



German Chemical Society
Gesellschaft Deutscher Chemiker

GDCh-Advisory Committee
on Existing Chemicals of
Environmental Relevance (BUA)

2-Nitrophenol

(2-Hydroxy-nitrobenzene)

4-Nitrophenol

(4-Hydroxy-nitrobenzene)

BUA Report 75
(February 1992)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1993

GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA)

Chairman:

Prof. Dr. E. Bayer, Institut für Organische Chemie der Universität Tübingen

Members:

Dr. G. Alfke, Mineralölwirtschaftsverband e. V., Hamburg
Prof. Dr. K. Ballschmiter, Abteilung Analytische Chemie und Umweltchemie der Universität Ulm
Dr. R. Bias, BASF AG, Emissionsüberwachung und Ökologie, Ludwigshafen a. Rh.
Dr. B. Broecker, HOECHST AG, Abteilung Umweltchemikalien/Verbrauchersicherheit, Frankfurt am Main
Prof. Dr. O. Fränzle, Geographisches Institut der Universität Kiel
Prof. Dr. F. H. Frimmel, DVGW-Forschungsstelle am Engler-Bunte-Institut der Universität Karlsruhe
Prof. Dr. H.-P. Gelbke, BASF AG, Toxikologie, Ludwigshafen a. Rh.
Prof. Dr. H. Greim, GSF - Institut für Toxikologie, Neuherberg (Vice Chairman)
Dr. H. Jungen, Deutsche Wissenschaftliche Gesellschaft für Erdöl, Erdgas und Kohle e. V., Hamburg
Dir. und Prof. Dr. D. Kayser, Bundesgesundheitsamt, Berlin
Prof. Dr. P. Müller, Institut für Biogeographie, Universität des Saarlandes, Saarbrücken
Dir. und Prof. Dr. E. Offhaus, Umweltbundesamt, Berlin
Dr. R. Ott, Deutsche Shell Chemie GmbH, Eschborn/Ts.
Prof. Dr. U. Schlottmann, Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit, Bonn
Dr. N. Schön, BAYER AG, LE Umweltschutz/AWALU, Leverkusen
Vizepräsident Dr. A. Troge, Umweltbundesamt, Berlin

Guests:

Dr. K. H. Adlfinger, Initiative umweltrelevante Altstoffe, Frankfurt am Main
Prof. Dr. R. Kümmer, Technische Hochschule Leuna-Merseburg
Prof. Dr. Dr. W. Mücke, Institut für Toxikologie und Umwelthygiene der TU München
Dr. J. Oberhansberg, BG Chemie, Heidelberg

In collaboration with:

Dr. S. Ettl, Institut für Organische Chemie der Universität Tübingen
Dr. E. Futterer, Hoechst AG, Frankfurt am Main
Dr. G. Könecker, Fraunhofer-Institut für Toxikologie und Aerosolforschung, Hannover
Prof. Dr. K. Levsen, Fraunhofer-Institut für Toxikologie und Aerosolforschung, Hannover
Frau Dr. I. Mangelsdorf, GSF - Institut für Toxikologie, Neuherberg
Frau Dipl.-Biol. V. Müller, Fraunhofer-Institut für Toxikologie und Aerosolforschung, Hannover
Dr. G. Rosner, Fraunhofer-Institut für Toxikologie und Aerosolforschung, Hannover
Frau Dr. H. Sterzl-Eckert, GSF - Institut für Toxikologie, Neuherberg
Dr. D. Vogel, Institut für Organische Chemie der Universität Tübingen
Frau Dipl.-Biol. L. Weis, Institut für Organische Chemie der Universität Tübingen
Frau Dr. K. Widmann, Institut für Organische Chemie der Universität Tübingen

GDCh Office:

Dr. H. Behret, GDCh, Frankfurt am Main

2-Nitrophenol

(2-Hydroxy-nitrobenzene)

4-Nitrophenol

(4-Hydroxy-nitrobenzene)

BUA Report 75

(February 1992)

edited by the GDCh-Advisory
Committee on Existing Chemicals
of Environmental Relevance

Beratergremium für
Umweltrelevante Altstoffe (BUA)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1993

Dr. H. Behret
Gesellschaft Deutscher Chemiker
Postfach 90 04 40
D-60444 Frankfurt am Main

Translated by R. Hicks

This book was carefully produced. Nevertheless, authors, editors and publisher do not warrant the information contained therein to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

The use of general descriptive names, trade names, trademarks, etc. in a publication, even if not specifically identified, does not imply that these names are not protected by the relevant law and regulations.

Die Deutsche Bibliothek — CIP-Einheitsaufnahme

2-Nitrophenol : (2-Hydroxy-nitrobenzene). 4-Nitrophenol : (4-Hydroxy-nitrobenzene). (February 1992) / GDCh Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) - Stuttgart: Hirzel ; Stuttgart : Wiss. Verl.-Ges., 1993
(BUA report; 75)
ISBN 3-7776-0554-9

NE: Gesellschaft Deutscher Chemiker / Beratergremium für Umweltrelevante Altstoffe: BUA report

ISSN 0938-9393

All rights reserved. No part of this publication may be translated, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without permission in writing from the publisher.

© 1993 S. Hirzel Verlag, Birkenwaldstraße 44, 70191 Stuttgart

Printed in acid-free and low-chlorine paper.

Printing and binding: Zehnersche Buchdruckerei, Speyer
Printed in F.R. Germany

Foreword

The German Chemicals Act (Chemikaliengesetz - ChemG) of 1980 stipulates that certain existing chemicals must be reported to the competent authority, if they exhibit properties which indicate that they may be hazardous, either alone or in combination with other substances.

In the summer of 1982, an Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) was set up by the German Chemical Society (Gesellschaft Deutscher Chemiker - GDCh). It brings together representatives from the scientific community, the chemical industry and the governmental authorities. This Advisory Committee is responsible for elaborating appropriate solutions for substances of relevance for health and the environment on the basis of voluntary measures. It selects and examines existing chemicals from the aforementioned angles. The testing and evaluation are based on scientific criteria alone.

It was, therefore, necessary to develop priority setting procedures. In a first phase reports were only prepared for priority chemicals. Within the framework of a first priority setting procedure, chemicals were compiled from several priority lists and 135 chemicals were selected for detailed substance reports.

In a second priority setting procedure the survey of the German Chemical Industry Association (VCI) on all substances with a production volume of more than 10 tons per year was used as a starting list. Since this survey covered 4,600 chemicals, BUA decided to process the corresponding list in several stages. The first stage included approx. 1,050 substances with a production volume of more than 1,000 tons per year.

Detailed reports are drawn up on chemicals suspected of having a hazard potential and abridged reports on those presenting only a minor hazard potential, according to the current state of knowledge.

The detailed BUA reports take in both the published literature and data from industry. If data for the evaluation of the chemicals are not available, additional studies are recommended and the results are published as updates to the reports. The reports serve as a basis for the instigation of administrative measures, when there are indications of risks to health or the environment.

Tübingen, May 1993

Ernst Bayer
Chairman of the Advisory Committee
on Existing Chemicals
of Environmental Relevance

Contents

Summary and Conclusions	XI
--------------------------------------	-----------

Recommendations.....	XX
-----------------------------	-----------

2-Nitrophenol and 4-Nitrophenol

(2-Hydroxy-nitrobenzene and and 4-Hydroxy-nitrobenzene)

1. Chemistry of 2-Nitrophenol and 4-Nitrophenol	1
1.1 Chemical Identity	1
1.2 Composition of the Technical Product	2
1.3 Chemical Properties	2
2. Physical Properties	4
2.1 2-Nitrophenol	4
2.2 4-Nitrophenol	6
3. Analysis	9
3.1 Determination in Air	9
3.2 Determination in Water	9
3.2.1 Extraction and Enrichment	9
3.2.2 Analysis	10
3.3 Determination in Soil, Sediment and Biological Material	13
4. Emissions into the Environment through Production, Processing, Use and Waste Disposal	14
4.1 The Production Process	14
4.2 Manufacturers and Processors, Production Volume, Export, Import, Total Consumption	15
4.3 Processing, Use and Amounts Consumed	17
4.3.1 Processing	17
4.3.2 Use	18
4.4 Emissions into the Atmosphere	19
4.4.1 Emissions through Production and Processing	19
4.4.1.1 Emissions through Production	19
4.4.1.2 Emissions through Processing	19
4.4.2 Emissions through Use	20

4.4.3	Other sources of Emissions into the Atmosphere	20
4.4.3.1	Direct Emissions through Automobile Exhaust	20
4.4.3.2	Indirect Emissions through Photochemical Formation	21
4.4.3.3	Emissions through the Degradation of Plant Protection Products.....	23
4.5	Emissions into the Hydrosphere	23
4.5.1	Emissions through Production and Processing	23
4.5.1.1	Emissions through Production	23
4.5.1.2	Emissions through Processing	24
4.5.2	Emissions through Use	25
4.5.3	Other Sources of Emissions into the Hydrosphere	25
4.6	Emissions into the Geo- and Biosphere	27
4.7	Emissions from Waste and Waste Treatment	28
4.8	Summary of Emissions into the Environment	29
5.	Occurrence in the Environment	31
5.1	Atmosphere	31
5.2	Hydrosphere	33
5.3	Geosphere	35
5.4	Biosphere	35
5.5	Natural Sources	36
6.	Environmental Behaviour	37
6.1	Transformation, Degradation and Degradation Products	37
6.1.1	Biological Degradation	37
6.1.1.1	Aerobic Degradation in Tests with Inoculation	37
6.1.1.2	Studies of Aerobic Degradation in Natural Water and Sediment and at Low Substrate Concentrations	48
6.1.1.3	Anaerobic Degradation	57
6.1.1.4	Degradation with Pure Cultures and Degradation Products	60
6.1.1.5	Degradation in Animals	64
6.1.2	Hydrolytic Degradation	64
6.1.3	Photochemical Degradation	65
6.1.3.1	Photochemical Degradation in Air	65
6.1.3.2	Photochemical Degradation in Water	66
6.2	Accumulation	68
6.2.1	Bioaccumulation	68
6.2.2	Geoaccumulation	72

6.3	Distributional Behaviour and Transport Processes within and between Environmental Compartments	72
6.3.1	Henry's Law Constant	74
6.3.2	n-Octanol/Water Partition Coefficient	75
6.3.3	Coefficients of Soil Sorption	76
6.4	Fate in the Environment	77
7.	Ecotoxicology	82
7.1	Effect on Aquatic Organisms	82
7.1.1	Microorganisms	82
7.1.2	Plants	82
7.1.3	Invertebrates	87
7.1.4	Vertebrates	96
7.2	Effects on Terrestrial Organisms	101
7.2.1	Microorganisms	101
7.2.2	Plants	101
7.2.3	Invertebrates	103
7.2.4	Vertebrates	103
7.3	Effects on Ecosystems	106
8.	Toxicity in Mammals	108
8.1	General Effects	108
8.2	Mode of Action	109
8.3	Metabolism Toxicokinetics	109
8.3.1	Absorption and Distribution	109
8.3.2	Biotransformation and Elimination	110
8.4	Acute Toxicity	115
8.5	Skin and Eye Irritation/Corrosion	118
8.6	Sensitisation	119
8.7	Subacute, Subchronic and Chronic Toxicity	119
8.8	Mutagenicity	121
8.9	Carcinogenicity	127
8.10	Reproduction Toxicity	127
8.11	Effects on the Immune System	129
8.12	Other Effects	129
8.13	Effects on Man	130
9.	Substance-Specific Regulations	131
10.	Literature	134

BUA Report on 2-Nitrophenol and 4-Nitrophenol

(2-Hydroxy-nitrobenzene and 4-Hydroxy-nitrobenzene)

Summary and conclusions

Ecological aspects

Occurrence and distribution in the compartments

In the Federal Republic of Germany (data from 1988/89) 2-nitrophenol is converted exclusively into 2-nitrophenetol, a starting product in the manufacture of azo pigments. 4-Nitrophenol is also used as an intermediate. In the Federal Republic of Germany (data from 1988/89) this is converted exclusively into 4-aminophenol, which itself is an intermediate in the manufacture of the analgesic 4-acetaminophenol (paracetamol).

In the Federal Republic of Germany production (data from 1988/89) is 500 tonnes per year of 2-nitrophenol and 2000 tonnes per year of 4-nitrophenol, of which approximately 20 tonnes per year are exported.

Discharge into the environment via waste water from production and processing is estimated (data from 1988/89) in the Federal Republic of Germany to be approximately 93 kg per year of 2-nitrophenol and approximately 64 kg per year of 4-nitrophenol, of which approximately respective 18 and 54 kg per year come from production and respective 75 and < 10 kg per year from processing. During manufacture an additional discharge occurs through exhaust air: approximately 2.5 kg per year of 2-nitrophenol and approximately 10 kg per year of 4-nitrophenol. Because of the physico-chemical properties, transfer from the hydrosphere to the atmosphere is possible with 2-nitrophenol, but unlikely with 4-nitrophenol. The 2-nitrophenol or 4-nitrophenol emitted into the atmosphere is scavenged by precipitation.

Further, probably greater entries occur through direct emission into the air from automobiles. Due to insufficient data, it is not possible to quantify the amount released, but it could be in the lower tonnage per year range (< 16 tonnes per year). Of even greater importance could be the transformation of monoaromatics to nitrophenols, whereby the majority of the precursor substances (benzene, toluene) again come from automobile emissions.

An unquantifiable entry into the hydrosphere occurs through the scavenging of airborne nitrophenols by precipitation. In 1989, an entry of maximum 120 tonnes into the geosphere and biosphere occurred through the use of the pesticides parathion and parathion-methyl which are registered in the Federal Republic of Germany and broken down abiotically or biotically via 4-nitrophenol.

In rural areas (Switzerland, 1985) the concentration of 2-nitrophenol in the air is estimated, from rainwater concentrations and the rain/air partition coefficients, to be in the lower $\mu\text{g}/\text{m}^3$ range. Pollution of the air in the Federal Republic of Germany with 2- and 4-nitrophenol can be derived from the concentrations found in precipitation. These were 0.1 - 5.7 $\mu\text{g}/\text{l}$ 2-nitrophenol and 0.5 - 24 $\mu\text{g}/\text{l}$ 4-nitrophenol in 1984 and 1988. Similar concentrations were found in Switzerland and the USA.

The concentration of 2-nitrophenol in the Rhine River near Düsseldorf in 1984 was below the detection limit of 0.5 $\mu\text{g}/\text{l}$. In the Rhine River and the Schelde River in the Netherlands, measurements of 0.1 - 1.3 $\mu\text{g}/\text{l}$ 2-nitrophenol and < 0.1 $\mu\text{g}/\text{l}$ 4-nitrophenol were recorded between 1978 and 1982. Up to 0.25 $\mu\text{g}/\text{l}$ 2-nitrophenol and 0.65 $\mu\text{g}/\text{l}$ 4-nitrophenol were found in the surface water of agricultural regions (The Netherlands, 1982) and in river sediment (Canada, 1988) up to 610 $\mu\text{g}/\text{kg}$ 4-nitrophenol has been recorded.

2- and 4-nitrophenol could not be found in aquatic organisms (fish) (Japan, 1979). No further data on the occurrence in aquatic and terrestrial organisms are available.

In 1978, concentrations of up to 113 µg/l 4-nitrophenol (average < 10 µg/l) were found in the urine of occupationally non-exposed US Americans. This is probably a result of the use of parathion as a pesticide.

Degradability

2- and 4-nitrophenol are, under aerobic conditions, inherently biodegradable. Microbial decomposition can occur in natural waters and in soil after adaptation. The degree and rate of decomposition depend, among others, on the concentration of the substance, the climate and the microbial population. Under anaerobic conditions, on principal a slow biodecomposition by adapted microorganisms is to be expected. In the sea, due to the low nutrient concentrations and microbial counts, 2- and 4-nitrophenol can only be degraded very slowly, if at all.

Hydrolysis could not be proven. 4-Nitrophenol can be decomposed photochemically in water near the surface. Half-lives in the region of a few hours up to several weeks were determined experimentally. There are no results available on this for 2-nitrophenol.

A half-life of approximately 18 days was given for the reaction of 2-nitrophenol with OH-radicals in the atmosphere; no experimental data are available for 4-nitrophenol. The calculated half-life for both nitrophenols is 3.7 days.

Accumulation

Studies on the bioaccumulation in fish resulted in bioconcentration factors of up to 76 for 2-nitrophenol and up to 280 for 4-nitrophenol. Both 2- and 4-nitrophenol are classed as non- or weakly accumulative in the MITI list.

The sorption on soil is low; under anaerobic conditions, enrichment is possible in soil water.

Effects on aquatic and terrestrial organisms

The toxic threshold concentrations for various aquatic microorganisms (bacteria, protozoa) were 0.4 - 27 mg/l for 2-nitrophenol and 0.83 - 56 mg/l for 4-nitrophenol.

For green algae, the EC_{50} values for the inhibition of cell multiplication or yield range, independent of test duration (6 - 192 h), from 0.39 to 8.4 mg/l for 2-nitrophenol and from 2.3 to 32 mg/l for 4-nitrophenol. The 48 h EC_{50} value for the inhibition of chlorophyll biosynthesis was 6.8 mg/l for 2-nitrophenol and 10.4 mg/l for 4-nitrophenol. The photosynthesis of marine algae was inhibited by 25 - 34 mg/l 4-nitrophenol (6 h EC_{50} value).

In the daphnia test for mobility 24 h EC_0 values of 5 - 12 mg/l 2-nitrophenol and 2 - 7 mg/l 4-nitrophenol, and 24 h EC_{50} values of 25 - 110 mg/l 2-nitrophenol and 10 - 12 mg/l 4-nitrophenol were recorded. The 48 h EC_0 values were 2.5 mg/l 2-nitrophenol and 1 mg/l 4-nitrophenol. The highest non effective concentrations (NOEC) in the 21-day daphnia reproduction test differ considerably in two comparable tests for 2-nitrophenol with 5 and 0.032 mg/l. The lowest threshold level for 4-nitrophenol was 0.15 mg/l (NOEC not determined); moreover, NOEC values of 1.3 and 5 mg/l were recorded.

The toxic threshold concentration for asexual reproduction in marine and estuary polyps was 5.7 - 40 mg/l 2-nitrophenol and 6.8 - 13 mg/l 4-nitrophenol; a 6-day LC₅₀ value of 0.5 mg/l and a 6-day LC₀ value of 0.08 mg/l were determined for the toxic effect of 4-nitrophenol on the survival rate of the larvae and young of sea squirts (*Ascidia*).

With respect to the acute fish toxicity of 2-nitrophenol, LC₅₀ values of 46 - 150 mg/l were recorded for various fish species in the static/semistatic test (duration 24, 48, 96 h). In static tests the LC₅₀ values (24, 48 h) of 4-nitrophenol were in the region of 8.3 - 28 mg/l. In the flow through test the lowest 96 h LC₅₀ value recorded was 7.93 mg/l 4-nitrophenol. In the 28-day test with the zebrafish (*Brachydanio rerio*) an NOEC value (with reference to behavioural changes) of 2 mg/l 2-nitrophenol was recorded.

In a longer-term exposure of a marine fish species (sheeps head minnow, *Cyprinodon variegatus*) from the egg-stage to 28 days after hatching, 16 mg/l 4-nitrophenol in the flow through System resulted in a reduction in the hatching rate to 2 % (control: 89 %) and led to the death of all hatched young. No effects could be determined below 16 mg/l. Exposure of a freshwater fish (zebrafish) to 4-nitrophenol under comparable conditions resulted in sex-specific marked ultra structural changes in the liver already at a concentration of 1 mg/l.

At concentrations of 2 and 20 mg/kg soil, 4-nitrophenol had a stimulating effect on the bioactivity of terrestrial micro organisms (CO₂ exchange, ATP level, enzyme activity), whilst 200 mg/kg had an inhibitive effect.

In higher plants the fresh weight (shoots above ground) was reduced with 14-day EC₅₀ values of 52 - 420 mg/kg soil for 2-nitrophenol and 35 - 260 mg/kg for 4-nitrophenol. The 14-day EC₀ value for 2-nitrophenol was 10 mg/kg.

In the earthworm contact test a 48 h LC₅₀ of 5.9 µg/cm² for 2-nitrophenol and 0.7 - 2.7 µg/cm² for 4-nitrophenol was determined. The earthworm test with artificial soil mixture produced 14 day LC₅₀ values of 250 - 500 mg/kg substratum for 2-nitrophenol and 38 – 67 mg/kg for 4-nitrophenol.

Macrophytes, algae and copepods proved to be more sensitive to 4-nitrophenol after 2 months' exposure (5 and 10 mg/l) in a model ecosystem (artificially populated pond) than in laboratory tests. Macrophytes introduced into the pond disappeared with the exception of one species within one year after exposure. After population fluctuations in some families and species, the composition of the plankton normalized in the second year after exposure.

Toxicological Aspects

4-Nitrophenol^{*)}

4-Nitrophenol is resorbed through the skin: in rabbits and dogs 35 % and 11 % respectively of the dermal, non-occlusively applied dose (357 µg were resorbed within 7 days).

After oral, intraperitoneal or intravenous application, 4-nitrophenol is quickly distributed in the body and excreted within 24 hours mainly via the kidneys and liver in the urine. 4-Nitrophenol glucuronide or 4-nitrophenol sulphate occur as metabolites.

In single oral or dermal application, 4-nitrophenol is low toxic (LD₅₀ rat oral 220 - 620 mg/kg body weight; dermal 1024 - 1300 mg/kg body weight). After a single administration, symptoms are described as increase in the respiratory rate, lying in the prone or lateral position, tonic-clonic

This chapter was written in cooperation with BG Chemie (Employment Accident Insurance Fund of the Chemical Industry).

convulsion as well as episthotonus. In cats, 4-nitrophenol did not cause formation of methaemoglobin.

After oral administration of 4-nitrophenol in rats in the 28- day test, slight liver damage was observed in the lowest (70 mg/kg bw/day) and also in the middle dose groups (210 mg/kg bw/day), so that no NOEL (no observed effect level) can be recorded. Studies on chronic toxicity with oral application are not available. After repeated dermal application, dose dependent skin irritations were recorded in rats, but no systemic effects.

4-Nitrophenol has proved to be slightly irritating to the skin. From the results of two studies, it is presumed that 4-nitrophenol has a strong irritative effect on the mucous membrane, although in an additional study the irritation was only slight.

In the maximization test on guinea-pigs, a weak sensitizing effect of the compound was observed.

In a wide range of in vitro test systems, 4-nitrophenol showed no genotoxic effect. Tests on *Drosophila melanogaster* in vivo were also negative.

The carcinogenicity of topically applied 4-nitrophenol was studied in mice as part of the National Toxicology Program. This study did not show any signs of carcinogenic effects. From the results of tests on mice and rats, no toxic effects on reproduction can be attributed to the compound.

In vitro, 4-nitrophenol inhibited the cellular immune response (inhibition of the interleukin-2 System and correlating to the lymphocyte proliferation after mitogenic stimulation).

In vitro, the substance had a cytotoxic effect on animal as well as on plant cells.

There is one occupational medical report indicating a possible sensitizing effect of 4-nitrophenol. Beyond that, there is no information on acute and chronic intoxication of humans and no epidemiological data.

2-Nitrophenol

The intake of 2-nitrophenol was only investigated in model tests with isolated skin preparations of nude mice. The permeability of 2-nitrophenol was 4 - 8 times higher than that of 4-nitrophenol. From the very low amount of information available on 2-nitrophenol, it can be presumed that metabolism and elimination of this compound are similar to those of the well-studied 4-nitrophenol.

In contrast to 4-nitrophenol, formation of methaemoglobin has been proven in cats.

In single oral or dermal application, 2-nitrophenol is less toxic than 4-nitrophenol (LD₅₀ rat oral 2830 - 5376 mg/kg body weight; dermal > 2000 mg/kg body weight). After a single administration, symptoms are described as increase in the respiratory rate, tonic-clonic convulsion as well as episthotonus.

In the 28-day test with oral administration of 2-nitrophenol in rats, no substance-specific symptoms were observed with the selected doses (22/67/200 mg/kg bw/day). A NOEL cannot be deduced. Studies on chronic toxicity are not available.

2-Nitrophenol has proved to be slightly irritating to the skin with reversible reaction and has no irritative effect on the mucous membrane. In guinea-pigs, no sensitizing effect of the compound was observed.

In several Ames tests (with and without metabolic activation) as well as in a bacterial DNA repair test, 2-nitrophenol was not mutagenic.

Studies on the carcinogenicity, reproduction toxicity and immunotoxicity are not available.

There is no information on acute and chronic intoxication of humans and no epidemiological data.

Recommendations

Ecology

The concentrations of 2- and 4-nitrophenol measured in the hydrosphere and atmosphere cannot be accounted for from the low emissions during manufacture and processing. It is presumed that predominantly direct emissions from motor vehicles and photochemical reactions of monoaromatics, which mainly come from automobile exhaust (benzene/toluene), are responsible for this. Studies relevant to the outdoor environment should therefore be carried out to investigate the photochemical behaviour of monoaromatics, and of the secondarily formed nitrophenols.

Toxicology

No NOEL can be deduced for 4-nitrophenol from the existing subchronic toxicity test. The final report of a study carried out in the USA should therefore be awaited in order to evaluate the chronic effect.

A 28-day test with oral administration to investigate target organs and the NOEL is recommended for 2-nitrophenol, if exposure at the workplace is to be expected.

Tests on the reproduction toxicity of 2-nitrophenol and additional tests on the reproduction toxicity of 4-nitrophenol are not considered to be of high priority, since significant exposure, if at all, is only to be expected at the workplace. Determination of the concentration at the workplace is therefore necessary for both substances.