone or 4-pyridone was similar with human microsomal fractions obtained from liver and kidney (71). Lung microsomal fraction was less effective. Compared to rat, human liver microsomal fractions were approximately ten times more efficient. Phenobarbital treatment could, however, increase the activity in rat liver.

Cytochrome P-450 has been shown to have a primary role in the catalysis of pyridine N-oxide production (51). Administration of pyridine (100 mg/kg) induced elevated levels of cytochrome P-450 in rat liver (38, 39), indicating that chronic exposure to pyridine might cause an increased biotransformation of this substance.

The enzyme that catalyzes the N-methylation of pyridine has been shown to be confined to the cytosol and to utilize S-adenosyl-L-methionine as the methyl donor (23). Pyridine N-methyltransferase activity in rabbit tissues was shown to increase several fold by dialysis, indicating the presence of an endogenous inhibitor (23).

Elimination

Pyridine is eliminated through the lungs, skin, feces, and urine, as free base and as metabolites (33, 52). Depending on the animal species and the dose, up to 70 % of the administered dose is recovered in the 24-hour urine collection (20, 21).

In a Russian study it was reported that the major quantity of an intraperitoneal administration to rat of 0.4 g/kg was removed within the first three days (66).

Conclusion

Very little information is available about the metabolism of pyridine in man. Two males received a very low dose of pyridine p.o. and only some urinary metabolites were analyzed. Approximately 30 % and 10 % of the administered dose was recovered as pyridine N-oxide and N-methylpyridinium ion, respectively, in the 24-h urine samples (21). Studies using experimental animals have shown that the biotransformation of pyridine is both species- and dose-dependent. In addition, there is no information about other than urinary metabolites. Jori *et al.* (33) concluded in 1983 that the knowledge of the kinetics and metabolism of pyridine is totally inadequate and that information on metabolic fate is based either on very old publications or on recent studies which were not specifically designed to study pyridine metabolism. No *in vivo* studies on man have appeared thereafter.

Toxicological mechanisms

No studies that were aimed at investigating the mechanisms of pyridine toxicity have been found in the literature. It is possible though that pyridine interferes with endogenous pyridine nucleotide metabolism. Pyridine may also act on nicotinic receptors (43). It has been suggested that the metabolism of pyridine increase its toxicity. The N-oxide of pyridine is a more potent toxicant than the parent compound (61), and the metabolite 3-hydroxypyridine is a potential teratogen (51).

Clugnet & Laget (17) suggest that that the effects of pyridine on the motor behaviour of experimental animals may be due to acetylation in the blood of pyridine to 3-acetylpyridine, which affects cerebellar functions. However, that such an acetylation occurs has not been established.

General toxicological effects in animals

Short-term exposure

Pyridine has a narcotic action when administered to experimental animals. Effective doses by any route produce weakness, ataxia, salivation, and unconsciousness, but convulsions are uncommon. With exposure to pyridine vapors there are symptoms of moderate mucous membrane irritation. Pyridine has relatively low acute toxicity. In most cases the oral LD_{50} for small animals exceeds 1 g/kg (60). There is a general depression of the CNS and death results from respiratory paralysis (43, 59). In various bird species LD_{50} for pyridine has been estimated to exceed 1 g/kg (62).

The acute dermal lethal dose of pyridine for rabbits was 1120 mg/kg (7). This value is only slightly higher than the oral LD_{50} (for rat), indicating that pyridine is effectively absorbed through the skin

For rats, inhalation of pyridine vapor for 4 h yielded an LD_{Lo} of 4000 ppm (49). Concentrated vapor (23200 ppm) caused 100% mortality within 1.5 h (60).

Long-term exposure

Rats receiving 0.1% pyridine in the diet (approximately 50 mg/kg body weight/day, (59)) gradually lost weight and died within 2-4 weeks (12). The livers and kidneys revealed acute lesions and some of the livers exhibited well marked cirrhosis. Addition of 0.5% methionine to the diet decreased the toxicity of pyridine. Another group of rats in this study received 0.164 % in the diet of the pyridine metabolite methylpyridinium ion (as chloride), this dosage being equivalent to 0.1% pyridine. All six animals survived and showed continual growth. Two were sacrificed on the 32nd day and were found to have histologically essentially normal livers and kidneys.

In another study it was shown that pyridine toxicity decreased when the choline and casein content of the diet increased (11). Pyridine administered daily by subcutaneous injection or by stomach tube proved to be less toxic than when given in the diet (11).

Sprague-Dawley rats (10 male and 10 female rats in each group) were given pyridine by gavage at dosages of 0, 0.25, 1.0, 10.0, 25.0, or 50.0 mg/kg for 90 days (5). The male rats given the highest dose of pyridine (50 mg/kg) showed statistically significant decreased body weights (days 57-85) and total weight gain. Inflammatory hepatic lesions were found in 70% of the animals compared to 10% in the controls. In females, 50 mg/kg caused mild hepatotoxicity with significantly increased absolute and relative liver weights. Inflammatory hepatic lesions appeared in 20% of the females in this group. Increased relative liver weights were also found in females, but not in males, given 10 or 25 mg/kg. In this study no significant histopathological or clinical findings related to the neurological systems were found that could be definitely attributed to exposure to pyridine.

The MTD for rats injected subcutaneously, twice weekly for four weeks, was found to be less than 180 mg/kg. Twice weekly injections of 100 mg/kg for one year did not produce any changes in mortality relative to controls (45).

Four rabbits dosed orally for 5-7 days with 44 mg/kg pyridine showed no noticeable effects (58).

Administration to mice of pyridine in the drinking water (2.0 µl/ml) for 3 months induced a significant increase in lipid peroxidation in striatum and cerebellum (57).

Repeated exposure of rats (7 h/day, 5 days/week for 6 months) to either 10 or 50 ppm pyridine vapor did not change either the growth rate or mortality when compared to controls; however increased liver weight/body weight ratios were noted in the treated rats (8, 28).

Continuous inhalational exposure of rats for two months at 1 mg/m^3 (0.3 ppm) caused minor effects on CNS function and blood protein composition, while 0.1 mg/m^3 was without effect (41).

Chronic exposure of guinea pigs to vapors of commercial-grade pyridine for 4 months (3 h/day) at a concentration of 1000 mg/m^3 caused loss of body weight, depression of body temperature and hypochromic anemia (66). A histopathological examination of some of the animals showed hepatic cirrhosis, focal necrosis and fatty liver cells.

Intragastric administration to albino rats of pyridine at doses of 0.25 and 0.125 mg/kg during 100 days led to decreases in body weights and disturbances in the functional state of the liver. A pyridine dose of 0.0125 mg/kg did not affect the body weight of the rats. The speed with which conditioned reflex was produced in mice was not altered by exposure to 0.0125 mg/kg (66).

General toxicological effects in humans

Browning states that pyridine is less toxic in animals than in human beings (13).

Most of the effects observed in man are transient, involving the CNS and gastrointestinal tract. Despite its relatively large industrial and some medical use, reports of injurious effects of pyridine in man have been relatively uncommon (15).

Short-term exposure

A fatal case from accidental ingestion of "half a cupful" of commercial pyridine was reported by Helme in 1893 (31). Initially there was vomiting. Later there was slight cyanosis, a choking sensation, precordial and abdominal pain, and a raised temperature, pulse and respiration. There was no abnormality of the urine. Delirium and acute congestion of the lungs preceded death which occurred 43 hours after the ingestion. Autopsy revealed that the major lesions were inflammatory and were situated in the respiratory tract, the oesophagus and the stomach. There were a few fatty patches in the liver.

Browning notes a case of acute narcosis in a man who had been employed in cleaning a tank-waggon that had contained pyridine (no further details were given) (13).

Another case of acute poisoning is noted in (60). In this case a woman had been decontaminating a pyridine spillage for 15 to 20 minutes. Symptoms did not occur for ten hours and then intensified until the third day. They included speech disorders and what was recorded as "rather diffused cortical affliction" which

receded after thiamine therapy. There were no symptoms from the upper respiratory tract .

The probable lethal dose is 0.5-5.0 g/kg (54), and a LD_{Lo} for man was 500 mg/kg p.o. (48).

OSHA states that a vapor concentration in air of 3600 ppm is immediately dangerous to life and health (54).

Long-term exposure

Ludwig reported in 1935 two cases of pyridine poisoning from its industrial use (44). In one case a chemist, who had worked with crude pyridine for six months, suffered from disturbance of equilibrium, facial paralysis and attacks of loss of consciousness. These symptoms disappeared when the man stopped working with pyridine. In the other case, the symptoms after two years' exposure were paralysis of the ocular muscles with nystagmus, facial paralysis, hemiparesis with anaesthesia to heat and paraesthesia of the left side of the face, right-sided excessive perspiration, cerebellar ataxia, bladder paralysis, difficulty of hearing and neuralgic headache. The author considered these symptoms similar to Wernicke's pseudo-encephalitis.

In the treatment of epilepsy, short-term administration of 0.6 ml pyridine 3 or 4 times a day was found by Pollock *et al.* to cause minor complaints of anorexia, nausea, occasional vomiting and headache, faintness, weakness and mental depression (58). Treatment was continued in two cases for up to two months, resulting in severe liver and kidney damage (in one case fatal).

Transient symptoms from the CNS and the GI tract, without associated liver and kidney damage, have occurred in individuals exposed to pyridine concentrations averaging 125 ppm, 4 hours a day, for 1 to 2 weeks (60).

Teisinger (67) reported seven cases of chronic pyridine poisoning in a chemical plant where air samples showed concentrations of 20-42 mg/m^3. The symptoms were headache, temporary vertigo, nervousness, sleeplessness, together with occasional digestive troubles, particularly nausea and vomiting. No objective clinical signs were found in any of the cases.

In a Russian review it was noted that an examination of 88 production employees inhaling pyridine vapors at concentrations of 10 to 20 mg/m^3 showed signs of myocardial degeneration, symptoms of chronic gastritis, functional CNS changes, and sensitivity disturbances of the polyneuritic type. The incidence of these alterations increased with the duration of employment (66).

Effects on organs

Skin and mucous membranes

With exposure to pyridine vapors there are symptoms of moderate mucous membrane irritation (60). Liquid pyridine is severely irritant to skin (66). Skin irritation in rabbits is described as mild after application of 10 mg/24 h (open Draize test) or 500 mg/24 h (standard Draize test) (50).

In rabbits, the primary irritation index was estimated to 4.8 (maximum possible score=8) (26). Necrosis was observed on the scarified skin of all animals. On the intact skin individual differences were important; very slight to severe erythema with rare necrosis, no or slight oedema. In all cases no regeneration occurred after

72 h. Histopathological examination showed both lesions of necrosis and regeneration phenomena.

Pyridine acts as a photosensitizer in skin (27). Skin eruptions provoked by light, and limited to exposed surfaces, have been induced by pyridine in humans (9).

In the "maximization test" by Kligman, performed on humans, the allergenic potential of pyridine was classified as weak (grade 1) (25).

Eye

Pyridine vapor is irritating to the eyes and lids. Pure pyridine applied to rabbit eyes caused moderate injury (graded 7 on a scale of 1 to 10 after 24 h). However, an aqueous solution (0.08 M) of pyridine applied to the denuded cornea or injected into the corneal stroma caused no reaction (29).

Dutertre-Catalla *et al.* (26) classify pyridine as severely irritating to the eye. Pyridine is not only irritating but also corrosive and necrotizing for the eye.

. In a human experiment, 0.098-0.11 mg/m^3 (0.0295-0.033 ppm) pyridine temporarily affected the sensitivity of the eye to light (15, 41). The practical significance of this finding is unclear.

Lung

Rats were exposed to pyridine vapor at a concentration of 15 mg/m^3 for 60 days. During the first six days this exposure resulted in a depression of lipid formation in pneumocytes, with a reduction of protein synthetic activity of cells and a reduction in the amount of phospholipids in the surfactant. Signs of adaptation appeared the following weeks, but after the 36th day there was a fall of phospholipids in the alveolar cells and in the surface-active lining of the alveoli (56).

No data from human exposure is available.

Digestive organs

Rats exposed to pyridine (0.2 mg/l) and Ca^{2+} (100 mg/l) in their drinking water showed a thickening of the mucous membrane folds of the stomach, abundant mucous in the stomach with small amounts in the duodenum, as well as catarrhal symptoms and ulceration. When Mg^{2+} was added instead of Ca^{2+} no catarrhal symptoms or ulcerations were seen (40).

In humans, chronic exposure to pyridine may affect the GI tract and cause digestive troubles (44, 60, 67).

Liver and kidney

Chronic exposure to pyridine is toxic to the liver and kidneys. The kidney is less sensitive to pyridine-induced damage than the liver is (28).

In studies by Baxter *et al.*, already referred to (10, 11, 12), 0.1% pyridine in the diet given to rats caused death in 2-4 weeks. The principal lesions were found in the livers and the kidneys, and it was presumed that death was due to disturbances in the functions of these organs.

Rats given 50 mg/kg pyridine by gavage for 90 days showed inflammatory hepatic lesions in some of the animals (5). Increased liver weights were also noted.

Exposure to pyridine by inhalation may also cause liver damage. Guinea pigs exposed to 1000 mg/m^3 pyridine (3h/day, 4 months) exhibited toxic effects in the liver (66).

A single exposure of rats to 5000 or 10000 mg/m^3 for 40 minutes affected the kidneys' capacity to produce ammonia and their contribution to sustaining acid-alkaline balance in the body (66).

In a study where 17 anaesthetized dogs were given pyridine at various dose levels between 88 and 880 mg/kg body weight intravenously (LD_5 to LD_{50}), significant and dose-dependent increases in serum GOT and blood urea were noted, as well as decreases in serum alkaline phosphatase, indicating liver and kidney damages (70).

In man, the treatment of epilepsy with pyridine (1.85 - 2.4 ml per day for up to two months) caused progressive parenchymal destruction of the liver in two cases (58).

Heart

In the rat, intravenous administration of pyridine in doses between 1 and 15 mg/kg caused tachycardia and a small fall in blood pressure. Higher doses, up to 75 mg/kg, produced marked bradycardia and hypotension, with changes in the ECG (43). The vasodilator effect of pyridine is also referred to.

ACGIH notes that large doses of pyridine are toxic to the heart (2). It is not clear whether this refers to humans.

Nervous system

Pyridine has a narcotic action when administered to experimental animals. Effective doses by any route produce weakness, ataxia, unconsciousness and salivation (60). Also in man cases with CNS symptoms, including headache, dizziness, and fatigue, have been reported from exposures to pyridine vapor (13, 44, 59, 67).

By intravenous administration the narcotic dose in rabbits is 110 mg/kg (13, 58).

In the Wistar rat, large, i.e. more than 100 mg/kg, intravenous injections of pyridine through the jugular vein caused alterations of the spontaneous neo- and archeo-cortical bioelectrical activities (17). These alterations were reversible. Chronic treatment of rats with intraperitoneal injections of more than 330 mg/kg pyridine affected the motor behaviour of the animals. The duration of this experiment is not specified.

In an experiment on dogs, intravenous administration of pyridine (88-880 mg/kg) affected the nervous system. Commonly observed manifestations were salivation, myosis, lacrimation, nasal secretion, micturition, cloudy cornea, apnoea and death by cardiac failure, which invariably followed administration of a dose of 880 mg/kg i.v. (70).

A Russian paper states that the minimal concentration of pyridine that changed the pattern of bending reflex in rabbits by a 4-minute exposure was 400 mg/m^3. The lowest effective dose that acted on the unconditioned reflex response was 12.5 to 25 mg/kg (66).

Inhalation of high concentrations of pyridine (5000 or 10000 mg/m^3 for 40 minutes) caused accumulation of ammonia in the brain of the test rats 1 to 3 days after the exposure (66). As previously mentioned, pyridine in the drinking water (2.0 µg/ml for 3 months) caused increased lipid peroxidation in mouse brain (57).

In an *in vitro* system using cultured mouse neuroblastoma cells, pyridine inhibited the respiratory activity of the cells only at very high concentrations (ED_{50}=40 mM) (69).

Biochemical effects

Chronic administration of pyridine to rabbits and rats has been shown to induce cytochrome P-450, and to result in an increased biotransformation of pyridine and also of N-nitrosodimethylamine, alcohols and aniline (36, 51). A single injection of pyridine (10 to 200 mg/kg, i.p.) caused a dose-dependent induction of cytochrome P-450 (P450IIE1) in rat liver (38). Pyridine has also been shown to inhibit the metabolism, and thereby the clastogenicity, of benzene (30), as well as reversibly inhibit the respiratory burst in porcine and human neutrophils (32). Aromatic L-amino acid decarboxylase may be affected by pyridine (34), and pyridine has also been shown to change ammonia metabolism (66).

Reproductive effects and effects of pregnancy

When injected into chicken eggs at a dosage of 20 mg per egg, pyridine caused typical muscular hypoplasia of the legs and, very rarely, skeletal abnormalities of the neck and face. These effects were decreased with nicotinamide supplementation (42).

Pregnant guinea pigs showed increased sensitivity to the toxic effects of pyridine at chronic exposure to 1000 mg/m^3 (66).

Mutagenicity and genotoxicity

Santodonato (61) notes that pyridine was not mutagenic in an extensive assay using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA1536, and TA100. The compound was tested at 1, 10, and 100 µg/plate with or without the addition of a metabolic activation system (from 7 rat tissues). EPA reports that assays in *Salmonella typhimurium* tester strains TA98, TA100, TA1535 and TA1537 were negative following pyridine incubation (max. 10 µl sample per plate) with or without added metabolic activation (47).

A significant increase in forward mutation frequency was seen in *S. typhimurium* strain TM677 with microsomal activation (35). The minimum dose with mutagenic effect was 6 mM. For comparison, benzo(a)pyrene was mutagenic at 4 µM. However, in another study, using the same strain and 25 mM pyridine as the highest concentration, no mutagenesis was reported (63).

In the *Drosophila* sex-linked recessive lethal test pyridine was inactive in a feeding test and gave questionable results after injection (68). Also in the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay, pyridine was found not to be mutagenic (46).

Negative results were also obtained in a test on *Drosophila*, where pyridine was administered throughout the larval development of the flies at 0.01, 0.1 or 1 mM concentration in the food. Surviving treated adults, as well as the F_1 and F_2 progenies, were screened for tumors and developmental abnormalities (19).

In cultured Chinese hamster cells, Abe & Sasaki (1) reported a significant, but not dose-related, increase in the frequency of sister-chromatid exchanges, while no chromosome aberrations were found. The concentrations of pyridine used were 1, 2, and 5 mM.

In a spot test in *E. coli*, no increase in reverse mutants to Trp^+ were produced following pyridine exposure (55).

Pyridine caused a slight induction of mitotic aneuploidy in yeast at 0.8-1.3 % (73). It was suggested that pyridine interfered with tubulin assembly and disassembly causing a malfunctioning of spindle fiber microtubules.

Pyridine has also been tested for its ability to inhibit intercellular communication in the metabolic cooperation assay using Chinese hamster V79 cells and found to be negative (16).

A cooperative program on short-term assays for carcinogenicity in Japan 1973-1978 came to the conclusion that pyridine is not mutagenic (37). The assay systems used were *S. typhimurium* TA100 and TA98 (mutations), *Bacillus subtilis* (*rec* assay, without metabolic activation), hamster lung fibroblast cells (chromosome aberrations, sister chromatid exchanges), rat bone marrow cells (chromosome aberrations *in vivo*), and silk worms (mutations).

Carcinogenicity

In a study by Mason et al. (45), pyridine was administered to rats (Fischer 344) by subcutaneous injection at 3, 10, 30, or 100 mg/kg twice weekly for one year. An additional six-month latency period was allowed prior to autopsy. The incidence of injection site, mammary or total tumors was not increased in pyridine-exposed animals compared to unexposed or vehicle controls.

Hepatic nodules were reported in some rats exposed to pyridine in the diet at 0.20-0.29 % for up to 4 months (11). Lesions were not invasive and no metastases were seen, indicating their benign nature.

Santodonato (61) notes that the National Toxicology Program has conducted a chronic carcinogenicity bioassay of pyridine in which the compound was administered by gavage to rats (F344) and mice (B6C3F1), and that this bioassay has been completed and the technical report been drafted (NCI/NTP Technical Report No. 283). The report has not yet been published though. It is probably this study which is referred to in ref. (24), where it is noted that pyridine caused a positive trend for mononuclear cell leukemia in male Fischer 344 rats in a 2-year study performed by the NCI/NTP. The incidences of leukemia were 23 %, 40 % and 45% in the control, low-dose (25 mg/kg) and high-dose (50 mg/kg) groups.

Pyridine treatment also accelerated the rate of tumor growth in a cellular transplant model for leukemia in Fischer rats (24). Pyridine was given in the drinking water at doses of 0, 0.5 or 1.0 mg/ml and these doses were meant to replicate those used in the 2-year study.

A long term animal study for carcinogenesis of pyridine was scheduled to start in 1990 (53).

Dose-effect and dose-response

No dose-response data from controlled studies on man have been found in the literature. Dose-effect relations are also difficult to establish due to poor exposure data. Effects of pyridine on man are summarized in Table 1.

Some dose effect data from animal studies are shown in Tables 2 and 3.

Table 1. Summary of reported effects of pyridine on man

Exposure levels	Effect	Ref.
0.17 ppm	Odor threshold	(4)
10 ppm	Objectionable odor	(60)
700 ppm	Nose irritation threshold	(4, 65)
Occupational exposure 6-13 ppm	CNS symptoms, e.g. headache, nervousness, sleeplessness, and occasional digestive troubles	(67)
125 ppm, 4h/day for 1 to 2 weeks	Transient symptoms from the CNS and GI tract	(60)
Inhalation of unknown dose	Acute narcosis	(13)
Inhalation during 15-20 min. of unknown dose	Speech disorders 10h later	(60)
Occupational exposure to crude pyridine for six months	Disturbance of equilibrium, facial paralysis, attacks of loss of consciousness. Reversible effects.	(44)
Occupational exposure for 2 years	Wernicke's pseudo-encephalitis	(44)
1.85-2.4 ml p.o. daily for 10-30 days	Anorexia, nausea, occasional vomiting and headache, weakness, depression.	(58)
1.85-2.4 ml p.o. daily for up to two months	These were two epileptics. One died as a consequence of pyridine anti-convulsant treatment. Liver and kidney damage.	(58)
Half a cup p.o.	Died after 43h. Inflammatory lesions in the respiratory tract, the oeso-phagus and the stomach.	(31)
500mg/kg p.o.	LD_{Lo}	(48)

Table 2. Some dose-effect data for animals exposed to pyridine

Exposure	Species	Effect	Ref.
1500 mg/kg p.o	mouse	LD_{50}	(49)
1120 mg/kg, dermal	rabbit	Lethal dose	(7)
891 mg/kg p.o.	rat	LD_{50}	(49)
880 mg/kg i.v.	dog	LD_{50}	(49)
360 mg/kg i.v.	rat	LD_{50}	(49)
330 mg/kg i.p. duration unknown	rat	Altered motor behaviour	(17)
180 mg/kg s.c., twice weekly, 1 year	rat	Maximal tolerated dose	(45)
110 mg/kg i.v.	rabbit	Narcosis	(13, 58)
100 mg/kg i.v.	rat	Alterations of bioelectrical activities	(17)
75 mg/kg i.v.	rat	Bradycardia, hypotension, changes in the ECG	(43)
50 mg/kg p.o., 90 days	rat	Some inflammatory hepatic lesions	(5)
12.5-25 mg/kg	rat	ED_{Lo}, unconditioned reflex response	(66)
0.25 mg/kg, intragastric, 100 days	rat	Decrease in body weight, liver function disturbance	(66)
2.0 µg/ml in drinking water, 3 months	mouse	Brain lipid peroxidation	(57)

Table 3. Some dose-effect data for animals exposed to pyridine vapor

Exposure	Species	Effect	Ref.
23200 ppm, 1.5 h	rat	Lethal dose	(60)
4000 ppm, 4 h	rat	LD_{Lo}	(49)
1545-3090 ppm, 40 min	rat	Changes in ammonia metabolism	(66)
309 ppm, 3h/day, 4 months	guinea pig	Decrease in body weight and body temperature, hypochromic anemia, liver damage	(66)
10 or 50 ppm, 7h/day, 5 days/week for 6 months	rat	Increased relative liver weight	(8, 28)
4.6 ppm, 60 days	rat	Reduction of phospholipids in alveolar cells and in the surface-active lining of the alveoli	(56)
0.3 ppm, 2 months	rat	Minor effects on CNS function and blood proteins	(41)

Risk evaluation

Occupational exposure of pyridine is mainly through inhalation of its vapors. Pyridine may also enter the body through the skin. Accidental ingestion of pyridine has occurred. There are no data that indicate that pyridine accumulates in the body.

Exposure to pyridine vapors is irritating to the eyes and respiratory tract. Liquid pyridine is also irritating to the skin. Pyridine has moderate acute toxicity in mammals, including man. Long-term toxicity data are scarce. Mild symptoms of CNS injury (e.g., nausea, headache) may result from exposure to approximately 10 ppm. In rats, exposure to 10 ppm for three months caused increased liver weights. Most individuals can detect pyridine at a concentration in air of less than 1 ppm. The odor is not a reliable warning property though, since olfactory fatigue occurs quickly. High doses of pyridine cause liver and kidney damage.

The majority of short-term tests for mutagenicity and genotoxicity of pyridine are negative. The results of a chronic bioassay for carcinogenesis of pyridine in rat and mice, performed by the NTP and completed in 1985, have not yet been published. According to (24) a positive trend for mononuclear cell leukemia was found in the 2-year study, indicating that pyridine might accelerate the progression of this spontaneous (in Fischer rats) tumor.

The critical effect of exposure to pyridine is its effects on the central nervous system and the liver. The unpleasant, nauseating odor might be a problem at even lower exposures.

Summary

Warholm M. DEC and SCG Basis for an Occupational Health Standard. Pyridine. Arbete och Hälsa 1991:49, pp 1-20.

Pyridine is used as a solvent and as an intermediate in the production of e.g. pharmaceutical and agricultural chemicals. Occupational exposure is mainly through inhalation of its vapors. Pyridine has an unpleasant, nauseating odor and it is irritating to the eyes, skin and respiratory tract. Mild symptoms of CNS injury (e.g., nausea, headache) may result from exposure to approximately 10 ppm. Higher doses cause liver and kidney damage. Most studies on mutagenicity and genotoxicity are negative. The critical effect of pyridine seems to be its effects on the central nervous system and the liver.

Key words: Pyridine, Occupational standards, Irritation, Odor, CNS effects, Liver effects.

Sammanfattning

Warholm M. DEC and SCG Basis for an Occupational Health Standard. Pyridine. Arbete och Hälsa 1991:49, sid 1-20.

Pyridin används som lösningsmedel samt som intermediär vid tillverkning av bl.a. läkemedel och jordbrukskemikalier. Yrkesmässig exponering sker huvudsakligen genom inandning av pyridinångor. Pyridin har en skarp och obehaglig lukt samt är irriterande för ögon, hud och andningsvägar. Exponering för ca. 10 ppm kan påverka det centrala nervsystemet och ge upphov till huvudvärk och illamående. Högre doser orsakar skador på lever och njurar. De flesta studier över mutagenicitet och genotoxicitet har varit negativa. Den kritiska effekten av pyridin tycks vara påverkan på det centrala nervsystemet och levern.

Nyckelord: Pyridin, Hygieniskt gränsvärde, Irritation, Lukt, CNS-påverkan, Leverpåverkan.

References

1. Abe S, Sasaki M. Chromosome aberrations and sister chromatid exchanges in Chinese hamster cells exposed to various chemicals. J Natl Cancer Inst 58 (1977) 1635-1641.
2. ACGIH. Pyridine. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH (1986) 507.
3. Ahlström R, Berglund B, Berglund U, Lindvall T, Wennberg A. Impaired odor perception in tank cleaners. Scand J Work Environ Health 12 (1986) 574-581.
4. Amoore JE, Hautala E. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. J Appl Toxicol 3 (1983) 272-290.
5. Anderson RC. 90-Day subchronic oral toxicity in rats. Test material: Pyridine. Report No. EPA/530-SW-88-016A, 1987.
6. Anonymous. Pyridine. Natl Saf News 100 (1969) 63-65.
7. Anonymous. Pyridine. Industrial Bio-Test Laboratories, Inc., Northbrook, IL, Data Sheet No. 14-4/70, 1970.
8. Anonymous. Pyridine. The Safety Practitioner 4 (1986) 44-45.
9. Arena JM. Poisoning. 2nd ed. Charles C. Thomas, Springfield, IL, 1970.
10. Baxter JH. The mechanisms of the liver and kidney injury produced by toxic substances. I. Some effects of pyridine and their prevention by methionine. J Clin Invest 25 (1946) 908,
11. Baxter JH. Hepatic and renal injury with calcium deposits and cirrhosis produced in rats by pyridine. Am J Pathol 24 (1948) 503-525.
12. Baxter JH, Mason MF. Studies of the mechanisms of liver and kidney injury. IV. A comparison of the effects of pyridine and methyl pyridinium chloride in the rat. J Pharmacol Exp Ther 91 (1947) 350-356.
13. Browning E. Pyridine. In: Toxicity and metabolism of industrial solvents. Elsevier Publishing Company, Amsterdam (1965) 304-309.
14. Cain WS, Leaderer BP, Cannon L, Tosun T, Ismail H. Odorization of inert gas for occupational safety: Psychophysical considerations. Am Ind Hyg Assoc J 48 (1987) 47-55.
15. CEC. Solvents in commun use. Health risks to workers. Commission of the European Communities, Royal Society of Chemistry, London, UK (1988) 215-234.
16. Chen T-H, Kavanagh TJ, Chang CC, Trosko JE. Inhibition of metabolic cooperation in Chinese hamster V79 cells by various organic solvents and simple compounds. Cell Biol Toxicol 1 (1984) 155-171.
17. Clugnet MC, Laget P. Compared effects of pyrrolidine and pyridine on rat neo- and archeo-cortex. In: Remond A, Izard C (Eds.) Electrophysiological Effects of Nicotine. Elsevier/North-Holland Biomedical Press (1979) 49-59.
18. Cometto-Muniz JE, Cain WS. Thresholds for odor and nasal pungency. Physiol Behav 48 (1990) 719-725.
19. Corwin HO, Gottlieb FJ. Anthracene-induced melanotic tumors in *Drosophila*. Environ Res 15 (1978) 327-331.
20. D'Souza J, Caldwell J, Smith RL. Species variation in the N-methylation and quaternization of [^{14}C]pyridine. Xenobiotica 10 (1980) 151-157.
21. Damani LA, Crooks PA, Shaker MS, Caldwell J, D'Souza J, Smith RL. Species differences in the metabolic C- and N-oxidation, and N-methylation of [^{14}C]pyridine *in vivo*. Xenobiotica 12 (1982) 527-534.
22. Damani LA, Disley LG, Gorrod JW. The in vivo N-oxidation of 3-substituted pyridines following their intraperitoneal administration. In: Gorrod JW (Ed.) Biological Oxidation of Nitrogen. Elsevier/North-Holland Biomedical Press (1978) 157-162.

23. Damani LA, Shaker MS, Crooks PA, Godin CS, Nwosu C. N-Methylation and quaternization of pyridine *in vitro* by rabbit lung, liver and kidney N-methyltransferases: an S-adenosyl-L-methionine-dependent reaction. Xenobiotica 16 (1986) 645-650.

24. Dieter MP, Jameson CW, French JE, Gangjee S, Stefanski SA, Chhabra RS, Chan PC. Development and validation of a cellular transplant model for leukemia in Fischer rats: A short-term assay for potential anti-leukemic chemicals. Leuk Res 13 (1989) 841-849.

25. Dupuis G, Benezra C. Allergic Contact Dermatitis to Simple Chemicals. A Molecular Approach. Marcel Dekker Inc., New York and Basel, 1982.

26. Dutertre-Catalla H, Phu-Lich N, Huyen VN, Olivier L, Truhaut R, Claude J-C. Eye and skin irritation induced by picolines. Arch Toxicol (Suppl) 13 (1989) 428-432.

27.Fisher AA. Contact Dermatitis. 3rd ed. Lea & Febiger, Philadelphia (1986) 899.

28. Gehring PJ. Pyridine, homologues and derivatives. In: Parmeggiani L (Ed.) Encyclopaedia of Occupational Health and Safety. 3rd ed. Vol. 2. International Labour Office, Geneva (1983) 1810-1812.

29. Grant WM. Toxicology of the eye. 2nd ed. Charles C. Thomas, Springfield, IL (1974) 867-868.

30. Harper BL, Legator MS. Pyridine prevents the clastogenicity of benzene but not of benzo(a)pyrene or cyclophosphamide. Mutat Res 179 (1987) 23-31.

31. Helme GE. A fatal case of pyridine poisoning. Br Med J 2 (1893) 844.

32. Iizuka T, Kanegasaki S, Makino R, Tanaka T, Ishimura Y. Pyridine and imidazole reversibly inhibit the respiratory burst in porcine and human neutrophils: Evidence for the involvement of cytochrome b553 in the reaction. Biochem Biophys Res Commun 130 (1985) 621-626.

33. Jori A, Calamari D, Cattabeni F, Di Domenico A, Galli CL, Galli E, Silano V. Ecotoxicological profile of pyridine. Working party on ecotoxicological profiles of chemicals. Ecotoxicol Environ Saf 7 (1983) 251-275.

34. Juorio AV, Yu PH. Effects of benzene and pyridine on the concentration of mouse striatal tryptamine and 5-hydroxytryptamine. Biochem Pharmacol 34 (1985) 3774-3776.

35. Kaden DA, Hites RA, Thilly WG. Mutagenicity of soot and associated polycyclic aromatic hydrocarbons to *Salmonella typhimurium*. Cancer Res 39 (1979) 4152-4159.

36. Kaul KL, Novak RF. Inhibition and induction of rabbit liver microsomal cytochrome P-450 by pyridine. J Pharmacol Exp Ther 243 (1987) 384-390.

37. Kawachi T, Yahagi T, Kada T, Tazima Y, Ishidate M, Sasaki M, Sugiyama T. Cooperative programme on short-term assays for carcinogenicity in Japan. In: Montesano R, Bartsch H, Tomatis L (Eds.) Molecular and cellular aspects of carcinogen screening tests. Vol 27. International Agency for Research on Cancer, Lyon (1980) 323-330.

38. Kim SG, Novak RF. Induction of rat hepatic P450IIE1 (cyp 2E1) by pyridine: Evidence for a role of protein synthesis in the absence of transcriptional activation. Biochem Biophys Res Commun 166 (1990) 1072-1079.

39. Kim SG, Williams DE, Schuetz EG, Guzelian PS, Novak RF. Pyridine induction of cytochrome P-450 in the rat: Role of P-450j (alcohol-inducible form) in pyridine N-oxidation. J Pharmacol Exp Ther 246 (1988) 1175-1182.

40. Kondratyuk VA. Effect of pyridine dissolved in water on the mucous membrane of the stomach and intestines of experimental animals. Gig Sanit, Issue 11 (1974) 87-88.

41. Kristesashvili TS. Data to substantiate the maximum permissible concentration of pyridine in the atmosphere. Gig Sanit 30 (1965) 3-6.

42. Landauer W, Salam N. The experimental production in chicken embryos of muscular hypoplasia and associated defects of beak and cervical vertebrae. Acta Embryol Exp, Issue 1 (1974) 51-66.

43. Leslie GB, Hanahoe THP, Ireson JD, Sturman G. Some pharmacological properties of pyridine. Pharmacol Res Commun 5 (1973) 341-365.

44. Ludwig H. Zur Toxikologie des Pyridins und seiner Homologen. Arch Gewerbepathol Gewerbehyg 5 (1935) 654-664.

45. Mason MM, Cate CC, Baker J. Toxicology and carcinogenesis of various chemicals used in the preparation of vaccines. Clin Toxicol 4 (1971) 185-204.

46. McGregor DB, Brown A, Cattanach P, Edwards I, McBride D, Caspary WJ. Responses of the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay. II: 18 Coded chemicals. Environ Mol Mutagen 11 (1988) 91-118.

47. Monsanto Res. Corp. Salmonella mutagenicity assay of pyridine. EPA/OTS Document No. 878211746, 1983.

48. NIOSH. Registry of Toxic Effects of Chemical Substances. National Institute for Occupational Safety and Health, Cincinnati, OH, 1977.

49. NIOSH. Registry of Toxic Effects of Chemical Substances 1985-86. National Institute for Occupational Safety and Health, Cincinnati, OH, 1987.

50. NIOSH. Registry of Toxic Effects of Chemical Substances. National Institute for Occupational Safety and Health, Cincinnati, OH, 1989.

51. Novak RF, Kaul KL, Kim SG. Induction of the alcohol-inducible form of cytochrome P-450 by nitrogen-containing heterocycles: Effects on pyridine N-oxide production. Drug Metab Rev 20 (1989) 781-792.

52. Novello NJ. The fate of certain heterocyclic ring compounds in the animal body. J Biol Chem 74 (1927) 33-36.

53. NTP. Review of Current DHHS, DOE, and EPA Research Related to Toxicology. Fiscal year 1990. National Toxicology Program, Research Triangle Park, NC, 1990.

54. OSHA. Pyridine. In: OSHA Regulated Hazardous Substances. Health, Economic and Technological Data. Vol 2. Occupational Safety and Health Administration, Washington, DC (1990) 1689-1692.

55. Pai V, Bloomfield SF, Jones J, Gorrod JW. Mutagenicity testing of nitrogenous compounds and their N-oxidised products using Trp+ reversion in *E. coli*. In: Gorrod JW (Ed.) Biological Oxidation of Nitrogen. Elsevier/North-Holland Biomedical Press (1978) 375-382.

56. Perov OV. Condition of surfactant of the pulmonary alveoli and of pneumocyte lipid formation in subtoxic inhalation action of pyridine. Biull Eksp Biol Med 76 (1973) 29-32.

57. Pinsky C, Bose R. Pyridine and other coal tar constituents as free radical-generating environmental neurotoxicants. Mol Cell Biochem 84 (1988) 217-222.

58. Pollock LJ, Finkelman I, Arieff AJ. Toxicity of pyridine in man. Arch Intern Med 71 (1943) 95-106.

59. Reed RL. Pyridine. In: Buhler DR, Reed DJ (Eds.) Ethel Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Vol 2. Elsevier Science Publishers B. V. (1990) 259-267.

60. Reinhardt CF, Brittelli MR. Heterocyclic and miscellaneous nitrogen compounds. In: Clayton GD, Clayton FE (Eds.) Patty's Industrial Hygiene and Toxicology, 3rd ed. Vol 2A. John Wiley & Sons, New York (1981) 2719-2731.

61. Santodonato J et al. Monograph on human exposure to chemicals in the workplace: Pyridine. Center for Chemical Hazard Assessment, Syracuse Research Corporation, Syracuse, NY , Report No. SRC-TR-84-1119, 1985.

62. Schafer Jr. EW, Bowles Jr. WA, Hurlbut J. The acute oral toxicity, repellency, and hazard potential of 998 chemicals to one or more species of wild and domestic birds. Arch Environ Contam Toxicol 12 (1983) 355-382.

63. Seixas GM, Andon BM, Hollingshead PG, Thilly WG. The aza-arenes as mutagens for *Salmonella typhimurium*. Mutat Res 102 (1982) 201-212.

64. Shaker MS, Crooks PA, Damani LA. High-performance liquid chromatographic analysis of the *in vivo* metabolites of [^{14}C]pyridine. J Chromatogr 237 (1982) 489-495.

65. Sherman AH, Amoore JE, Weigel V. The pyridine scale for clinical measurement of olfactory threshold: A quantitative reevaluation. Otolaryngol Head Neck Surg 87 (1979) 717-733.

66. Tchircova EM. Pyridine. In: Izmerov NF (Ed.), Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals. International Register of Potentially Toxic Chemicals. United Nations Environment Programme. Vol 54. Centre of International Projects, GKNT, Moscow, 1984.

67. Teisinger J. Mild chronic intoxication with pyridine. Czech Med J 39 (1947). Abstract in J Ind Hyg Toxicol 30 (1948) 58.

68. Valencia R, Mason JM, Woodruff RC, Zimmering S. Chemical mutagenesis testing in *Drosophila*. III. Results of 48 coded compounds tested for the National Toxicology Program. Environ Mutagen 7 (1985) 325-348.

69. Varnbo I, Peterson A, Walum E. Effects of toxic chemicals on the respiratory activity of cultured mouse neuroblastoma cells. Xenobiotica 15 (1985) 727-733.

70. Venkatakrishna-Bhatt H, Shah MP, Kashyap SK. Toxicological effects of intravenous administration of pyridine in anaesthetized dogs. Toxicology 4 (1975) 165-169.

71. Wilke TJ, Jondorf WR, Powis G. Oxidative metabolism of ^{14}C-pyridine by human and rat tissue subcellular fractions. Xenobiotica 19 (1989) 1013-1022.

72. Zharikov GP, Titov NS. Kinetics of the absorption and elimination of pyridine and 3-methylpyridine during parenteral administration. Deposited Doc VINITI 2982-82, 1982.

73. Zimmermann FK, Gröschel-Stewart U, Scheel I, Resnick MA. Genetic change may be caused by interference with protein-protein interactions. Mutat Res 150 (1985) 203-210.

Insänt för publicering 1991-12-18

INSTRUKTION FÖR FÖRFATTARE

INNEHÅLL

I Arbete och Hälsa publiceras arbeten som utförts vid Arbetsmiljöinstitutet eller i vilka Arbetsmiljöinstitutets personal medverkat samt arbeten som utförts på Arbetsmiljöinstitutets uppdrag. Innehållet skall i första hand vara vetenskapliga originalarbeten, men även litteraturöversikter kan accepteras. Språket är i regel svenska. Doktorsavhandling skrivs vanligen på engelska.

MANUSKRIPT

Detaljerade manusanvisningar lämnas av institutets informationsenhet. Manuskriptet återges i samma skick som det skrivits ut. Manuskriptet inleds med ett titelblad, som med titeln (med versaler) i mitten och därunder författarnamnen. I övre vänstra hörnet skrivs Arbete och Hälsa, följt av årtal och löpnummer, t ex 1990:22. Numret utsätts efter ev trycklov och erhålls från informationsenheten (II), tel 08-730 98 48.

På sid 3 skrivs eventuellt ett kort **förord** som redogör för varför och hur arbetet utförts. I förordet bör även omnämnas personer som deltagit i arbetet utan att stå som medförfattare. Förordet undertecknas av projektledaren eller enhetschefen. På sid 4 bör **innehållsförteckningen** skrivas om inte manuskriptet är mycket kort.

SAMMANFATTNING

Sammanfattningar på svenska och engelska (Summary) skrivs efter texten. De bör omfatta högst ca 100 ord och inledas med arbetets författare och titel, löpnummer och uppgifter om sidantal, t ex Arbete och Hälsa 1980:5, sid 1–34. Efter texten utsätts **nyckelord** på svenska resp engelska (högst 10 per artikel). Språkgranskning av Summary görs när arbetet utsänds till referenter.

REFERENSER

Referenser skrivs efter sammanfattningarna och uppställs alfabetiskt med nummer i ordningsföljd.
Referenser anges i texten genom referenssiffran inom parentes.
Opublicerade data upptas inte i referenslistan utan i texten, t ex Pettersson (opubl 1975).
När författarnamn måste anges i texten skall författarlag med mer än två författare förkortas enl: Pettersson och medförf.
Referenser till abstracts bör inte göras.
Förkortningar av tidskrifter anges enligt Index Medicus.
Om originalartikeln ej varit tillgänglig för författaren kan istället någon referattidskrift citeras.
För de artiklar som ej är skrivna på nordiskt språk eller engelska, tyska eller franska, anges i stället titeln på engelska med angivande av originalspråk.

Exempel:

a tidskriftsartikel

1 Axelson NO, Sundell L. Mining lung cancer and smoking. Scand J Work Environ Health 4 (1978) 42–52.

2 Bergqvist U. Bildskärmsarbete och hälsa. En utvärdering av kunskapsläget. Arbete och Hälsa 9 (1986).

b kapitel ur bok

3 Birmingham DJ. Occupational dermatoses. In Clayton GD, Clayton FE (Eds). Patty's Industrial Hygiene and Toxicology, 3rd ed Vol 1. John Wiley & Sons, New York USA (1978) 203–235.

4 Kilbom Å, Hägg G. Manuell hantering. I Åstrand I. Arbetsfysiologi, 4th ed. Almqvist & Wiksell, Stockholm (1990) 136–141.

c bok

5 Klaassen CD, Amdur MO, Doull J (Eds). Casarett and Doull's Toxicology, 3rd ed. Macmillan Publ Co, New York USA 1986.

6 Olander O. Ventilation. Studentlitteratur, Lund 1982.

d artiklar inte skrivna på nordiskt språk, engelska, tyska eller franska

7 Toropkov V. The toxicology of trimellitic acid. Prof Zabol 4 (1968) 12–16 (på ryska, engelskt abstract).

e föredrag från symposium, seminarium el dyl

8 Voss M, Bergqvist U. Eye discomfort among VDT workers. Proceedings from Second international conference on Work with Display Units, Montreal, Canada September 11–14, 1989.

9 Åström A. Studier av vibrationers inverkan på balans. Nordisk hälsovetenskaplig konferens, Umeå 14–16 juni 1988.

FIGURER OCH TABELLER

Figurer sätts in i texten. Figurerna numreras i följd och förses med text, som förklarar figurernas innehåll.

Texten skrivs under figuren.

Tabeller sätts in i texten. Tabellerna numreras i följd och förses med text, som förklarar tabellernas innehåll. Tabelltexten skrivs ovanför tabellen.

På sista sidan längst ned skall anges dagen då manuskriptet inlämnas till redaktionen "Insänt för publicering 1990-00-00".

21. **Vlasta Molak:**
NIOH and NIOSH Basis for an Occupational Standard: Acrylamide: A Review of the Literature.
22. **Ronnie Lundström och Asta Lindmark:**
Akuta effekter på handens känsel efter exponering för stötformade vibrationer.
23. **Steve Kihlberg, Jan-Erik Hansson och Stig Johansson:**
Ergonomiska studier av manuella transporter med vagnar inom sjukvård och ombord på flygplan.
24. **Steve Kihlberg, Anders Kjellberg och Lars Lindbeck:**
Reaktionskrafter, rörelse, muskelaktivitet och upplevd belastning i hand/armsystemet av ryck från vinkelmutterdragare.
25. **Eva Vingård:**
Work, sports, overweight and osteoarthrosis of the hip.
26. **Bengt Åkesson:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 96. Dimetyletylamin.
27. **Marianne Byström, Ulf Landström och Anders Kjellberg**
Effekter av toner och bredbandigt buller på störningsupplevelse vid olika arbetsuppgifter
28. **Birgitta Meding:**
Handeksem. En epidemiologisk undersökning.
29. **Ewa Menckel. Med kommentarer av Lars Ettarp:**
Konsultativa förhållningssätt och aktivt ingripande. Företagshälsovård i olycksfallsförebyggande arbete.
30. **Rolf Alexandersson, Monica Dahlqvist, Göran Hedenstierna, Staffan Krantz, Nils Plato och Göran Tornling:**
Lungpåverkan och asbestexponering hos fordonsmekaniker. Asbestexponering i bil- och bussverkstäder – underlag för en lungfunktionsstudie. Lungpåverkan och asbestexponering hos fordonsmekaniker.
31. **Per Malmberg, Kjell Larsson, Anders Eklund, Britt-Marie Sundblad, Björn Sannagård, Lars Belin, Göran Blomquist och Monica Lundholm:**
Inflammatoriska förändringar i lungorna och immunstimulering hos svingårdsarbetare.
32. **Gunnar Rosén (Red):**
PIMEX. Föredrag vid en konferens om PIMEX-metoden. Solna 23 april 1991.
33. **Birgitta Kolmodin-Hedman, Britt-Inger Wenngren, Bertil Rudell, Ulrica Carstensen, Ulf Hammarström och Elsy Jönsson:**
Misstänkt hjärnstamsstörning hos svetsare vid två norrländska verkstadsindustrier.
34. **Håkan Nilsson, Sirkka Rissanen, Juhani Smolander, Kozo Hirata och Ingvar Holmér:**
Klimatfysiologisk belastning vid arbete i skyddsdräkter för asbestsanering.
35. **Anders Iregren, Andreas Seeber and Vesa Riihimäki:**
Acute effects from exposure to organic solvents: Experimental approaches and methods. Proceedings from a workshop held at the "Institut für Arbeitsphysiologie an der Universität Dortmund", March 7–9 1990.
36. **M. A. Maclaine Pont:**
DEC and NEG Basis for an Occupational Health Standard. Methyl methacrylate.
37. **Lisbeth E. Knudsen:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 97. Dimethylsulfoxid.
38. **Sven Byström:**
Physiological response and acceptability of isometric intermittent handgrip contractions.
39. **Gunnar Aronsson och Anneli Strömberg:**
Sociala och psykologiska riskfaktorer i yrkesgrupper med omfattande datoranvändning.
40. **Åsa Kilbom, Marja Mäkäräinen, Lena Sperling, Roland Kadefors, Lennart Liedberg:**
Betydelsen av verktygsutformning och individfaktorer vid arbete med plåtsax.
41. **Eva Vingård, Lars Alfredsson, Evy Fellenius, Christer Hogstedt:**
Risken för män i fysiskt tunga yrken att förtidspensioneras på grund av sjukdomar i rörelseapparaten.
42. **Ronnie Lundström, Mats Hagberg, Kerstin Johansson, Asta Lindmark, Tohr Nilsson:**
Handens känselfunktion hos plåtslagare och montörer utsatta för vibrationer.
43. **Marit Skogstad och Petter Kristensen:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 98. Trikloreten.
44. **Per Malmberg:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 99. Mikroorganismer.
45. **Gunnar Damgård Nielsen och Susanna Heissel Petersen:**
Nordiska Expertgruppen för Gränsvärdesdokumentation. 100. Acrolein.
46. **Gunnar Aronsson och Anneli Strömberg:**
Copingmönster vid datoravbrott och datorstörningar. En empirisk studie vid televerket, ett landsting och en kommun.
47. **Jessica Elert:**
The pattern of activation and relaxation during fatiguing isokinetic contractions in subjects with and without muscle pain.
48. **Gudrun Hedberg, Karl Anders Jacobsson, Urban Janlert och Stina Langendoen:**
Riskindikatorer för ischemisk hjärtsjukdom i en kohort av manliga yrkesförare.
49. **Margareta Warholm:**
DEC and SCG Basis for an Occupational Health Standard: PYRIDINE.

Skriftserien Arbete och Hälsa är utgiven av Arbetsmiljöinstitutet. Ytterligare exemplar kan rekvireras från:
ARBETSMILJÖINSTITUTET
Förlagstjänst
171 84 Solna.
Tel: 08-730 98 00

Graphic Systems AB, Göteborg 1992
KoF 185 2001

ISBN 91-7045-151-6
ISSN 0346-7821

RAPPORTEN VAN DE WERKGROEP VAN DESKUNDIGEN
(op alfabetische volgorde)

	RA
Acetaldehyde	6/92
Acrylaten	13/87
Aflatoxine B1, B2, G1 en G2	6/87
Allylglycidylether	1/92
Amyl acetate	4/90
Aniline	2/89
Anorganisch Lood	2/80
Anorganische Kwikzouten	3/82
Arc welding fume particles not containing chromium and nickel	1/93
Arseenverbindingen (Anorganische)	2/84
Asbest	1/84
Asbest, Evaluatie van risico op kanker bij beroepshalve blootstelling aan (aanvullend op RA 1/84)	9/89
Benzeen	5/89
Beryllium and Beryllium compounds	4/88
Blootstelling, Gezondheidskundige aspecten van het begrip en van het meten/schatten ervan	8/90
Butadiene(1,3-)	5/90
Cadmium	5/80
Caprolactam	4/84
Carbon disulphide	9/92
Carbon monoxide	7/92
Carbonylfluoride and PTFE Pyrolysis products	3/88
Carcinogene stoffen	3/80
Chloor	6/80
Chloroform	7/87
Chroom en chroomverbindingen	6/85
Cyclohexane	15/90
Cyclohexanol	3/90
Dibroomethaan	5/87
Dichloorethaan (1,1-)	8/87
Diisocyanates	3/91
Dimethyl- en diethylsulfaat	12/90
Dimethylamine	10/90
Dimethylhydrazine	2/87
Dinitro-ortho-cresol (4,6-)	4/87
Dioxaan (1,4-)	1/87
Epichloorhydrine	1/86
Ethyl acrylate	6/90
Ethyl acetate	10/91
Ethyl Methanesulphonate (EMS)	4/89
Ethyl amine	7/90
Ethylbenzene	9/91
Ethyleenoxide	6/89
Fenylhydrazine	2/87
Fluorcarbons(except FC11)	15/87
Fluorine compounds(inorganic)	1/89
Fluorine	1/89
Formaldehyde	3/87
Fosfine	1/80

Fijn hinderlijk stof; gezondheidskundige aspecten van bijlage 3 bij de Nationale MAC-lijst 1989	9/90	
Gasoline	3/92	
Hexaan (n-)	11/87	
Hexachlorobenzene	2/88	
Hexanone (2-)	2/90	
Hydrazine	2/87	
Hydrogenfluorine	1/89	
Hydroxyethylhydrazine	2/87	
Isopropylglycidylether	1/92	
Isopropoxyethanol (2-)	12/87	
Koolmonoxide (Carbon monoxide)	2/79	(7/92)
Kwikalkylverbindingen - Korte keten	5/82	
Kwikverbindingen (Organische)	4/82	
Lachgas (Nitrous oxide)	2/85	(2/92)
Lasrook (Arc welding fume....nickel)	1/93	
Mangaan	1/82	
Metallisch Kwik	5/81	
Methyl acrylate	1/90	
Methyleenchloride (Methylene chloride)	1/83	(8/92)
Methyl ethyl ketone	16/90	
Methyl isobutyl ketone	4/91	
Methyl Methanesulphonate (MMS)	4/89	
Methylbromide	13/90	
Monochloorethaan	2/82	
Monoketones (7/8 Carbon chain Aliphatic)	14/90	
n-Heptaan	1/81	
Nikkel en nikkelverbindingen	3/85	
Nitropropaan (2-)	1/85	
Nitrous oxide	2/92	
Ozone	4/92	
Para-Dichloorbenzeen	1/88	
Pentaan	2/81	
Phthalic anhydride	3/89	
Piperazine	7/91	
Polyvinyl chloride (PVC) dust	2/93	
Propoxyethanol (2-)	12/87	
Propoxyethylacetate (2-)	12/87	
Pyridine	3/93	
Selenium en verbindingen	7/89	
Silicon dioxide, Crystalline forms of	5/92	
Stikstofdioxide	5/85	
Styreen	8/89	
Talc dusts	6/91	
Tetrahydrofuran	1/91	
Thiourea	11/90	
Tolueen Diisocyanaat	4/80	
Tolueen	2/91	
Trichloorethaan(1,1,1-)	3/81	
Trichloorethyleen	3/83	
Trichlorofluoromethane	14/87	
Triethylamine	2/83	
Trimethylamine	9/87	
Vanadium metaal en anorganische verbingingen	10/87	
Wood dust	8/91	
Xylene	5/91	
Zwaveldioxide	4/85	

Publikaties arbeidsinspectie

Publikatiebladen

CODE		PRIJS
P 1	Inhoud verbandtrommels Middelen voor de Eerste hulp bij ongevallen op het werk Vijfde druk 1993	*f* 7,50
P 41	Zittend en staand werk, ergonomische aspecten Vierde druk 1993	*f* 16,-
P 77	Het tegengaan van beroepshuidaandoeningen Tweede druk 1983	*f* 10,-
P 88-2	Gevaarlijke stoffen in de haven; Veilig stuwen in containers; Veilig stuwen van containers Eerste druk 1984	*f* 13,-
P 89	Blauwzuur; Veilige behandeling in de haven Derde druk 1983	*f* 10,-
P 90	Zwavelwaterstof; Veilige behandeling in de haven Tweede druk 1982	*f* 10,-
P 91	Zwavelkoolstof; Veilige behandeling in de haven Tweede druk 1982	*f* 10,-
P 92	Chloor; Veilige behandeling in de haven Derde druk 1982	*f* 10,-
P 93	Chloorwaterstof; Veilige behandeling in de haven Tweede druk 1982	*f* 10,-
P 94	Fosgeen; Veilige behandeling in de haven Derde druk 1984	*f* 11,-
P 95	Allylalcohol; Veilige behandeling in de haven Derde druk 1984	*f* 11,-
P 96	Fluor; Veilige behandeling in de haven Tweede druk 1982	*f* 10,-
P 97	Fluorwaterstof; Veilige behandeling in de haven Derde druk 1984	*f* 11,-
P 98	Acetoncyaanhydrine; Veilige behandeling in de haven Tweede druk 1984	*f* 11,-
P 99	Chloorpicrine; Veilige behandeling in de haven Tweede druk 1984	*f* 11,-
P 100	Acrylnitril; Veilige behandeling in de haven Tweede druk 1981	*f* 10,-
P 101	Zwaveldioxide; Veilige behandeling in de haven Tweede druk 1982	*f* 10,-
P 102	Epichloorhydrine; Veilige behandeling in de haven Tweede druk 1984	*f* 11,-
P 103	Allylchloride; Veilige behandeling in de haven Tweede druk 1984	*f* 11,-
P 104	Broom; Veilige behandeling in de haven Derde druk 1986	*f* 11,-
P 105	Broomwaterstof; Veilige behandeling in de haven Tweede druk 1984	*f* 10,-
P 107	Acetonitril; Veilige behandeling in de haven Tweede druk 1986	*f* 11,-
P 108	Methylbromide; Veilige behandeling in de haven Derde druk 1984	*f* 11,-

Chemie (gevaarlijke stoffen)

CODE		PRIJS
P 109	Acroleïne; Veilige behandeling in de haven Derde druk 1984	*f* 11,-
P 110	Loodakylverbindingen; Veilige behandeling in de haven Tweede druk 1984	*f* 11,-
P 111	Paration; Veilige behandeling in de haven Tweede druk 1984	*f* 11,-
P 112-1	Ademhalingsbeschermingsmiddelen; Overzicht en toepassing Vierde druk 1985	*f* 14,-
P 112-2	Ademhalingsbeschermingsmiddelen; Overzicht en beschrijving Eerste druk 1985	*f* 20,-
P 112-3	Keuzetabel Ademhalingsbeschermingsmiddelen Tweede druk 1983	*f* 15,-
P 130	Laboratoria; Veiligheid bij gebruik van gevaarlijke stoffen Eerste druk 1982	*f* 26,-
P 130-1	Laboratoria; Veiligheid en hygiëne Algemeen Tweede druk 1982	*f* 16,-
P 134-1	Zweminrichtingen; Wettelijke bepalingen Derde druk 1982	*f* 11,-
P 134-2	Zweminrichtingen; De opslag en het gebruik van natrium hypochloriet (—chloorbleekloog) Vierde druk 1988	*f* 11,-
P 134-3	Zweminrichtingen; De opslag en het gebruik van zoutzuur Vierde druk 1988	*f* 11,-
P 134-4	Zweminrichtingen; De opslag en het gebruik van zwavelzuur Vierde druk 1988	*f* 11,-
P 134-5	Zweminrichtingen; De opslag en het gebruik van kooldioxide Eerste druk 1980	*f* 12,-
P 139	Verfverwerking Tweede druk 1986	*f* 13,-
P 145	Nationale MAC-lijst 1992 Achtste druk 1992	*f* 16,-
PMAC	Zakboek MAC-waarden 1989	*f* 9,-
P 167	Chemisch reinigen van textiel Eerste druk 1987	*f* 13,-
P 171-1	Vaklokalen en theorievaklokalen; Scheikunde Eerste druk 1988	*f* 14,-
P 172-1	Arbeidsveiligheidsrapport; Leidraad aanwijzing AVR-plichtige installaties Eerste druk 1988	*f* 14,-
P 172-1E	Occupational Safety Report; Designatory guidelines for AVR-mandatory installations First edition 1988	*f* 14,-
P 172-2	Arbeidsveiligheidsrapport; Leidraad voor het samenstellen Eerste druk 1989	*f* 15,-
P 172-2E	Occupational Safety Report; Guideline for compilation Eerste druk 1990	*f* 15,-
P 182	Gevarenzone-indeling met betrekking tot gasontploffingsgevaar Eerste druk 1992	*f* 27,-
P 184	Werken met beeldschermen Eerste druk 1992 ISBN 9039903735	*f* 20,-

Concept-publikatiebladen

CODE		PRIJS
CP 1	Het werken met recombinant DNA in CI- en CII-laboratoria Eerste druk 1980	f 19,-
CP 8	Veilig werken met PCB's en apparaten die PCB's bevatten Eerste druk 1985	f 20,-
CP 19	Tapruimten en taplokalen voor gevaarlijke stoffen Eerste druk 1990	f 21,-
CP 22	Tankauto's; Laden en lossen van gevaarlijke stoffen Eerste druk 1990	f 15,-
CP 35	Produktiekennisgeving in het kader van het kennisgevingsstelsel Wet Milieugevaarlijke Stoffen Eerste druk 1992	f 17,50
CP 36	Ergonomische richtlijnen voor informatieoverdracht bij procesbesturing Eerste druk 1992	f 22,50

Voorlichtingsbladen

CODE		PRIJS
V 1-E	The impact op modifications in the process-industry on safety Eerste druk 1981	f 11,-
V 5	Technische inspectie van installaties in de procesindustrie; Enkele principes en achtergronden Eerste druk 1982	f 21,-
V 5-E	Technical inspection of installations in the process-industry; Basic principles and background Eerste druk 1983	f 21,-
V 6	Instrumentele beveiligings- en gevaardetectiesystemen in de procesindustrie; Enkele principes en grondslagen Eerste druk 1984	f 29,-
V 7	Procesveiligheidsanalyse; Aanzet tot het opsporen van inherente procesgevaren Eerste druk 1984	f 31,-
V 7-E	Process safety analysis; Incentive for the identification of inherent process hazards Eerste druk 1985	f 30,-
V 9	Beroepshuidaandoeningen; Handleiding onderzoek Eerste druk 1985	f 32,-
V 11	Checklist procesinstallaties; Aandachtspunten voor een veilig ontwerp Tweede druk 1986	f 31,-
V 11-E	Checklist processing plants Tweede druk 1989	f 26,-
V 14	Explosiebestendige controlegebouwen in de procesindustrie Eerste druk 1977	f 11,-
V 18	Procedures in de procesindustrie; Voorbeelden en voorstellen met betrekking tot het ontwikkelen, invoeren en beheren van procedures in de procesindustrie Eerste druk 1989	f 25,-

CODE		PRIJS
V 18-E	Procedures in the process industry; Examples and proposals concerning development, introduction and controlof procedures in the process-industry Eerste druk 1989	f 21,-
V 23	Gevaren van statische elektriciteit in de procesindustrie Tweede druk 1991 ISBN 9053071903	f 36,-

Concept-voorlichtingsbladen

CODE		PRIJS
CV 2	Hoe te handelen bij blootstelling aan longbeschadigende gassen of dampen Eerste druk 1981	f 21,-
CV 4	Acrylnitril; Technisch-arbeidshygiënische voorzieningen Eerste druk 1983	f 26,-
CV 12	Ademhalingsbescherming; Fysiologische en gezondheidsaspecten Eerste druk 1989	f 24,-
CV 14	Veiligheid van gebouwen in de procesindustrie; Aandachtspunten bij ontwerp, constructie en gebruik Eerste druk 1989 ISBN 9053070028	f 39,-
CV 21	Procesbeheersingssystemen aandachtspunten voor een veilige en correcte toepassing Eerste druk 1991 ISBN 905307192X	f 34,-
CV 28	Afgasbehandelingssystemen Eerste druk 1992 ISBN 9053072993	f 25,-

Studies

CODE		PRIJS
S 20	Acute intoxicaties in de werksituatie April 1986	f 20,-
S 20-1	Acute intoxicaties in de werksituatie Februari 1989	f 20,-
S 20-2	Acute intoxicaties in de arbeidssituaties in 1989 Maart 1991	f 19,-
S 20-3	Acute intoxicaties in de arbeidssituaties in 1990 September 1991	f 20,-
S 28	Blaastumoren als beroepsziekten ten gevolge van blootstelling aan chemische stoffen Oktober 1986	f 34,-
S 29-1	Chronische effecten tengevolge van blootstelling aan organische oplosmiddelen; Samenstelling, voorkomen, blootstellingsniveaus en effecten December 1986	f 26,50
S 29-2	Chronische effecten tengevolge van blootstelling aan organische oplosmiddelen; Effecten van blootstelling aan organische oplosmiddelen op het centrale zenuwstelsel November 1986	f 21,50
S 30	Protocollen voor de bedrijfsgezondheidszorg; Verzamelband	f 12,-
S 30-1	Algemeen April 1987	f 19,-
S 30-2	Benzeen April 1987	f 9,-
S 30-3	Styreen April 1987	f 9,-

CODE		PRIJS
S 30-4	Xylenen April 1987	f 9,-
S 30-5	Trichlooretheen April 1987	f 9,-
S 30-6	Tetrachlooretheen April 1987	f 9,-
S 30-7	Zwavelkoolstof April 1987	f 9,-
S 30-8	Lood en zijn ionverbindingen Juni 1988	f 9,-
S 30-9	Chloroform Juni 1989	f 9,-
S 30-10	Molybdeen en anorganische molybdeenverbindingen Juni 1989	f 9,-
S 30-11	Metallisch kwik (A); Kwikzouten (B); Organische kwikverbindingen Juni 1989	f 9,-
S 30-12	Mangaan en anorganische mangaanverbindingen Juni 1989	f 9,-
S 30-13	Antimoon en antimoonverbindingen Juni 1989	f 9,-
S 30-14	Tetraethyllood; Tetramethyllood Juni 1989	f 9,-
S 30-15	Methanol Juli 1990	f 9,-
S 30-16	Fenol Juli 1990	f 9,-
S 30-17	n-Hexaan Juli 1990	f 9,-
S 30-18	Methyl-n-butylketon (2-hexanon) Juli 1990	f 9,-
S 30-19	Isopropylbenzeen (cumeen) Juli 1990	f 9,-
S 47	Werkterreinanalyse van trichloormonofluormethaan (freon-11) December1988	f 21,50
S 48	Werkterrein-analyse van hexachloobenzeen December 1988	f 12,50
S 49	Werkterreinanalyse van 1,3-butadieen December 1988	f 19,-
S 50	Beroepsmatige blootstelling aan organische stof en de daarmee samenhangende risico's voor de gezondheid December 1988	f 47,50
S 62	Werkterreinanalyse van anorganische oplosbare fluoriden April 1989	f 26,50
S 63	Werkterreinanalyse van 1,2-dichloor-ethaan April 1989	f 20,-
S 64	Werkterreinanalyse van aniline Tweede druk 1991 ISBN 9053071415	f 21,50
S 65	Werkterreinanalyse van cyclohexanol April 1989	f 17,50
S 116	Arbeidsomstandigheden in de chemische industrie April 1991 ISBN 9053071628	f 35,-

Commissie preventie van rampen door gevaarlijke stoffen

CODE		PRIJS
CPR 2	Model voor risico-evaluatie van opslag van gevaarlijke stoffen, vloeistoffen en gassen Eerste druk 1982	f 19,-
CPR 3	Organische peroxiden; Opslag Eerste druk 1982	f 29,-
CPR 3-E	Storage of organic peroxides Eerste druk 1982	f 30,-
CPR 4	Experimenten met chloor (rapporten) Eerste druk 1979	f 46,-
CPR 5	Vloeibare zuurstof; Opslag van 0,45 -100 m3 Eerste druk 1983	f 21,-
CPR 6	Vloeibare zwaveldioxide Eerste druk 1983	f 32,50
CPR 7	De bewaring van springstoffen en ontstekingsmiddelen Eerste druk 1983	f 14,-
CPR 8-1	Supplement Autogas (LPG) Supplement 1988	f 22,50
CPR 8-2	LPG-Tankwagens Eerste druk 1985	f 27,50
CPR 8-3	Distributiedepots voor LPG (Butaan, Propaan en hun mengsels) Eerste druk 1991 ISBN 9053071652	f 42,50
CPR 9-1	Vloeibare aardolieprodukten; Ondergrondse opslag in stalen tanks en afleverinstallaties voor motor-brandstof Concept vijfde druk 1991	f 26,-
CPR 9-2	Vloeibare aardolieprodukten; Bovengrondse opslag kleine installaties Eerste druk 1985	f 29,-
CPR 9-3	Vloeibare aardolieprodukten; Bovengrondse opslag grote installaties Eerste druk 1984	f 36,-
CPR 9-5	Vloeibare aardolieprodukten; Ondergrondse opslag van vloeibare produkten in kunststof tanks Eerste druk 1992 ISBN 9039903727	f 27,50
CPR 10	Chloor; Opslag en gebruik Tweede druk 1983	f 36,-
CPR 11-1	Propaan; Het gebruik van propaan op bouwterreinen Eerste druk 1984	f 35,-
CPR 11-2	Propaan (5 m3); De opslag van propaan en butaan in stationaire bovengrondse reservoirs met een inhoud groter dan 0,15 m3 en ten hoogste 5 m3 Eerste druk 1986	f 34,-
CPR 11-3	Propaan; Opslag van propaan en butaan in stationaire bovengrondse- en terpreservoirs met een inhoud groter dan 5 m3 en ten hoogste 150 m3 Eerste druk 1990 ISBN 9053070591	f 36,-
CPR 11-4	Propaan; Toepassing van propaan in wegenbouwmachines en onkruidbestrijdingsmachines Eerste druk 1990 ISBN 9053070605	f 19,-
CPR 11-5	Propaan vulstations van butaan- en propaanflessen Concept eerste druk 1991	f 41,-
CPR 12	Methoden voor het bepalen en verwerken van kansen Eerste druk 1985	f 127,50
CPR 12-E	Methods for determining and processing probabilities Eerste druk 1988	f 127,50
CPR 13	Ammoniak; Vervoer, opslag en toepassingen Tweede druk 1988	f 46,-
CPR 14	Methoden voor het berekenen van fysische effecten Eerste druk 1988	f159,-
CPR 14-E	Methods for the calculation of physical effects Tweede druk 1991	f156,-

CODE		PRIJS
CPR 15-1	Opslag gevaarlijke stoffen in emballage; Opslag van vloeistoffen en vaste stoffen (0 tot 10 ton) Tweede druk 1990 ISBN 9053070338	*f* 20,-
CPR15-1E	Storage of Packaged Hazardous Materials; Storage of liquids and solids (0-10 tons) Eerste druk 1992	*f* 19,-
CPR 15-2	Opslag gevaarlijke stoffen, chemische afvalstoffen en bestrijdingsmiddelen in emballage; opslag van grote hoeveelheden Eerste druk 1991 ISBN 9053072128	*f* 22,50
CPR 15-3	Opslag van bestrijdingsmiddelen in emballage; Opslag van bestrijdingsmiddelen in distributiebedrijven en aanverwante bedrijven (vanaf 400 kg) Eerste druk 1990 ISBN 9053071024	*f* 21,-
CPR15-3E	Storage of Packaged pesticides Storage of pesticides in distribution and related enterprises (in excess of 400 kg) Eerste druk 1992	*f* 21,-
CPR 16	Methoden voor het bepalen van mogelijke schade aan mensen en goederen door het vrijkomen van gevaarlijke stoffen Eerste druk 1990	*f*159,-
CPR 16E	Methods for the determination of possible damage to people and objects resulting from releases of hazardous materials Eerste druk 1992	*f*159,-

R-bladen

CODE		PRIJS
R 1	Voorlopige richtlijnen voor de beveiliging van stookinstallaties met een maximum belasting groter dan 600 kW in de procesindustrie en die gestookt worden met gasvormige of vloeibare brandstoffen Eerste druk 1978	*f* 29,-
R 1-E	Provisional guidelines for the safeguarding of fuel-burning installations with a maximum try and fired gaseous or liguid fuels Eerste druk 1979	*f* 36,-
R 2-E	Guide for the classification of hazardous areas in zones in relation to gasexplosion hazards and to the installation and selection of electrical apparatus Eerste druk 1980	*f* 31,-
R 3-E	Hazard and operability study; Why? When? How? Eerste druk 1979 (Nederlandse uitgave zie V2)	*f* 24,-

Overige publikaties

CODE		PRIJS
OP 1	Experimenten met acrylnitril Eerste druk 1971	*f* 19,-
OP 1-E	Experiments with Acrylonitrile Eerste druk 1972	*f* 19,-
OP 2	Experimenten met acrylnitril; Blusproeven (Nederlands en Engels) Eerste druk 1972	*f* 20,-
OP 3	Experimenten met chloor Eerste druk 1975	*f* 16,-
OP 3-E	Experiments with chlorine Eerste druk 1975	*f* 16,-
OP 9	Leidraad voor oliepijpleidingen Eerste druk 1973	*f* 21,-
OP 12	De opslag en het vervoer van acrylnitril Eerste druk 1970	*f* 22,50
OP 14	De opslag en het gebruik van fosgeen Eerste druk 1977	*f* 31,-
OP 17	Voorlopige richtlijn voor de beveiliging van met olie/aardgas gestookte éénbranderinstallaties met een maximum belasting groter dan 600 kW Eerste druk 1975	*f* 13,-

Gezondheidskundige adviezen van de werkgroep van deskundigen ter vaststelling van MAC-waarden

CODE		PRIJS
RA 2/79	Grenswaarde Koolmonoxyde	*f* 29,-
RA 1/80	Grenswaarde Fosfine	*f* 15,-
RA 2/80	Grenswaarde anorganisch lood	*f* 22,50
RA 3/80	Grenswaarde Carcinogene stoffen	*f* 20,-
RA 4/80	Grenswaarde Tolueen Diisocyanaat	*f* 9,-
RA 5/80	Grenswaarde Cadmium	*f* 20,-
RA 6/80	Grenswaarde Chloor	*f* 16,-
RA 1/81	Grenswaarde n-Heptaan	*f* 14,-
RA 2/81	Grenswaarde Pentaan	*f* 11,-
RA 3/81	Grenswaarde 1,1,1,-Trichloorethaan	*f* 22,50
RA 5/81	Grenswaarde metallisch kwik	*f* 16,-
RA 1/82	Grenswaarde Mangaan	*f* 21,-
RA 2/82	Grenswaarde Monochloorethaan	*f* 14,-
RA 3/82	Grenswaarde anorganische kwikzouten	*f* 19,-
RA 4/82	Grenswaarde organische kwikverbindingen (uitsluitend phenyl-kwik en alkoxyalkylverbindingen)	*f* 16,-
RA 5/82	Grenswaarde kwikalkylverbindingen korte keten (uitsluitend methylkwik en ethylkwik)	*f* 22,50
RA 1/83	Grenswaarde Methyleenchloride	*f* 21,-
RA 2/83	Grenswaarde Triethylamine	*f* 20,-
RA 3/83	Grenswaarde Trichloorethyleen	*f* 22,50
RA 1/84	Asbest	*f* 35,-
RA 2/84	Grenswaarde anorganische Arseenverbindingen (exclusief Arseenwaterstof)	*f* 25,-
RA 4/84	Grenswaarde Caprolactam	*f* 21,-
RA 1/85	Grenswaarde 2-Nitropropaan	*f* 15,-
RA 2/85	Grenswaarde Lachgas	*f* 26,-
RA 3/85	Grenswaarde Nikkel en nikkelverbindingen	*f* 26,-
RA 4/85	Grenswaarde Zwaveldioxide	*f* 21,-
RA 5/85	Grenswaarde Stikstofdioxide	*f* 19,-
RA 6/85	Grenswaarde Chroom en chroomverbindingen	*f* 25,-
RA 1/86	Grenswaarde Epichloorhydrine	*f* 24,-
RA 1/87	Grenswaarde 1,4-Dioxaan	*f* 16,-
RA 2/87	Grenswaarde Hydrazine, dimethylhydrazine, hydroxyethyl-hydrazine en fenylhydrazine	*f* 26,-
RA 3/87	Grenswaarde Formaldehyde (engelse uitgave)	*f* 27,50
RA 4/87	Grenswaarde 4,6-Dinitro-orhtocresol	*f* 16,-
RA 5/87	Grenswaarde Dibroomethaan	*f* 16,-
RA 6/87	Grenswaarde Aflatoxine B1, B2, G1 en G2	*f* 20,-

CODE		PRIJS
RA 7/87	Grenswaarde Chloroform	f 22,50
RA 8/87	Grenswaarde 1,1-Dichloorethaan	f 11,-
RA 9/87	Grenswaarde Trimethylamine	f 16,-
RA 10/87	Grenswaarde Vanadium metaal en anorganische verbindingen	f 20,-
RA 11/87	Grenswaarde n-Hexaan	f 26,-
RA 12/87	Grenswaarde 2-Propoxyethanol, 2-Propoxyethyl acetate, 2-Isopropoxyethanol	f 11,-
RA 13/87	Grenswaarde Acrilaten	f 16,-
RA 14/87	Grenswaarde Trichlorofluoromethane (engelse uitgave)	f 20,-
RA 15/87	Grenswaarde Fluorcarbons (except FC11) (engelse uitgave)	f 26,-
RA 1/88	Grenswaarde Para-Dichloorbenzeen	f 19,-
RA 2/88	Grenswaarde Hexachloorbenzeen (engelse uitgave)	f 30,-
RA 3/88	Grenswaarde Carbonylfluoride and PTFE Pyrolysis products (engelse uitgave)	f 14,-
RA 4/88	Grenswaarde Beryllium and Beryllium compounds (engelse uitgave)	f 27,50
RA 1/89	Grenswaarde Fluorine, Hydrogenfluoride and Inorganic Fluoride Compounds (engelse uitgave)	f 27,50
RA 2/89	Grenswaarde Aniline (engelse uitgave)	f 21,-
RA 3/89	Grenswaarde Phtalic anhydride (engelse uitgave)	f 15,-
RA 4/89	Grenswaarde Ethyl Methanesulphonate (EMS) Methyl Methanesulphonate (MMS) (engelse uitgave) ISBN 9053070354	f 27,50
RA 5/89	Grenswaarde Benzeen ISBN 9053070362	f 13,-
RA 6/89	Grenswaarde Ethyleenoxide ISBN 9053070370	f 16,-
RA 7/89	Grenswaarde Selenium en verbindingen ISBN 9053070389	f 22,50
RA 8/89	Grenswaarde Styreen ISBN 9053070397	f 21,-
RA 9/89	Evaluatie van het risico op kanker bij beroepshalve blootstelling aan asbest ISBN 9053070559	f 15,-
RA 1/90	Grenswaarde Methyl acrylate (engelse uitgave) ISBN 9053070648	f 17,-
RA 2/90	Grenswaarde 2-Hexanone (engelse uitgave) ISBN 9053070656	f 21,-
RA 3/90	Grenswaarde Cyclohexanol (engelse uitgave) ISBN 9053070702	f 20,-
RA 4/90	Grenswaarde Amyl acetate (engelse uitgave) ISBN 9053070710	f 14,-
RA 5/90	Grenswaarde 1,3 Butadiene (engelse uitgave) ISBN 9053070834	f 21,-
RA 6/90	Grenswaarde Ethyl acrylate (engelse uitgave) ISBN 9053070818	f 19,-
RA 7/90	Grenswaarde Ethylamine (engelse uitgave) ISBN 9053070826	f 16,-
RA 8/90	Gezondheidskundige aspecten van het begrip blootstelling en van het meten/schatten ervan	f 32,50
RA 9/90	Fijn hinderlijk stof; gezondheidskundige aspecten van bijlage 3 bij de Nationale MAC-lijst 1989 ISBN 9053071067	f 27,50
RA 10/90	Grenswaarde dimethylamine (engelse uitgave) ISBN 9053071105	f 20,-
RA 11/90	Grenswaarde thiourea (engelse uitgave) ISBN 9053071091	f 14,-

CODE		PRIJS
RA 12/90	Grenswaarde dimethyl- en diethylsulfaat ISBN 9053071113	f 17,-
RA 13/90	Grenswaarde methylbromide (engelse uitgave) ISBN 9053071121	f 22,50
RA 14/90	Grenswaarde 7/8-carbon chain aliphatic monoketons: 2-heptanone, 3-heptanone, ethylamylketone, methylisoamylketone (engelse uitgave) ISBN 905307113X	f 21,-
RA 15/90	Grenswaarde cyclohexane (engelse uitgave) ISBN 9053071148	f 17,-
RA 16/90	Grenswaarde methyl ethyl ketone (engelse uitgave) ISBN 9053071296	f 21,-
RA 1/91	Grenswaarde tetrahydrofuran (engelse uitgave) ISBN 9053070710	f 22,50
RA 2/91	Grenswaarde tolueen ISBN 9053071482	f 26,-
RA 3/91	Grenswaarde diisocyanates (engelse uitgave) ISBN 9053071636	f 27,50
RA 4/91	Grenswaarde methyl isobutyl ketone (engelse uitgave) ISBN 9053072055	f 21,-
RA 5/91	Grenswaarde xylene (engelse uitgave) ISBN 9053072098	f 34,-
RA 6/91	Grenswaarde talc dusts (engelse uitgave) ISBN 9053072101	f 24,-
RA 7/91	Grenswaarde piperazine (engelse uitgave) ISBN 9053072438	f 20,-
RA 8/91	Grenswaarde wooddust (engelse uitgave) ISBN 9053072446	f 29,-
RA 9/91	Grenswaarde ethylbenzene (engelse uitgave)	f 26,-
RA10/91	Grenswaarde ethyl acetate (engelse uitgave)	f 22,50
RA 1/92	Grenswaarde allyl glycidil ether and isopropyl glycidyl (engelse uitgave)	f 20,-
RA 2/92	Grenswaarde Nitrous oxide (engelse uitgave)	f 24,-
RA 3/92	Grenswaarde Gasoline (engelse uitgave)	f 25,-
RA 4/92	Grenswaarde Ozone (engelse uitgave)	f 25,-
RA 5/92	Grenswaarde Crystalline forms of silicon dioxide (free silica) (engelse uitgave)	f 27,50
RA 6/92	Grenswaarde Acetoldehyde (engelse uitgave)	f 21,-
RA 7/92	Grenswaarde Carbon Monoxide (engelse uitgave)	f 18,40
RA 8/92	Grenswaarde Methylene Chloride (engelse uitgave)	f 21,-
RA 9/92	Grenswaarde Carbon Disulphide (engelse uitgave)	f 37,50
RA 1/93	Grenswaarde arcwelding fume particles not containing chromium and nickel (engelse uitgave) ISBN 9039904618	f 30,-
RA 2/93	Grenswaarde Polyvinyl Chloride (engelse uitgave) ISBN 9039905177	
RA 3/93	Grenswaarde Pyridine (engelse uitgave) ISBN 9039905185	

Signaalintekening en clusters met 25% korting

U wilt goed gedocumenteerd zijn op uw vakgebied? Wanneer u zich abonneert op één of meerdere onderstaande signaalintekeningen ontvangt u automatisch alle nieuwe publikaties van de Arbeidsinspectie op uw vakgebied met een korting van 25% op de normale verkoopprijs. U kunt tevens complete clusters bestellen met alle publikaties op uw vakgebied. Vermelde prijzen zijn indicaties.

Alle publikaties van de Arbeidsinspectie tezamen
bestelcode DGACOMPLEET, ca. *f* 12.000,-
bestelcode signaalintekening BGSICPL
Complete set publikatiebladen
bestelcode DGAPBLAD, ca. *f* 1500,-
bestelcode signaalintekening BGSIPBLAD
Bouwbedrijf
bestelcode DGABOUW, ca. *f* 625,-
bestelcode signaalintekening BGSIBOUW
Havenbedrijf
bestelcode DGAHAVEN, ca. *f* 620,-
bestelcode signaalintekening BGSIHAVEN
Land-, tuin- en bosbouw
bestelcode DGALAND, ca. *f* 630,-
bestelcode signaalintekening BGSILAND
Houtbewerking
bestelcode DGAHOUT, ca. *f* 610,-
bestelcode signaalintekening BGSIHOUT
Metaalnijverheid
bestelcode DGAMETAAL, ca. *f* 650,-
bestelcode signaalintekening BGSIMETAAL
Garagebedrijf
bestelcode DGAGARAGE, ca. *f* 350,-
bestelcode signaalintekening BGSIGARAGE
Chemie (gevaarlijke stoffen)
bestelcode DGACHEMIE, ca. *f* 4225,-
bestelcode signaalintekening BGSICHEMIE
Elektrotechniek
bestelcode DGAELEKTRO, ca. *f* 150,-
bestelcode signaalintekening BGSIELEKTRO
Hijs- en hefwerktuigen
bestelcode DGAHIJS, ca. *f* 168,-
bestelcodesignaalintekening BGSIHIJS

Nieuwsbrief

Actuele informatie over nieuw verschenen publikaties van de Arbeidsinspectie.
Verschijnt periodiek. Bestelcode BGNWSDGA, prijs van een jaarabonnement *f* 79,- (incl. BTW en verzendkosten).

Catalogus

De catalogus publikaties Arbeidsinspectie geeft een volledig overzicht van alle uitgaven van de Arbeidsinspectie. U kunt deze gratis aanvragen en/of een abonnement nemen op de nieuwe edities.
Bestelcode TSCATDGA
Bestelcode abonnement BGTSCATDGA

Adressen

Informatie over de activiteiten van de Arbeidsinspectie is te verkrijgen bij onderstaande adressen.

Arbeidsinspectie

1e district
Maastricht
Postbus 300, 6200 AH
Sint Pieterskade 26, 6212 AD
Telefoon (043) 219251
Telefax (043) 213052

2e district
Breda
Postbus 90109, 4800 RA
Vismarktstraat 28, 4811 WE
Telefoon (076) 223400
Telefax (076) 229470

3e district
Rotterdam
Stadionweg 43c, 3077 AS
Postbus 9580, 3007 AN
Telefoon (010) 4798300
Telefax (010) 4797093

4e district
Nieuwegein
Postbus 7001, 3430 JA
Florijnburg 41, 3437 SR
Telefoon (03402) 94511
Telefax (03402) 40905

5e district
Zoetermeer
Postbus 3013, 2700 KN
Boerhaavelaan 3, 2713 HA
Telefoon (079) 710101
Telefax (079) 511773

6e district
Amsterdam
Leeuwendalersweg 21,1055 JE
Telefoon (020) 5812612
Telefax (020) 864703

7e district
Groningen
Postbus 30016, 9700 RM
Engelse Kamp 4, 9722 AX
Telefoon (050) 225880
Telefax (050) 267202

8e district
Deventer
Postbus 5011, 7400 GC
Smedenstraat 284, 7411 RD
Telefoon (05700) 14745
Telefax (05700) 17208

Bestel/faxbiljet RA-rapporten Arbeidsinspectie

Graag ontvang ik rechtstreeks/via boekhandel_____
de hieronder vermelde uitgaven

AANTAL	CODE	
		naam
		t.a.v.
		adres
		postcode
		plaats
		functie
		Handtekening

Stuur een kopie van dit bestelbiljet naar: Sdu Uitgeverij Plantijnstraat, afd. Verkoop Publikaties Arbeidsinspectie (K2301), postbus 20014, 2500 EA Den Haag
Rechtstreeks bestellen kan ook: **telefoon** (070) 378 98 84, **fax** (070) 381 77 71

Genoemde prijzen zijn incl. BTW, excl. verzendkosten. Prijswijzigingen voorbehouden

Arbeidsinspectie
Kijk op gezond en veilig werk

Sdu Uitgeverij Plantijnstraat

BESTELADRES PUBLIKATIES ARBEIDSINSPECTIE

Sdu Uitgeverij Plantijnstraat
Afdeling Verkoop Arbeidsinspectie, kamer 2301
Postbus 20014, 2500 EA Den Haag
Telefoon (070) 378 98 84, Fax (070) 381 77 71

ISBN 90 399 0518 5