IPCS INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Health and Safety Guide No. 100

CRESOLS HEALTH AND SAFETY GUIDE

UNEP

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Health and Safety Guide No. 100

CRESOLS
HEALTH AND SAFETY GUIDE

This is a companion volume to
Environmental Health Criteria 168: Cresols

Published by the World Health Organization for the International
Programme on Chemical Safety (a collaborative programme of the United
Nations Environment Programme, the International Labour Organisation,
and the World Health Organization)

WORLD HEALTH ORGANIZATION, GENEVA 1996

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

WHO Library Cataloguing in Publication Data

Cresols: health and safety guide.

(Health and safety guide ; no. 100)

1.Cresols - adverse effects 2.Anti-infective agents
3.Occupational exposure 4. I.Series

ISBN 92 4 151100 1 (NLM Classification: QD 341.P5)
ISSN 0259-7268

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Computer typesetting by HEADS, Oxford OX8 8NY, England

The Federal Ministry for the Environment, Nature Conservation
and Nuclear Safety (Federal Republic of Germany) provided
financial support for, and undertook the printing of, this publication

Printed by Wissenschaftliche Verlagsgesellschaft mbH · D-70009 Stuttgart 10

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CONTENTS

INTRODUCTION

The Environmental Health Criteria (EHC) monographs produced by the International Programme on Chemical Safety include an assessment of the effects on the environment and on human health of exposure to a chemical or combination of chemicals, or physical or biological agents. They also provide guidelines for setting exposure limits.

The purpose of a Health and Safety Guide is to facilitate the application of these guidelines in national chemical safety programmes. The first three sections of a Health and Safety Guide highlight the relevant technical information in the corresponding EHC. Section 4 includes advice on preventive and protective measures and emergency action; health workers should be thoroughly familiar with the medical information to ensure that they can act efficiently in an emergency. Within the Guide is a Summary of Chemical Safety Information which should be readily available, and should be clearly explained, to all who could come into contact with the chemical. The section on regulatory information has been extracted from the legal file of the International Register of Potentially Toxic Chemicals (IRPTC) and from other United Nations sources.

The target readership includes occupational health services, those in ministries, governmental agencies, industry, and trade unions who are involved in the safe use of chemicals and the avoidance of environmental health hazards, and those wanting more information on this topic. An attempt has been made to use only terms that will be familiar to the intended user. However, sections 1 and 2 inevitably contain some technical terms. A bibliography has been included for readers who require further background information.

Revision of the information in this Guide will take place in due course, and the eventual aim is to use standardized terminology. Comments on any difficulties encountered in using the Guide would be very helpful and should be addressed to:

The Director
International Programme on Chemical Safety
World Health Organization
1211 Geneva 27
Switzerland

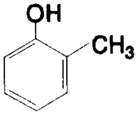
THE INFORMATION IN THIS GUIDE
SHOULD BE CONSIDERED AS A
STARTING POINT TO A COMPREHENSIVE
HEALTH AND SAFETY PROGRAMME

1. PRODUCT IDENTITY AND USES

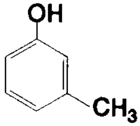
1.1 Identity

Common name: Cresols (*o*, *m*, *p*-isomers)

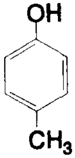
Common structure:



o-cresol



m-cresol



p-cresol

Common synonyms:

2-methyl phenol	3-methyl phenol	4-methyl phenol
2-hydroxy toluene	3-hydroxy toluene	4-hydroxyl toluene
o-cresylic acid	*m*-cresylic acid	*p*-cresylic acid
o-kresol (German)	*m*-kresol (German)	*p*-kresol(German)

Chemical formula: C_7H_8O

Common trade name:
cresylic acid (mixture of the three isomers)
cresylic acids (mixture of phenols)
tricresol (mixture of *o*, *m*, *p*- isomers)
dicresol (mixture of *m*- and *p*- isomers)
lysol (mixture of 60 cresol: 40 soap)

CAS registry number:

95-48-7 (*o*-cresol)	109-39-4 (*m*-cresol)	106-44-5 (*p*-cresol)

RTECS number:

G06300000	G06125000	G06475000

Relative molecular mass:	108.14	
Conversion factors:	air at 25 °C:	1 ppm = 4.42 mg/m^3 1 mg/m^3 = 0.23 ppm
	water:	1 ppm = 1 mg/litre
	solid or semi-solid:	1 ppm = 1 mg/kg

1.2 Physical and Chemical Properties

Cresols are isomeric substituted phenols with a methyl substituent at one of the *o*-, *m*-, or *p*- positions relative to the OH-group. Physically, they are white crystalline solids or yellowish liquids with a strong phenol-like odour. The compounds are highly flammable, moderately soluble in water and soluble in ethanol, ether, acetone, or alkali hydroxides. Chemically, these alkylphenols undergo electrophilic substitution reactions at the vacant *o*- or *p*- positions or undergo condensation reactions with aldehydes, ketones, or dienes.

Physical and chemical data on cresols are presented in the Summary of Chemical Safety Information (section 6).

1.3 Analysis

Cresols can be detected and quantified in a number of environmental media and biological samples. The most commonly used methods for determining the presence of cresols are gas chromatography-mass spectrophotometry (GC-MS) and high-performance liquid chromatography (HPLC). Sample detection limits are 1.33 ng/m^3 for air; 4-10 μg/litre for water; 300 μg/kg for soil and 0.5-1.0 mg/litre for urine. Air odour thresholds were reported to be 1.4-22, 0.007-1.2, and 0.002-0.04 mg/m^3 for *o*-, *m*-, and *p*-cresol, respectively.

1.4 Production and Uses

Cresols and cresol derivatives occur naturally in the oils of various flowering plants and trees, such as jasmine, easter lily, yucca, conifers, oaks, and sandalwoods. *p*-Cresol is found in the urine of animals and humans. Commercially, cresols are produced as by-products in the fractional distillation of crude oil and coal tars and in coal gasification. They are also formed as by-products during the combustion of wood, coal, and cigarettes. The various isomers can be manufactured by the methylation of phenols, toluene sulfonation and alkaline hydrolysis, or the hydrolysis of 2-isopropyltoluene or alkaline chlorotoluene. Worldwide production is not known; annual production in the USA for 1990 was reported to be 38.3 million kg.

Cresols have a wide variety of uses as solvents, disinfectants, or intermediates in the preparation of numerous products. They are commonly used in the production of fragrances, antioxidants, dyes, pesticides, and resins. In addition, *p*-cresol is used in the production of lubricating oils, motor fuels, and rubber polymers, while *m*-cresol is also used in the manufacture of explosives.

2. SUMMARY AND EVALUATION

2.1 Environmental Fate

Environmental transport of cresols occurs through the vapour phase of the atmosphere and from the atmosphere to surface water and soil by rain-scavenging. Because of their volatilization, binding to sediment, and biodegradation, only small amounts of cresols are found in water. In soils, cresols are slightly to highly mobile, depending on the K_{OC} value of the soil. Cresols have been detected in groundwater; therefore leaching does occur in soil.

2.2 Exposure

Exposure to cresols can occur through air, water, or food. The median air concentration of *o*-cresols was 1.578 $\mu g/m^3$ (0.359 ppb) for 32 source dominated sites in USA. In the USA, surface water concentrations ranged from below detection limits to 77 μg/litre. Levels of 204 μg/litre were reported in Japan in a river polluted from industrial effluents. Concentrations as high as 2100 μg/litre for *o*-cresol and 1200 μg/litre for mixed *m*- and *p*-cresols have been detected in waste waters. Concentrations of all three isomers in groundwater from undefined sources ranged from below detection limits to 100 mg/litre. Rainwater concentrations ranged from 240 to 2800 ng/litre for *o*-cresol and 380 to 2000 ng/litre for *p*- and *m*-cresol combined. Cresols have been detected in foods and beverages. Concentrations in spirit beverages ranged from 0.01 to 0.2 mg/litre. The amount in tobacco smoke was 75 μg/85-mm, non-filter, American cigarette. The general population can be exposed to cresols through air inhalation, drinking-water, food, and beverage ingestion, and dermal contact. In general, the lack of adequate monitoring data makes the quantitative estimate of daily intakes of cresol from these sources impossible. Occupational exposure levels in air as high as 5.0 mg/m^3 have been reported.

2.3 Uptake, Metabolism, and Excretion

Cresols are absorbed across the respiratory and gastrointestinal tracts and through the skin. The rate and extent of absorption of cresols have not been studied specifically; however, studies have shown that both gastrointestinal and dermal absorption are rapid and extensive. Cresols are distributed to all the major organs. The primary metabolic pathway for cresols is conjugation with glucuronic acid and inorganic sulfate. Minor metabolic pathways for cresols include hydroxylation of the benzene ring and side-chain oxidation. The main route of elimination of cresols from the body is renal elimination in the form of conjugates.

2.4 Effects on Organisms in the Environment

Observations on microorganisms, invertebrates, and fish are available and show that cresols may represent a risk to non-mammalian organisms at point sources with high cresol concentrations, but not in the general environment.

2.5 Effects on Experimental Animals and *In Vitro* Test Systems

Acute poisoning with cresol vapours is unlikely due to the low vapour pressure of these compounds. Mean lethal concentrations of cresols for rats have been reported to be 29 mg/m^3 for *o*- and *p*-cresols and 58 mg/m^3 for *m*-cresols. Oral LD_{50} values in rats have been reported to be 121, 207, and 242 mg/kg body weight for *o*-, *p*-, and *m*-isomers, respectively. Inter-species comparisons show that all three isomers are more toxic for mice than for rats and that toxicity increases with concentration. Systemic toxicity and death can result from dermal exposure. Dermal LD_{50} values in rabbits were 890, 2830, 300, and 2000 mg/kg body weight for *o*-, *m*-, *p*-, and mixed cresols, respectively. In rats, dermal LD_{50} values were 620, 1100, 750, and 825 mg/kg body weight for *o*-, *m*-, *p*-, and dicresol, respectively.

Cresols are highly irritating to the skin and eyes of rabbits, rats, and mice.

Short-term exposure to inhaled mixtures of *o*-cresol aerosol and vapours resulted in irritation of the respiratory tract, small haemorrhages in the lung, body weight reduction, and degeneration of heart muscle, liver, kidney, and nerve cells. Short-term (28-days) oral exposure to approximately 800 mg/kg body weight per day and above resulted in reduced body weights, organ weight changes, and histopathological changes in the respiratory and gastrointestinal tracts of rats. In mice similarly exposed to 1500 mg/kg body weight, more severe effects were reported and, at the highest concentrations, death resulted from exposure to *o*-, and *m*-, and *p*-cresols, but not from exposure to mixtures of the isomers.

Exposure of rats to vapours of *o*-, *m*-, or *p*-cresol for up to 4 months resulted in weight loss, reduced locomotor activity, inflammation of nasal membranes and skin, and changes in the liver. Oral exposures of up to 13 weeks of mice, rats, and hamsters resulted in mortality, tremors, reduced body weights, haematological effects, increased organ weights, and hyperplasia of nasal, and forestomach epithelium.

Oral and inhalation exposures to cresol isomers have resulted in lengthened estrus cycles, and histopathological changes in the uterus and ovaries of rats and mice. No adverse effects were observed on spermatogenesis in rats or mice. Mild fetotoxic effects have been reported in rats and rabbits exposed to *o*-, and *p*-cresols, but only minor treatment-related developmental effects have been reported. Some evidence of genotoxicity has been reported in *in vitro* studies with *o*- and *p*-cresols but not *m*-cresol. No positive results were obtained in *in vivo* studies; however, some evidence of promotive activities in skin has been reported. No studies of carcinogenicity have been reported for any cresol isomers.

2.6 Effects on Humans

Ingestion of cresols results in burning of the mouth and throat, abdominal pain, and vomiting. Target organs of ingested cresols in humans are the blood and kidneys and effects on the lungs, liver, heart, and central nervous system have also been reported. In severe cases, coma and death may result. Dermal exposure has been reported to cause severe skin burns, scarring, systemic toxicity, and death.

Occupational exposure to cresols usually results from dermal contact. Acute exposures have resulted in severe burns, anuria, coma, and death. Very few data are available regarding the reproductive effects of cresols and no data are available on carcinogenicity in humans.

3. CONCLUSIONS

3.1 Human Health

Cresols, at concentrations normally found in the environment, do not pose any significant risk for the general population. However, the potential for adverse health effects exists for specific subpopulations and under conditions of high exposure.

No information is available regarding the effects of long-term exposure to cresols. Thus, information to assess the carcinogenic hazard of cresols is inadequate. On the basis of the results of short-term studies, an NOAEL of 50 mg/kg body weight per day has been identified for all three isomers of cresols. Applying an uncertainty factor of 300 was recommended as follows: 10 to account for interspecies variation; 10 to account for the lack of long-term toxicity studies and possible genotoxic and promoting activity of cresols; and 3 to account for intraspecies variation based on the rapid and complete metabolism. Thus, an ADI of 0.17 mg/kg body weight per day can be developed for cresols.

NOAEL = 50 mg/kg per day
Uncertainty factor = 300
ADI = 0.17 mg/kg body weight per day.

3.2 Environment

Observations on microorganisms, invertebrates, and fish show that cresols may present a risk for non-mammalian organisms at point sources with high cresol concentrations, but not in the general environment.

4. HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

4.1 Human Health Hazards, Prevention and Protection, First Aid

The human health hazards associated with certain types of exposure to cresols, together with preventive and protective measures and first aid are shown in the Summary of Chemical Safety Information (section 6).

4.1.1 *Information for physicians*

High oral or dermal exposure to cresols may rapidly prove fatal. Exposed patients should be decontaminated and treated symptomatically. Maintenance of breathing and circulation is necessary in cases of severe poisoning. There is no specific antidote. Treatment of local lesions and systemic intoxication is symptomatic.

Monitor blood, liver, and kidney functions. Call the nearest Poisons Information Centre for further advice.

4.1.2 *Health surveillance advice*

The blood of individuals exposed to cresols on a frequent or long-term basis should be examined for haematological changes. Periodic medical examinations should also include testing of kidney and liver functions, and skin and eye sensitivity or irritation. Special attention should be given to pregnant females and females of child-bearing age.

4.2 Explosion and Fire Hazards

4.2.1 *Explosion hazards*

The vapours of cresols may become explosive when exposed to heat or flames; the flash-point is approximately 80 °C. Cylinders containing liquid may explode in heat.

4.2.2 *Fire hazards*

Highly flammable and volatile cresols can cause severe toxic effects, including burning and irritation of the skin, eyes, and nasal membranes.

4.3 Storage

Cresols should be stored in well-sealed containers in cool, well-ventilated areas, away from sources of ignition.

4.4 Transport

Transport should be in well-sealed, protective containers which should be labelled indicating the high flammability and corrosive and poisonous nature of the substance.

4.5 Spillage

In the case of spillage, wear protective gloves and glasses and avoid direct contact with skin. Evacuate and ventilate the area. Absorb leaking liquid in sand, earth, or inert material, and deposit in sealed containers. Collect powdered material in the most convenient and safe manner and deposit in a sealable container.

4.6 Disposal

Dispose of as hazardous waste.

5. HAZARDS FOR THE ENVIRONMENT AND THEIR PREVENTION

Cresols are present in the environment in the air, water, and soil, and may undergo rapid chemical and biological transformation. It is unlikely that cresols bioaccumulate in the environment or food chain.

Cresols are moderately toxic for aquatic bacteria, algae, and protozoa. The acute toxicity of cresols for invertebrates is low to moderate. Cresols have also been shown to be toxic for fish and birds.

Contamination of the environment can be reduced by controlling emissions from industrial point sources. In addition, proper methods for the storage, transport, and waste disposal of cresols are recommended to reduce the incidence of accidental releases of cresols into the environment.

6. SUMMARY OF CHEMICAL SAFETY INFORMATION

This summary should be easily available to all health workers concerned with, and users of, cresols. It should be displayed at, or near, entrances to areas where there is potential exposure to cresols, and on processing equipment and containers. The summary should be translated into the appropriate language(s). All persons potentially exposed to the chemical should also have the instructions in the summary clearly explained.
Space is available for insertion of the National Occupational Exposure Limit, the address and telephone number of the National Poison Control Centre, and local trade names.

SUMMARY OF CHEMICAL SAFETY INFORMATION

Cresols (*o*, *m*, *p* isomers)

C_7H_8O

Physical properties	*o*-cresol	*m*-cresol	*p*-cresol	Other characteristics
Relative molecular mass	108.14	108.14	108.14	White crystalline solid or yellowish liquid; soluble in ethanol, ethyl ether, acetone, benzene, aqueous alkali hydroxides; phenolic-like odour, highly corrosive, and strong irritant; highly reactive with metal (steel, chromium, aluminum) and their alloys; soluble in water
Melting point (°C)	30.94	12.22	34.74	
Boiling point (°C)	191.0	202.32	201.94	
Water solubility (25 °C)	25.95	22.70	21.52	
Relative density (25 °C)	1.135	1.030	1.154	
Vapour density	3.7	3.72	3.72	
Vapour pressure (25 °C)	0.31	0.143	0.13	
Flash point (°C)	81	86	86	
Ignition temperature (°C)	558	558	558	

Hazard/symptom	Prevention/protection	First aid
Skin: Irritant, corrosive; severe burns and scarring	Protective clothing, gloves, and shoes	Wash immediately with large amount of water; remove contaminated clothing; obtain medical care
Eyes: Corrosive, strong irritant; lacrimation, redness	Safety glasses	Wash with water continuously for 30 min; obtain medical care immediately

Inhalation: Irritation and burning of nasal membrane; burning in nose and throat	Adequate ventilation, use of respirators	Remove from exposure; provide fresh air and adequate ventilation; obtain medical care
Ingestion: Irritation and burning of mouth, throat, and gastrointestinal tract; vomiting	Store in properly sealed containers; avoid contact with food or beverages	Rinse mouth; obtain immediate medical care
Environment: Toxic for aquatic and terrestrial organisms	Avoid environmental releases from industrial processes and accidental spills	

Spillage	Storage	Fire and explosion
Evacuate and ventilate area; collect leaking liquid in sealed containers; absorb liquid in earth, sand, or inert material; wear protective clothing	Store away from food and incompatible materials (metals) in well-labelled containers and well-ventilated areas; sources of ignition/open flames, and smoking, must be prohibited	Flash-point 81-86 °C; may be explosive in reactions with metals; do not use near open fires; poisonous gas may be produced in a fire

7. CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

The information in the table on p. 21 has been extracted from the International Register of Potentially Toxic chemicals (IRPTC) legal file.

The reader should be aware that regulatory decisions about chemicals taken in a certain country can only be fully understood in the framework of the legislation of that country. Furthermore, the regulations and guidelines of all countries are subject to change and should be verified with the appropriate regulatory authorities before application.

7.1 Exposure Limit Values

Values for exposure limits are given in the table on page 21.

7.2 Specific Restrictions

Approved in the USA for use as a pesticide.

7.3 Labelling, Packaging, and Transport

In the USA, cresols (all isomers) have been designated as a hazardous substance R1987 and must be managed according to federal and/or state hazardous waste regulations.

7.4 Waste Disposal

In the USA, any sealed waste must be listed as hazardous waste, subject to handling, transport, storage, and disposal requirements, specified by CERLA, and the Clean Waste Act (effective date 1991). These regulations apply to all discharges.

As a commercial chemical, cresols must be identified as "toxic waste", subject to restrictions and disposal regulations, permitting, and notification (effective date 1989).

Any discharge into surface waters requires a permit under the Clean Water Act (effective date 1987).

CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

Exposure limit values

Medium	Specification	Country/ organization	Exposure limit description[a]	Value[b]	Effective date
Air	occupational	Argentina	8-h TWA	22 mg/m^3	May 1991
		Czech Republic	TWA	20 mg/m^3	1985
			CLV	40 mg/m^3	1985
		Germany	8-h TWA	22 mg/m^3	1991
			5-min STEL	44 mg/m^3	
		Japan	TWA	22 mg/m^3	1991
		Russian Federation	TWA	0.5 mg/m^3	1989
			CLV	1.5 mg/m^3	1989
		United Kingdom	8-h TWA	22 mg/m^3	1992
		USA (ACGIH)	TWA	22 mg/m^3	1989
Air	ambient	Russian Federation		0.02 mg/m^3 (*m*-, *p*-cresols) 0.028 mg/m^3 (*o*-cresol)	1983

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[a] TWA: time-weighted average;
CLV: ceiling value;
STEL: short-term exposure limit.

[b] Refers to *o*-, *m*-, *p*-cresols unless otherwise specified.

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