NIOSH

CRITERIA FOR A RECOMMENDED STANDARD.... OCCUPATIONAL EXPOSURE TO

CRESOL

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

criteria for a recommended standard....

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PREFACE

The Occupational Safety and Health Act of 1970 emphasizes the need for standards to protect the health and safety of workers exposed to an ever-increasing number of potential hazards at their workplace. The National Institute for Occupational Safety and Health has projected a formal system of research, with priorities determined on the basis of specified indices, to provide relevant data from which valid criteria for effective standards can be derived. Recommended standards for occupational exposure, which are the result of this work, are based on the health effects of exposure. The Secretary of Labor will weigh these recommendations along with other considerations such as feasibility and means of implementation in developing regulatory standards.

It is intended to present successive reports as research and epidemiologic studies are completed and as sampling and analytical methods are developed. Criteria and standards will be reviewed periodically to ensure continuing protection of the worker.

I am pleased to acknowledge the contributions to this report on cresol by NIOSH staff members and the valuable constructive comments provided by the Review Consultants on Cresol, the reviewers selected by the American Conference of Govermental Industrial Hygienists, and by Robert B.

O'Connor, M.D., NIOSH consultant in occupational medicine. The NIOSH recommendations for standards are not necessarily a consensus of all the consultants and professional societies that reviewed this criteria document on cresol. A list of review consultants and a list of the federal agencies to which the document was submitted are given on pages vi and vii.

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The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for the development of the criteria and recommended standard for cresol. David J. Brancato of this Division served as criteria manager. SRI International developed the basic information for consideration by NIOSH staff and consultants under contract No. CDC-99-74-31.

The Division review of this document was provided by Douglas L. Smith, Ph.D. (Chairman), Jon R. May, Ph.D., and Richard A. Rhoden, Ph.D., with Larry K. Lowry, Ph.D. (Division of Biomedical and Behavioral Science), Harry M. Donaldson (Division of Surveillance, Hazard Evaluations, and Field Studies), and Charles C. Hassett, Ph.D.

The views expressed and conclusions reached in this document, together with the recommendations for a standard, are those of NIOSH. These views and conclusions are not necessarily those of the consultants, other federal agencies or professional societies that reviewed the document, or of the contractor.

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  - National Institute of Environmental Health Sciences
  - National Institute of Neurological and Communicative Disease and Stroke

Consumer Product Safety Commission
- Bureau of Biomedical Science

Environmental Protection Agency
- Office of Assistant Administrator for Research and Development
- National Environmental Research Center
  - Health Effects Research Laboratory

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I. RECOMMENDATIONS FOR A CRESOL STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to cresol in the workplace be controlled by adherence to the following sections. The standard is designed to protect the health and provide for the safety of employees for up to a 10-hour workshift, 40-hour workweek, over a working lifetime. Compliance with all sections of the standard should prevent adverse effects of cresol on the health and safety of employees. The standard is measurable by techniques that are valid, reproducible, and available to industry and government agencies. Sufficient technology exists to permit compliance with the recommended standard. Although the workplace environmental limit is considered a safe level based on current information, it should be regarded as the upper boundary of exposure and every effort should be made to maintain the exposure at levels as low as is technically feasible. The criteria and standard will be subject to review and revision as necessary.

In this document, the term "cresol" applies to the ortho, meta, or para isomer of the aromatic organic compound $CH_3C_6H_4OH$ or to any combination of the three isomers in a mixture. Examples of commercial mixtures that often contain cresol are the cresylic acids, which are generally defined as mixtures of cresol, xylenols, and phenol in which 50% of the material boils above 204 C. The criteria and recommendation for cresol will apply to cresylic acid mixtures that contain cresol. The term "cresols," as used in this document, applies to information concerning both cresol and cresylic acids. The individual cresol isomers will be specified

when they are known, as will the composition of cresylic acid mixtures. Cresol has three major uses in the United States; over 60% of the total amount produced is consumed in the production of wire enamel solvents, phosphate esters, and phenolic resins.

There is often confusion between cresol and two other products, creosol and creosote, which are not a part of this recommendation. "Creosol," $CH_3O(CH_3)C_6H_3OH$, is a methoxy derivative of o-cresol, while "creosote" is a mixture of phenol and phenol derivatives obtained from the distillation of coal tar or wood tar.

The similarities between cresol and phenol are particularly evident in cases of skin contact. Past proposed standards have been set with the underlying assumption that what is applicable for phenol should be applicable for cresol. This assumption is true for recommendations concerning work practices, but recent experimental evidence suggests that the phenol analogy should not be applied to cresol when setting an environmental limit. The recommended environmental limit for cresol is based on available information about the effects from both short- and long-term exposure to cresol. The standard is designed to safeguard workers occupationally exposed to airborne cresol from impairment of motor function and from damage to the liver, kidneys, and pancreas.

"Occupational exposure" to cresol, because of systemic effects, absorption through the skin on contact, and possible dermal irritation, is defined as work in any area where cresol is produced, processed, stored, or otherwise used. The "action level" is defined as one-half the recommended time-weighted average (TWA) environmental limit. Adherence to all provisions of the standard is required if an employee is occupationally

exposed to airborne cresol at concentrations in excess of the action level. If the employee is occupationally exposed at concentrations equal to or below the action level, then all sections of the recommended standard except sections 4(c)(2) and 8(a) shall be complied with because adverse effects can be produced by skin and eye contact. If exposure to other chemicals also occurs, provisions of any applicable standards for the other chemicals shall also apply.

Section 1 - Environmental (Workplace Air)

(a) Concentration

When skin contact is prevented, exposure to cresol shall be controlled so that no employee is exposed to cresol at a concentration greater than 10 milligrams per cubic meter (mg/cu m) of air (2.3 parts per million parts of air by volume), determined as a time-weighted average (TWA) concentration for up to a 10-hour workshift and 40-hour workweek.

(b) Sampling and Analysis

Procedures for the collection and analysis of environmental samples shall be as provided in Appendix I or by any other methods shown to be at least equivalent in precision, accuracy, and sensitivity to the methods specified.

Section 2 - Medical

Medical surveillance shall be made available as outlined below to all persons subject to occupational exposure to cresol.

(a) Preplacement medical examinations shall include at least:

(1) Comprehensive medical and work histories with special emphasis directed to any preexisting disorders, particularly of the lungs, liver, kidneys, pancreas, nervous and cardiovascular systems, and skin.

(2) A physical examination giving special attention to the lungs, liver, kidneys, pancreas, skin, and nervous and cardiovascular systems.

(3) A urinalysis that includes a microscopic examination. Additional tests, such as complete blood counts and liver and kidney function tests, should be considered by the responsible physician.

(4) An evaluation of the worker's ability to use positive and negative pressure respirators.

(b) Periodic examinations shall be made available on at least an annual basis. These examinations shall include at least:

(1) Interim medical and work histories.

(2) A physical examination as described in (a)(2) and (3) of this section.

(c) Employees complaining of skin abnormalities, such as scaling, crusting, or irritation, that may be attributed to exposure to cresol shall be medically evaluated.

(d) Initial medical examinations shall be made available to all workers as soon as practicable after promulgation of a standard based on these recommendations.

(e) Employees and potential employees having medical conditions that could be directly or indirectly aggravated by exposure to cresol shall be counseled on the increased risk of impairment of their health from

working with this substance. All employees occupationally exposed to cresol shall be informed about the value of periodic medical examinations.

(f) In an emergency involving cresol, all affected personnel shall be provided with immediate first aid, followed by prompt medical evaluation and care. In the event of skin or eye contact with liquid cresol, contaminated clothing and shoes shall be removed immediately, and skin and eyes shall be flushed with copious amounts of water. In cases of splashes, spills, or leaks where significant skin or eye contact with or inhalation of the material occurs, appropriate medical personnel shall be notified. Medical attendants shall be informed of the possibility of delayed systemic effects, and the persons so exposed shall be observed for a minimum of 72 hours. Medical examinations as described for the periodic examinations shall be made available as warranted by the results of the 72-hour observation period.

(g) Pertinent medical records shall be maintained by the employer for all employees occupationally exposed to cresol. Such records shall be retained for at least 30 years after termination of employment. Records of environmental exposures applicable to an employee shall be included in the employee's medical records. These records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, and of the employer, employee, or former employee.

Section 3 - Labeling and Posting

All labels and warning signs shall be printed both in English and in the predominant language of non-English-reading workers. Illiterate

workers and workers reading languages other than those used on labels and posted signs shall receive information regarding hazardous areas and shall be informed of the instructions printed on labels and signs.

(a) Labeling

All bulk containers that hold cresol shall carry, in a readily visible location, a label that bears the trade name of the product, if appropriate, and information on the effects of exposure to the compound on human health. The information shall be arranged as in the example below.

CRESOL
(Trade Name)

DANGER!

CAUSES SEVERE BURNS
MAY BE FATAL IF ABSORBED THROUGH SKIN,
INHALED, OR INGESTED

Do not get on skin, in eyes or mouth, or on clothing.
Avoid breathing vapor.
Keep containers closed when not in use.
Use only with adequate ventilation.
Wash thoroughly after handling.

First Aid: Call a physician immediately. In case of skin or eye contact, immediately remove contaminated clothing and flush skin or eyes with large amounts of water for at least 15 minutes. If material is inhaled, remove victim to fresh air. If victim is not breathing, give artificial respiration. If breathing is difficult, give oxygen. If swallowed, give large quantities of water. Give at least 1 ounce of milk of magnesia or aluminum hydroxide gel in an equal amount of water. If these are not available, the whites of two or three eggs may be used. Do not induce vomiting. Never give anything by mouth to an unconscious person.

(b) Posting

In areas where exposure to cresol can occur, signs containing health hazard warning statements appropriate for this substance shall be posted in

readily visible locations. This information shall be arranged as in the example below.

DANGER!
CRESOL PRESENT IN AREA
(Isomer Name)

MAY BE FATAL IF ABSORBED THROUGH
SKIN, INHALED, OR INGESTED
CAUSES SEVERE BURNS

Do not get on skin, in eyes or mouth, or on clothing.
Avoid breathing vapor.

(c) When respirators are permitted under section 4(c), the following statement shall be added in large letters to the signs required in Section 3(b):

RESPIRATORY PROTECTION REQUIRED IN THIS AREA

(d) In any area where there is a likelihood of emergency situations arising, signs required by Section 3(b) shall be supplemented with signs giving emergency and first-aid instructions and procedures, the location of first-aid supplies and emergency equipment, and the locations of emergency showers and eyewash fountains.

Section 4 - Personal Protective Equipment

Engineering controls and safe work practices shall be used when needed to keep concentrations of airborne cresol at or below the prescribed limit and to minimize skin and eye contact. In addition, employers shall

provide protective equipment and clothing to employees when necessary.

(a) Eye Protection

Safety glasses with side shields shall be worn wherever there is occupational exposure to cresol. Chemical safety goggles or face shields (8-inch minimum) with goggles shall be provided by the employer and shall be worn during any operation in which particulate cresol may enter the eyes (29 CFR 1910.133).

(b) Skin Protection

Depending on the operations involved and the probable or likely extent of exposure, protective clothing and equipment, including gloves, aprons, suits, boots, and face shields (8-inch minimum) with goggles, shall be worn to prevent skin contact with particulate cresol.

(c) Respiratory Protection

(1) The use of respirators to achieve compliance with the recommended exposure limits is permitted only:

(A) During the time necessary to install or test the required engineering controls.

(B) During emergencies or during nonroutine operations, such as maintenance or repair activities, when the concentration of airborne cresol may exceed the permissible environmental limit.

(2) When use of a respirator is permitted, it shall be selected and used pursuant to the following requirements:

(A) The employer shall establish and enforce a respiratory protective program meeting the requirements of 29 CFR 1910.134.

(B) The employer shall provide respirators in accordance with Table I-1 and shall ensure that the employee uses the respirator provided when necessary. The respiratory protective devices provided in conformance with Table I-1 shall comply with the standards jointly approved by NIOSH and the Mining Enforcement and Safety Administration (MESA) as specified under the provisions of 30 CFR 11.

(C) Respirators specified for use in higher concentrations of cresol may be used in atmospheres of lower concentrations.

(D) The employer shall ensure that respirators are adequately cleaned and maintained and that employees are trained and drilled at least annually in the proper use and testing for leakage of respirators assigned to them.

(E) Respirators shall be easily accessible, and employees shall be informed of their location.

Section 5 - Informing Employees of Hazards

(a) Employees working in an area that may involve occupational exposure to cresol shall be verbally informed of the hazards of such employment, the symptoms associated with exposure to these substances, the appropriate emergency procedures to use, and the proper procedures for the safe handling and use of cresol.

TABLE I-1

RESPIRATOR SELECTION GUIDE FOR CRESOL

Concentration	Respirator Type Approved under Provisions of 30 CFR 11
Less than or equal to 500 mg/cu m	(1) Full facepiece respirator equipped with organic vapor canister or cartridge (2) Type C supplied-air respirator with full facepiece operated in demand (negative pressure) mode (3) Supplied-air impervious suit (4) Self-contained breathing apparatus with full facepiece operated in demand (negative pressure) mode
Less than or equal to 1,100 mg/cu m	(1) Type C supplied-air respirator with full facepiece operated in pressure-demand (positive pressure) mode (2) Type C supplied-air respirator operated in continuous-flow mode with full facepiece, hood, or helmet or impervious supplied-air suit
Greater than 1,100 mg/cu m or Emergency (entry into area of unknown concentration	(1) Self-contained breathing apparatus with full facepiece operated in pressure-demand mode or other positive pressure mode (2) Combination Type C supplied-air respirator with full facepiece operated in pressure-demand mode and auxiliary self-contained air supply

(b) A continuing education program, conducted on at least a yearly basis by qualified health and safety personnel, shall be instituted to ensure that employees whose jobs may involve exposure to cresol, including those engaged in maintenance and repair, have current knowledge of job hazards, proper maintenance procedures, and cleanup methods. Employees shall be informed of the general nature of the medical surveillance procedures and why it is advantageous to the workers to undergo these examinations. Each employee shall be told about the availability of the required information, which shall include, as a minimum, that prescribed in paragraph (c) of this section.

(c) Required information shall be recorded on the "Material Safety Data Sheet" shown in Appendix II or on a similar form approved by the Occupational Safety and Health Administration, US Department of Labor, and shall be kept on file, readily accessible to employees.

Section 6 - Work Practices

(a) Protective clothing and equipment, as set forth in Section 4, shall be worn by all employees engaged in operations where there is the possibility of skin or eye contact with particulate cresol.

(b) Engineering controls, such as process enclosure or local exhaust ventilation, shall be used as needed to keep airborne cresol within the recommended environmental limit.

(c) Equipment and systems used for handling and transferring cresol shall be enclosed to the extent feasible to prevent skin and eye contact. All equipment in which cresol is used shall be grounded,

including tanks, pipelines, and pumps.

(d) Storage, Handling, and General Work Practices

(1) Containers of cresol shall be kept tightly closed at all times when not in use. Storage shall be in well-ventilated areas away from heat and strong oxidizers. Containers shall be periodically inspected for leakage and deterioration.

(2) Written operating instructions and first-aid procedures shall be formulated and posted in areas where cresol is produced, processed, stored, or otherwise used.

(3) All equipment and systems used for handling and transferring cresol shall be inspected periodically for leaks. Valves, fittings, and connections shall be checked for tightness and good working order. Needed repairs and adjustments shall be made promptly.

(4) Before maintenance work is started, sources of cresol shall be eliminated from the affected area to the extent feasible. If the concentration of airborne cresol exceeds the recommended environmental limit, respiratory protective equipment shall be required during such maintenance work.

(5) Easily accessible, well-marked emergency showers and eyewash fountains shall be available in all work areas where cresol is produced, processed, stored, or otherwise used. In case of contact, the skin or eyes shall be flushed with large amounts of water for at least 15 mintues.

(6) Clothing that has become contaminated with cresol shall be either cleaned before reuse or disposed of. Contaminated clothing shall be kept in properly labeled, closed containers until it is laundered or

discarded. Anyone handling or responsible for cleaning contaminated clothing shall be informed about the hazards, relevant symptoms of overexposure, appropriate emergency procedures, and proper conditions and precautions for the safe handling of cresol. Materials that cannot be effectively decontaminated, such as leather and rubber, shall be discarded.

(7) Facilities, such as double lockers, shall be provided for each employee so clean and soiled clothing can be kept separate.

(8) Transportation and use of cresol shall comply with all federal, state, and local regulations.

(e) Emergency Procedures

Emergency plans and procedures shall be developed for all work areas where there is a potential for exposure to cresol. The measures shall include those specified below and any others considered appropriate for a specific operation or process. Employees shall be trained to implement the plans and procedures effectively.

(1) Prearranged plans shall be instituted for obtaining emergency medical care and for the transportation of injured workers. A sufficient number of employees shall be trained in first aid so that assistance is available immediately when necessary.

(2) Spills of cresol shall be cleaned up immediately. The area of the spill shall be posted and secured. Only authorized personnel, adequately protected and properly trained, shall be permitted to enter the area to shut off sources of cresol.

(3) Spilled liquids can be sorbed with vermiculite, dry sand, earth, or other appropriate material. If sufficient drainage to suitable collection basins is available, spilled liquid can be hosed away

with large quantities of water. Methods of waste disposal shall comply with federal, state, and local regulations.

(f) Confined Spaces

(1) Cleaning, maintenance, and repair of tanks, process equipment, and lines shall be performed only by properly trained, adequately protected, and supervised personnel.

(2) Entry into confined spaces, such as tanks, pits, tank cars, barges, and process vessels, shall be controlled by a permit system. Permits shall be signed by an authorized representative of the employer and shall certify that preparation of the confined space, precautionary measures, and personal protective equipment are adequate and that precautions have been taken to ensure that prescribed procedures will be followed.

(3) Before they are entered, confined spaces shall be inspected and tested for oxygen deficiency and for the presence of cresol and other known or suspected contaminants.

(4) No employee shall enter any confined space that does not have an entry large enough to admit an employee wearing safety harness, lifeline, and appropriate respiratory equipment as specified in Section 4(c).

(5) Confined spaces shall be ventilated while work is in progress to keep the concentration of airborne cresol at or below the recommended environmental limit, to keep the concentration of other contaminants below dangerous levels, and to prevent oxygen deficiency.

(6) Anyone entering a confined space shall be observed from the outside by another properly trained and protected worker. An

additional supplied-air or self-contained breathing apparatus with safety harness and lifeline shall be located outside the confined space for emergency use. The person entering the confined space shall maintain continuous communication with the standby worker.

Section 7 - Sanitation

(a) Plant sanitation shall meet the requirements of 29 CFR 1910.141.

(b) Food preparation, dispensing (including vending machines), and eating shall be prohibited in areas where cresol is produced, stored, processed, or otherwise used.

(c) Smoking shall be prohibited in areas where cresol is produced, processed, stored, or otherwise used.

(d) Employees who handle cresol shall be instructed to wash their hands thoroughly with soap or mild detergent and water before using toilet facilities or eating.

Section 8 - Monitoring and Recordkeeping Requirements

As soon as practicable after the promulgation of a standard based on these recommendations, employers shall determine by an industrial hygiene survey whether exposure to airborne cresol is in excess of the action level. Records of these surveys shall be kept, and if an employer concludes that air levels are at or below the action level, the records must show the basis for this conclusion. Surveys shall be repeated at least once every year and within 30 days of any process change likely to

result in an increased concentration of airborne cresol. When the industrial hygiene survey demonstrates that the environmental concentration of cresol exceeds the action level, the following requirements shall apply:

(a) Personal Monitoring

(1) A program of personal monitoring shall be instituted to identify and measure, or to permit calculation of, the exposure of each employee occupationally exposed to airborne cresol. Source and area monitoring may be used to supplement personal monitoring.

(2) In all personal monitoring, samples representative of the exposure to airborne cresol in the breathing zone of the employee shall be collected. Procedures for sampling and analysis of cresol shall be in accordance with Section 1(b).

(3) For each TWA concentration determination, a sufficient number of samples shall be taken to characterize employee exposures during each workshift. Variations in work and production schedules, as well as employee locations and job functions, shall be considered in decisions on sampling locations, times, and frequencies.

(4) Each operation shall be sampled at least once every 3 months or as otherwise indicated by a professional industrial hygienist. If an employee is found to be exposed at a level in excess of the TWA concentration limit, the exposure of that employee shall be measured at least once every week, control measures shall be initiated, and the employee shall be notified of the exposure and of the control measures being implemented. Such monitoring shall continue until two consecutive determinations, at least 1 week apart, indicate that employee exposure no

longer exceeds the environmental limit. Quarterly monitoring shall then be resumed.

(b) Recordkeeping

Records of environmental monitoring shall be kept for at least 30 years. These records shall include the dates and times of measurements, duties and location of the employees within the worksite, sampling and analytical methods used, number, duration, and results of the samples taken, TWA concentrations estimated from these samples, type of personal protective equipment used, if any, and employees' names. These records shall be available to the designated representatives of the Secretary of Labor, of the Secretary of Health, Education, and Welfare, of the employer, and of the employee or former employee.

II. INTRODUCTION

This report presents the criteria and the recommended standard based thereon which were prepared to meet the need for preventing occupational disease or injury arising from exposure to cresol. The criteria document fulfills the responsibility of the Secretary of Health, Education, and Welfare, under Section 20(a)(3) of the Occupational Safety and Health Act of 1970 to "...develop criteria dealing with toxic materials and harmful physical agents and substances which will describe...exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience."

The National Institute for Occupational Safety and Health (NIOSH), after a review of data and consultation with others, formalized a system for the development of criteria upon which standards can be established to protect the health and to provide for the safety of employees exposed to hazardous chemical and physical agents. The criteria and recommended standards should enable management and labor to develop better engineering controls resulting in more healthful work environments, and mere compliance with the recommended standards should not be regarded as a final goal.

The criteria and recommended standard for cresol are part of a continuing series of documents published by NIOSH. The proposed standard applies to the processing, manufacture, and use of, or other occupational exposure to, cresol as applicable under the Occupational Safety and Health Act of 1970. The standard was not designed for the population-at-large, and any extrapolation beyond the occupational environment is not warranted.

It is intended to protect against the development of systemic toxic effects and local effects on the skin and eyes of employees and be measurable by techniques that are valid, reproducible, and available to industry and governmental agencies.

The recommended standard for cresol applies to the individual cresol isomers either occurring alone or in various mixtures. Information found in the literature suggests that the toxicities of o-, m-, and p-cresol are similar and that exposure in the working environment is generally to a mixture of the three cresol isomers.

The major concern in occupational exposure to cresol is adverse effects on the skin, eyes, and respiratory tract. Cresol is both a vapor/aerosol hazard and liquid contact hazard that can result in severe chemical burns and systemic effects. The toxic effects from inhalation have not been adequately studied, but there is some information on the effects from short-term exposure. There is sufficient evidence to indicate that, when there is skin exposure, the toxicity of cresol is similar to that of phenol. In addition, the toxic effects produced by cresol and phenol given by routes of administration other than inhalation are also similar. Therefore, the recommended standard is based on available information on the effects of exposure to airborne cresol and on the similarities of acute toxicity between cresol and phenol that result from dermal contact with the compounds.

The development of the recommended standard for cresol suggested additional areas where further research would be beneficial. Studies, including epidemiologic studies, of the long-term health effects of exposure to cresol at concentrations around the recommended environmental

limit would aid in assessing the hazards of low-level exposure. Followup examinations of employees who have had skin contact with cresol would help to quantitate the risks of systemic effects from dermal exposure. Investigations of the carcinogenic, mutagenic, and teratogenic potential of cresol are also needed.

III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

The cresol isomers ($CH_3C_6H_4OH$) are monomethyl derivatives of phenol (or hydroxy derivatives of toluene) that have the methyl group ortho, meta, or para to the hydroxyl group. The three isomers can occur alone or in various mixtures, either with each other or with other compounds. A mixture containing all three isomers is often referred to as tricresol and has a boiling range between 191 and 203 C. Commercial cresylic acids usually contain cresol in combination with phenol and xylenols and are generally defined as mixtures in which 50% of the material boils above 204 C. The cresol isomers are usually the major components of cresylic acids. Some important chemical and physical properties of cresol are listed in Table XI-1 [1-7]. Although some of these properties differ among the isomers, the oil/water partition coefficients suggest that their biologic distribution may be similar.

Most nonsynthetic cresol used in industry is derived from petroleum or coal tar acids. Petroleum-based cresol is a byproduct of the naphtha-cracking process and is present in the spent caustic liquor used to wash petroleum distillate [8]. Coal tar acids are obtained from coke oven byproducts, gas-retort oven tars, and distilled tar byproducts [8]. The initial fractionation of petroleum or coal tar acids yields a phenolic mixture composed mainly of cresol, phenol, and xylenols. Pure o-cresol can be obtained by further distillation of this mixture, but because of their similar boiling points, the meta and para isomers of cresol must be

separated by other methods. Generally, these two isomers are used industrially as a mixture containing 40-65% m-cresol. Only small amounts of pure natural meta and para isomers are produced. There also are several methods of synthesizing the cresol isomers, particularly p-cresol. The catalyzed methylation of phenol is one of the methods used most often.

It is estimated that 151 million pounds of cresol and cresylic acids were produced in the United States in 1975, down 21% from 1974 [8]. The consumption of synthetic cresol varies to some extent from that of the natural products. Industry sources [8] estimated that, in 1975, 28% of natural cresol was used for production of wire enamel solvents, 20% for phosphate esters, 18% for phenolic resins, 6% for agricultural chemicals, 3% for disinfectants, 3% for ore flotation, 10% for miscellaneous purposes, and 12% for export. In 1969, 29% of synthetic cresol was consumed for phenolic resins, 26% for tricresyl phosphate, 11% for disinfectants, 17% for antioxidants and automotive products, 7% for ore flotation, and 10% for other purposes [8]. A major use of o-cresol is in the manufacture of the herbicides dinitro-o-cresol (DNOC) and 2-methyl-4-chlorophenoxyacetic acid (MCPA) [8]. p-Cresol is used largely to produce the antioxidant 2,6-di-tert-butyl-p-cresol (BHT), which is added to plastics and to food [8]. Cresylic acids and m,p-cresol mixtures are used to make phenolic resins, tricresyl phosphate, and cresyl diphenyl phosphate, the latter two used mainly as plasticizers [8]. Some minor uses of cresols are in the production of azo dyes and as perfume additives, nylon solvents, metal degreasing agents, and synthetic tanning agents [9].

NIOSH estimates that 11,000 people in the United States are occupationally exposed to cresol. This estimate is low, however, because

it does not include workers who are intermittently exposed to a widely used commercial degreasing agent that contains cresol. Some representative occupations are listed in Table XI-2 [8-10].

Historical Reports

Historical reports have described the dangers of exposure to cresol by ingestion and skin and eye contact. Such exposures have produced toxic effects on the central nervous system (CNS), lungs, liver, kidneys, pancreas, vascular system, skin, and eyes. Many attempted and successful suicides resulted from the ingestion of Lysol Disinfectant, which was introduced in 1860. It originally contained phenol, but, in 1872, a new Lysol preparation was introduced, which contained cresol (6-50%) as the active ingredient generally in glycerin or saponified linseed oil. Cresol was removed from Lysol preparations in the United States in 1951 and replaced by o-phenylphenol. Several other cresol solutions similar to Lysol, such as Compound Cresol Solution, U.S.P. and Cresol, N.F., are available and contain 15-50% cresol in saponified linseed or other suitable oil.

In 1922, Isaacs [11] described 52 cases of cresol poisoning, 2 of which were fatal. Most of the cases involved attempts at suicide by ingestion of Lysol, which the author reported as containing 25-50% cresol. Individuals had taken between 4 and 120 ml of the cresol preparation. The first signs of intoxication included abdominal pain and cramps, vomiting, and burning sensations of the mouth, throat, esophagus, and epigastrium. In the severe cases, cyanosis, unconsciousness, and respiratory failure

resulted. Body temperature was generally unaffected by cresol, but it was as low as 94.4 F in some individuals and as high as 99-100 F in others. The pulse of some patients became weak and rapid (100-136 beats/minute), but in others it was slow (66-80). Respiratory rates varied from 16 to 52/minute. Some cases involved dermal contact with cresol, which caused chemical burns. In cases where the eyes were exposed to cresol, the eyelids, corneas, and palpebral conjunctivae swelled and became congested.

Burg [12], in 1929, reported the effects of cresol on the lungs of a 24-year-old man who had attempted suicide by drinking 25 ml of Lysol. The man was found unconscious 2 hours later. He survived but developed pneumonia in both lungs, which the author believed was caused by aspirated Lysol that irritated the mucous membranes of the respiratory tract.

Dellal [13] reported in 1931 that a 31-year-old woman had died 4 days after she drank an unknown amount of Lysol. At autopsy, the pancreas showed acute hemorrhagic degeneration. Extensive fatty necrosis was found in the abdominal cavity, especially in the mesentery of the small intestine, and some congestion was present in the kidneys. This was the earliest mention found in the literature of a possible link between cresol and acute pancreatitis.

In 1933, Herwick and Treweek [14] stated that severe facial burns had developed in a 16-year-old girl exposed to Compound Cresol Solution. The girl had been hospitalized for a spinal graft. During anesthesia, she was placed in a prone position with her face resting for 2 hours in a rubber-cushioned mask. Afterward, her face had marked erythema where it had contacted the rubber on the mask. The skin condition worsened, and blistering developed. Disfiguring scars were still evident 1 year later.

One week before the girl was anesthetized, the mask apparently had been left overnight in a 10% solution of Compound Cresol Solution for sterilization.

Vance [15], in 1945, described the case of a 26-year-old woman, 4.5 months pregnant, who had introduced an unknown quantity of Lysol (50% cresol in saponified linseed oil) into her uterus to terminate the pregnancy. She was admitted to the hospital in a state of collapse. She was also cyanotic and semicomatose and had an extremely low blood pressure. Her breathing was rapid and labored, loud moist rales were detected in her lungs, and she was coughing up a bloodstained fluid. The woman died 75 minutes after being hospitalized. From the results of an autopsy, the author attributed death to pulmonary oil embolism and the action of cresol. He thought the latter may have caused erosion of the blood vessels and tissue necrosis that permitted the oil to enter the bloodstream.

Effects on Humans

The effects of cresols on humans in both occupational and nonoccupational situations have been observed after exposure by various routes, including skin and eye contact, inhalation, and ingestion.

(a) Dermal Exposure

Medical data from industrial plants where cresols are manufactured indicate that skin and eye contact are the major concerns in occupational exposure to cresols and are the cause of most worker injuries related to cresols [16(p 3)]. Effects recorded in the medical departments of these companies included skin and eye burns and irritation, dermatitis, and

conjunctivitis. One manufacturer reported 13 cases of chemical burns from exposure to cresols during 1970-1976 that required employees to miss one or more days of work. A company involved in the synthesis of p-cresol had 11 cases of burns from skin and eye contact in 1976. Maintenance workers and those involved in collecting cresol samples for analysis were at the greatest risk of exposure. The signs and symptoms related to skin contact with cresols were a burning sensation, erythema, localized anesthesia, and a brown discoloration of the skin. Although overt effects were reported, micro biochemical changes were not assessed.

The only report found in the published literature of a death from occupational exposure to cresols was one published by Cason [17] in 1959. It involved a 47-year-old male worker who fell into a vat of "ardrox," which the author called a derivative of cresylic acid. His clothing was removed immediately, and he was washed thoroughly before being taken to a hospital. He suffered burns on 15% of his body. Anuria developed 36 hours after the accident, and his blood urea nitrogen and potassium levels were elevated. On the 7th day, the man developed generalized rhonchi in both of his lungs, a pericardial rub, and precordial pain. He became comatose, developed congestive heart failure on the 10th day, and died 18 hours after becoming unconscious. No autopsy was performed.

In 1945, Klinger and Norton [18] described a case involving a one-time occupational exposure of a 41-year-old man who cleaned torpedo gear trains with a solvent containing 30% cresylic acid, 45% vegetable oil, and 25% water. The solution was diluted fivefold before use. The man worked for 5-6 hours with his unprotected hands and wrists immersed in the solvent most of the time. Later, the skin of his hands became dry and stiff, and

his right eye became watery. On the next day, the skin of his hands began to crack and peel, and the right side of his face and the area around the right ear became painful; his symptoms worsened, and he was hospitalized. The examining physician observed paralysis on the right side of the face, eversion and drooping of the right lower eyelid, sagging of the right corner of the mouth and elevation of the left corner, lacrimation of the right eye, and impaired speech. The skin of the hands and wrists was still dry and peeling, and the underlying tissue was erythematous. The patient's condition was diagnosed as facial peripheral neuritis. Results from red, white, and differential blood cell counts, a hemoglobin determination, and a urinalysis all were normal. The patient was treated with ointments applied to the hands and wrists and with "anti-neuritic vitamins" for the facial neuritis. The authors reported that the prognosis was good.

Goodman [19] reported, in 1933, the effects of skin contact with cresols on silkmill employees. A 21-year-old man developed reddened, ulcerated areas on the fingers of both hands. The redness had been present for 4 of the 8 months he had worked in the mill. Through a series of patch tests, the author concluded that the dermatitis was caused by contact with an antimildew solution that contained the cresol isomers and cresylic acid. After further investigation, nine other workers were identified with dermatitis caused by contact with the antimildew solution.

Zalecki [20] examined employees of several factories in Poland to determine the prevalence of occupational skin disorders. Some of the workers had been exposed to cresol in a cable plant, a rubber plant, and several plants manufacturing synthetic chemicals. Dermatitis, observed most often, was present in 0.75 and 1.3% of the workers in the cable and

rubber plants, respectively. Since many other chemicals were used in these factories, dermatitis could not be attributed specifically to cresol exposure. In a plastics plant, 6 of 30 people examined had dermatitis that was localized on the hands. During the summer months, dermatitis also developed on the face of an unspecified number of workers. The author attributed the dermatitis chiefly to exposure to cresol and phenol.

Nonoccupational dermal exposure to cresol has also resulted in injury and death. In 1975, Green [21] described the case of a male infant who had about 20 ml of a 90% cresol solution in water accidentally poured over his head. Within 5 minutes, the baby was unconscious and cyanotic. He died 4 hours later. Chemical burns were evident on about 7% of his skin. Examination of the internal organs revealed edema, hemorrhagic effusions from the peritoneum, pleura, and pericardium, and congestion in the brain and kidneys. The blood contained 12 mg of cresol/100 ml. Microscopic examination of the tissues revealed destruction of the epidermis with loss of the stratum corneum, extensive centrilobular and midzonal necrosis of the liver, edema of the brain, and signs of early acute tubular necrosis of the kidneys.

These reports of dermal exposures [17-21] show that cresols can produce chemical burns and dermatitis following skin contact. Cresols are rapidly absorbed through the skin and produce effects on the CNS, liver, kidneys, and vascular system.

(b) Inhalation

Because the cresol isomers have low vapor pressures, inhalation of appreciable amounts of their vapors in working environments under normal conditions is unlikely. However, at high process temperatures, vapors can

be produced and may lead to adverse effects upon inhalation. In addition, inhalation of particulate cresol as an aerosol is possible.

In 1939, Corcos [22] presented a study of 34 French workers who were involved in the manufacture of synthetic resins used to produce automobile brake linings. The resins were prepared by combining cresol with formaldehyde in the presence of a condensation agent (ammonia). Because of the high process temperature, cresol vapor was produced and inhaled by the workers. No temperature and vapor concentration data were reported. Seven workers were examined. They were 23-32 years old and had been working for 18 months to 3 years in a plant where resins were prepared in an open tank located in a poorly ventilated room. Blood pressure, Ambard's constant (the ratio of the urea concentration in the blood to that in the urine), and Chvostek's sign (a test for facial muscle spasms, possibly related to blood calcium imbalance) were determined in these workers. During the medical examination, the seven workers complained of headaches that were most severe at the start of the working day and of nausea that was often accompanied by vomiting. Four of the seven workers were hypertensive, as indicated by blood pressure readings of 170/130, 180/120, 170/100, and 160/120. Two of these workers had elevated Ambard's constants, three had marked tremors, and two had positive Chvostek's signs. Radiography showed that the four hypertensive workers also had slightly enlarged hearts, although they were within normal limits.

About 6 months later, after additional ventilation had been installed in the factory, Corcos [22] reexamined these seven workers. Although their arterial pressures had returned to normal and their tremors were less marked, the workers still had digestive disorders, which the author

attributed to continued exposure to cresol vapor because of inadequate ventilation in the plant.

In another study of the same plant, Corcos [22] observed 27 male and female workers (age range not specified) and noted similar but less severe effects than those previously mentioned.

In 1974, NIOSH conducted a Health Hazard Survey of maintenance shop workers exposed to degreasing agents that contained cresol and phenol [23]. Samples taken from the general room air adjacent to the degreaser vats had concentrations of 0.02-10 ppm (0.08-38 mg/cu m), expressed as total phenols. (See Chapter IV for details on environmental data.)

Medical interviews were conducted with several of the shop mechanics at the end of the workday [23]. Questions were directed towards finding whether there were any problems with dermatitis or any effects on the eyes, nose, or throat. One employee complained about the cresol-phenol odor released when the degreaser vat was refilled. No adverse health effects were determined from the interviews. However, the cresol/phenol concentration of 10 ppm (38 mg/cu m), measured as an area sample, was not representative of the true work procedure. Normal procedure required degreaser vats to remain covered. Covers of these vats were removed for the purpose of placing material to be degreased into them and then replaced. The report did not indicate that the workers remained in the area of the degreaser vats for any lengthy period. Thus, the association of the area sample measured as total phenol (38 mg/cu m cresol/phenol) with no health effects is diminished greatly.

Uzhdavini et al [24,25], in two reports that concentrated on the toxicity of cresol in animals (see Animal Toxicity), briefly mentioned the

irritant effects of o-cresol on the nasal mucosa of humans. Ten subjects were exposed to o-cresol vapor at a concentration of 6 mg/cu m (1.4 ppm). Eight individuals had complaints that included dryness and constriction in the nose, irritation of the throat, and an unspecified taste sensation. The authors did not specify the duration of exposure or how the cresol vapor was generated or sampled.

The reports [22-24] on exposure to cresol by inhalation, described above, indicate that cresol vapor has an unpleasant odor, can cause irritation of the upper airways, and may be responsible for nervous system and vascular disturbances.

(c) Other Routes of Exposure

Reports have also described the effects of cresol solutions used in suicide attempts and as abortifacients. In 1956, Presley and Brown [26] presented the cases of four women, 18-35 years old, who had Lysol-induced abortions. When the women were hospitalized because of vaginal bleeding, it was discovered that Lysol, which the authors described as a mixture of 50% cresol and saponified linseed oil, had been introduced into the uterus of each one. One of the women, who reportedly had been given Lysol by her physician 2 days before, had an elevated temperature (104 F), pulse rate (100), and white blood cell count (35,000), a low hemoglobin value (7.5 g%), blood and albumin in her urine, and extensive hemolysis at the time she was hospitalized. The authors stated that the white blood cell count and hemoglobin value were probably inaccurate because of hemolysis. The woman developed abdominal cramps, moist rales in both lungs, hyperpnea, and pulmonary edema and died 12 hours after entering the hospital. Autopsy revealed massive hemolysis in all tissues, especially the liver and

kidneys, acute hemoglobinuric nephrosis, focal necrosis of the liver, and pulmonary oil embolism.

The other three women examined by Presley and Brown [26] survived the abortions. They all had elevated body temperatures and pulse rates. Two had extremely low hematocrits (27% and 11%) and hemoglobin values (7.0 g% and 3.3 g%), while the third had a hematocrit of 34% and a hemoglobin value of 11.1 g%. The white blood cell counts were elevated in two women (14,250 and 24,000) and were not reported for the third.

The most recent case of pancreatic damage from cresol ingestion found in the literature was described by Klimkiewicz et al [27] in 1974. A 49-year-old woman ingested 250 ml of 40% ethyl alcohol and 250 ml of Lysol, which the authors reported contained 50% cresol in potassium soap. She was unconscious when admitted to the hospital and suffered from respiratory disturbance. A medical examination revealed high blood pressure, rapid pulse rate, low hemoglobin concentration, and a low red cell count. Kidney problems, which worsened during the next 3 days, were indicated by the presence of blood in the urine, oliguria with accompanying metabolic acidosis, accumulation of nitrogen metabolites in the blood, and blood electrolyte imbalance. Dialysis was performed, but the patient's condition remained serious. There were also indications (strong stomach pains, no peristaltic sounds) that either the stomach or the intestinal wall had been perforated, but surgery revealed acute inflammation of the pancreas with peritoneal involvement. The woman was treated with diuretics, which gradually relieved the excess nitrogen metabolites, electrolyte imbalance, oliguria, and acidosis. In 3 weeks, the patient's general condition began to improve, although she had developed lobar pneumonia in the left lung.

The authors attributed the kidney malfunction to the direct action of cresol and the pancreatitis to the irritant action of both the cresol and alcohol, including the alcohol that had been consumed prior to the incident. They suggested that these compounds, by directly irritating the mucous lining of the duodenum, constricted the sphincter of the pancreatic and bile ducts and thereby disrupted drainage of pancreatic fluid. The authors attributed the woman's survival, despite pancreatic complications, to the early dialysis, which they thought had quickly reduced the amount of circulating cresol.

The reports [11,12,15,26,27] dealing with the ingestion of Lysol and with its introduction into the uterus demonstrate that it can produce vascular effects, necrosis of the liver and kidneys, and pancreatic involvement. These effects were attributed to the cresol contained in Lysol.

Epidemiologic Studies

No reports of epidemiologic studies of workers exposed to cresol were found in the literature.

Animal Toxicity

Animal studies have investigated the local and systemic effects of exposure to cresols by skin contact, by inhalation, and by oral, subcutaneous, and intravenous administration.

(a) Dermal Exposure

In 1941, Campbell [28] described the toxicities of cresol and several cresylic acids derived from petroleum or coal tar. The chemical constituents of the cresylic acids were not specified. In one experiment, groups of two to six rats of unstated sex and age were dermally exposed to various coal tar-derived mixtures or to high-boiling, petroleum-derived cresylic acids. The mixtures and the doses applied are given in Table III-1. Each dose was placed on a 1-sq-cm gauze patch, which was applied to the clipped abdominal skin and covered with adhesive plaster. The patch and plaster were kept in place for 1 hour, and then they were removed and the skin was washed. The survivors received another similarly applied dose the following day and were observed for 1 week.

TABLE III-1

DOSES OF CRESOL SOLUTIONS APPLIED TO RATS

Solution	Dose* (ml/kg)
Coal tar-derived mixtures	
(1) Commercial cresylic acid	1.0 or 2.0
(2) Soluble cresylic disinfectant	1.0 or 2.25
(3) Commercial soluble cresylic disinfectant	1.0 or 3.5
(4) Saponified Cresol Solution, U.S.P	1.0 or 1.7
Petroleum-derived cresylic acids	1.0

*Each rat was given one of the specified amounts once or twice, depending on whether it survived the first application.

Adapted from Campbell [28]

The petroleum-derived cresylic acid mixtures were less toxic than the others [28]. They caused, at most, slight skin discoloration and occasional superficial erosion of the skin. The other four mixtures caused convulsions and death, as well as skin discoloration ranging from a reddish brown to a dark bluish brown. Convulsions, beginning 5-30 minutes after application and lasting up to 4 hours, occurred after two applications of mixtures 1 and 4, after the first application of 2.25 ml/kg of mixtre 2, and after each of two applications of 1 ml/kg of mixtures 2 and 3. Rats that recovered from the convulsions appeared practically normal the next day. Deaths occurred 0.5-2 hours after a single application of 1.0 or 2.0 ml/kg of mixture 1, 1.0 ml/kg of mixture 2, 3.5 ml/kg of mixture 3, and 1.7 ml/kg of mixture 4. Death also followed the second application of 1.0 ml/kg of mixture 2 and the second application of 1.0 ml/kg of mixture 3. The author concluded that coal tar-derived cresols were more irritating to the skin than petroleum-derived cresols.

Uzhdavini et al [25], as part of a study of various cresol and xylenol isomers (see also sections (b) and (c) in Animal Toxicity), reported on the toxicities of these compounds after application to the skin of rats and mice. The three cresol isomers and 2,4-xylenol, which is a liquid isomer, were applied to the skin of rats. The solid xylenol isomers, 2,6-, 3,4-, 3,5-, and 2,5-, were applied to the skin of rats in crystalline form. Also, 2,6-xylenol in a solution of ethyl alcohol was applied to the skin of mice. The LD50 values were 620, 1,100, and 750 mg/kg for o-, m-, and p-cresol, respectively. 2,4-Xylenol had an LD50 of 1,040 mg/kg in rats, while the LD50 for 2,6-xylenol in ethyl alcohol was 920 mg/kg in mice. No deaths resulted from exposure to any of the other

solid xylenol isomers. All of the xylenols were said to have produced necrosis following skin contact.

Back and colleagues [29] determined the LD50 value for a cresol mixture containing the three isomers in unspecified concentrations. The mixture was applied to the skin of female albino New Zealand rabbits weighing about 5 pounds each. Cresol was administered as an undiluted liquid to the clipped back and sides of rabbits and kept in place with a gauze patch covered by latex rubber or vinyl plastic for 24 hours. Mortality was recorded for 14 days. The authors determined that the dermal LD50 was 1,782 mg/kg.

The dermal LD50 values of the three cresol isomers were determined in albino rabbits (sex unspecified) by a commercial laboratory [30]. The undiluted cresol isomers at four dose levels were each applied to groups of five rabbits weighing between 2.3 and 2.7 kg. Each compound was applied to clipped skin, which was covered with a plastic sleeve for 24 hours. The animals were observed for signs of poisoning, including mortality and evidence of dermal irritation, for 14 days. Gross autopsies were performed on all rabbits.

The LD50 values for o-, m-, and p-cresol were 1,380, 2,050, and 301 mg/kg, respectively [30]. It is not known why in this particular study the reported LD50 value for p-cresol was greatly different from the values for o- and m-cresol. This disparity in LD50 values for the isomers was not indicated in other studies [25,30,31]. Rabbits exposed to m-, o-, and p-cresol at concentrations that ranged from 1,000 to 3,160, 681 to 2,150, and 215 to 618 mg/kg, respectively, exhibited signs of skin irritation,

hyperemia, convulsions, tremors, and death. No abnormalities were observed in animals that survived 14 days after exposure.

In 1972, Shelley and Raque [32] reported that topical application of black laundry ink, which they had used to mark experimental groups of mice, produced depigmentation of the hair in these animals. Two years later, Shelley [33] published the results of a study that investigated the various components of the laundry ink to determine which ones were responsible for pigment loss. Female CBA/J agouti mice were exposed, in groups of five, to various compounds, including phenol and o-, m-, and p-cresol, each at a 0.5% concentration in acetone, or to acetone alone. The hair of the lower back of the animals was plucked or clipped, and each compound was applied topically three times/week for 6 weeks as a mist spray from a tuberculin syringe. Thirty black 6-week-old male mice of the C57 BL/6J strain were similarly exposed to p-cresol at a concentration of 0.5% in acetone. All animals were observed for 6 months after the last dose for any changes in hair color.

p-Cresol produced patterned depigmentation in two of five agouti mice in both the plucked and clipped groups [33]. In two other mice in the plucked group, new hair was totally white. Both the plucked and clipped mice showed what the author described as "occult loss of pigment in the hair." The surface color remained and hid the fact that there was pigment loss in 90% of the hair shaft. Only the tip of the new hair contained pigment. This change was still noted 6 months after the last application of p-cresol. Patches of pigment loss were also observed in the C57 BL/6J mice following application of p-cresol. In the C57 BL/6J strain, a local corrosive effect and a depigmentation of the epidermis were also seen after

repeated applications of p-cresol. Phenol was the only other compound tested that produced the "occult" loss of pigment. The effect from phenol, however, was scarcely apparent after 6 months. Neither o- nor m-cresol produced any changes in hair color. The results of the experiment thus indicated to the author that p-cresol was the chemical responsible for producing hair depigmentation after application of the laundry ink.

Boutwell and Bosch [34] reported on the tumor-promoting action of cresol and xylenols in 2- to 3-month-old tumor-susceptible female mice of the Sutter strain. The fur was shaved from the mid-dorsal region of the mice with electric clippers 1 week prior to application of 9,10-dimethyl-1,2-benzanthracene (DMBA). The mice were not shaved again because of the possibility of mechanical irritation and damage to papillomas. Solutions of DMBA, cresol, and xylenol were applied to the backs of mice as indicated in Table III-2. A single application of DMBA in benzene or acetone was given 1 week prior to the start of xylenol or cresol treatment. The cresol and xylenol isomers, as 20% solutions in benzene, were applied twice weekly for 11 and 19 weeks, respectively. Some mice were given m- or p-cresol two times/week for 19 weeks after a single application of DMBA in benzene, and xylenols were applied to some mice twice weekly for 20 weeks with no prior DMBA treatment. Mice were inspected for tumors once a week, and tumor diagnosis was confirmed by microscopic identification. Tumor yields and survival rates for the various groups of mice are given in Table III-2.

Application of each of the three cresol isomers in benzene after treatment with DMBA in benzene or acetone resulted in a large increase in the number of surviving mice with papillomas compared to the number after

TABLE III-2

CARCINOGENESIS PROMOTING EFFECTS OF CRESOL AND XYLENOL IN MICE

DMBA Solution (25 μl)	Test-agent Solution (25 μl)	Duration (Weeks)	No. of Survivors/ Original	Percent Survivors with Pa*	Average Pa/ Survivor	Percent Survivors with Ca*
0.3% in acetone	None (benzene control)	12	12/12	0	0	0
"	20% o-cresol in benzene	12	17/27	59	1.35	0
"	20% m-cresol in benzene	12	14/29	50	0.93	0
"	20% p-cresol in benzene	12	20/28	35	0.55	0
0.3% in benzene	None (benzene control)	20	18/20	0	0	0
"	5.7% m-cresol in benzene	20	17/20	24	0.24	0
"	5.7% p-cresol in benzene	20	14/20	29	0.36	0
"	None (control)	15	16/20	13	0.13	0 (6 at 53 wk)
"	20% 2,4-xylenol in benzene	15	28/30	50	1.21	11 (18 at 23 wk)
"	20% 2,6-xylenol in benzene	15	27/30	30	0.44	4 (11 at 23 wk)
"	20% 3,4-xylenol in benzene	15	21/30	95	2.66	0 (14 at 23 wk)

TABLE III-2 (CONTINUED)

CARCINOGENESIS PROMOTING EFFECTS OF CRESOL AND XYLENOL IN MICE

DMBA Solution (25 μl)	Test-agent Solution (25 μl)	Duration (Weeks)	No. of Survivors/ Original	Percent Survivors with Pa*	Average Pa/ Survivor	Percent Survivors with Ca*
0.3% in benzene	20% 3,5-xylenol in benzene	15	20/30	40	0.90	0 (5 at 23 wk)
None	10% 2,4-xylenol in benzene	20	26/29	31	0.66	0 (12 at 28 wk)
"	10% 2,5-xylenol in benzene	20	25/30	24	0.40	0 (8 at 28 wk)
"	10% 2,6-xylenol in benzene	20	26/30	8	0.15	0
"	10% 3,4-xylenol in benzene	20	28/29	50	0.71	4 (14 at 28 wk)
"	10% 3,5-xylenol in benzene	20	22/30	55	0.91	5 (14 at 28 wk)

*Pa=papilloma; Ca=Carcinoma

Adapted from Boutwell and Bosch [34]

application of only DMBA in benzene or acetone, but there were no carcinomas due to cresol [34]. Application of the xylenols in benzene after DMBA produced a higher incidence of papillomas and carcinomas than treatment with just DMBA in benzene. When the xylenols in benzene were given with no prior DMBA treatment, both papillomas and carcinomas

developed. Although benzene alone was not evaluated, no tumors were produced when benzene was given after initial application of DMBA. This would indicate that the xylenols, not benzene, produced tumors in the test mice. Cresol alone was not tested.

(b) Inhalation

Campbell [28] exposed an unstated number of white mice to an atmosphere saturated with cresylic acid vapors either for one 5-hour period or for 1 hour/day for 10 consecutive days. The age and sex of the mice, the concentration of the vapor mixture, and the way the vapors were generated were not specified. The mice were exposed either to a coal tar-derived or to one of five different petroleum-derived cresylic acids. The single 5-hour exposures resulted in no deaths. However, exposures to three of the petroleum-derived cresylic acids and to the coal tar-derived cresylic acid for 1 hour/day for 10 days caused death in a few mice. Irritation of the nose and eyes was a common observation in mice from all of the materials tested.

Inhalation studies of the three cresol isomers were conducted by a commercial laboratory [30] using 18 male albino Charles River rats, averaging 209 g in weight and divided into three groups of six rats each. Each group of rats was placed in a 56-liter inhalation chamber and exposed for a single 1-hour period to a dynamically circulated mixture. Vapor was generated by passing air through undiluted liquid cresol, but it was not clear whether an elevated temperature was needed. The rats were placed in the chamber after the concentration had reached 99% of the theoretical maximum concentration. The concentrations attained were 0.71 mg/liter (710 mg/cu m or 161 ppm) for m- and p-cresol and 1.22 mg/liter (1,220 mg/cu m or

280 ppm) for o-cresol. The rats were observed for signs of toxicity until, at the end of 14 days, they were killed and autopsies were performed. All of the rats survived exposure to the cresol isomers. Evidence of toxicity was observed only in rats exposed to o-cresol. They showed generalized inactivity and lacrimation. No abnormalities were observed grossly at autopsy.

Uzhdavini et al [24] examined the effects of o-cresol inhalation on animals of various species. The authors stated that sufficient o-cresol vapor to produce signs of toxicity after a single exposure could not be generated because of its low vapor pressure. Therefore, animals were exposed to a mixture of o-cresol vapor and aerosol generated under static conditions, possibly by warming the material as stated in a subsequent study [25]. Mice (sex and age not given) were exposed to o-cresol, described as vapor and aerosol, at concentrations that varied in the chamber from 26 to 76 mg/cu m (average, 50 mg/cu m) for 2 hours daily, 6 days/week, for 1 month [24]. Control mice were also used. It was recognized that, in addition to the mice being exposed to o-cresol by inhalation, percutaneous penetration was also possible. Although it was not stated by the authors, apparently the mice were killed after the 1-month exposure, and autopsies were performed.

Irritation, presumably of the mucous membranes of the respiratory tract, was noticed in the mice in the first few minutes of exposure [24]. In 18-20 days, the ends of the tails of some exposed mice fell off. The exposed mice gained weight more slowly than controls, but the organ-to-body weight ratios of unspecified internal organs were unchanged in both the experimental and control groups. Microscopic and gross examinations were

performed on several tissues. The CNS contained excess blood, and degenerative changes had occurred in the nerve cells and glial elements. Hyperemia, edema, and a proliferation of cellular elements were observed in the respiratory tract. There were small hemorrhagic patches in the lungs, and the mucous membranes of the airways were inflamed. Degenerative changes of the myocardial fibers were noted, and there were indications of protein degeneration in the liver and kidney cells.

In another part of this study, rats and guinea pigs (number not given) were exposed to o-cresol vapor for 6 hours/day, 5 days/week, for 2 months, and then for 4 hours/day, 5 days/week, for another 2 months [24]. The results were compared with those from control animals. The mean concentration during the exposure period was 9.0 ± 0.9 mg/cu m. In the experiments with rats, the authors measured what they identified as the elementary conditioned defensive reflex, leukocyte levels in the peripheral blood, and leukoid and erythroid elements in the bone marrow. Bone marrow smears at unspecified intervals were also studied. Hexobarbital narcosis was tested in the rats as an indirect measure of liver function. In the experiments with guinea pigs, the blood elements were analyzed, and results of electrocardiograms (ECG's) were briefly mentioned.

By the end of the 2nd month, all exposed rats had lost the defensive reflex [24]. This reflex was also depressed in control rats, but at a slower rate. At 2 months, 30% of the controls still demonstrated the conditioned reflex, and less than 10% still manifested it by 4.5 months. The exposed male rats had a greater number of leukocytes in the peripheral blood (about 22,000/cu mm) than did the controls (about 14,000/cu mm), especially by the 4th month of exposure. One month after exposure to

cresol had ended, the leukocyte count in the exposed rats had returned to essentially control values. No effects on leukocyte count in female rats were described. After rats were exposed to o-cresol for 4 months, some changes in bone marrow were reported. Exposed rats had a statistically significant decrease in the numbers of elements in the erythroid series compared to controls, which was reflected in a statistically significant difference in the leukoid-to-erythroid ratio (1.3:1 in exposed rats and 2.1:1 in controls). After the 4-month exposure, the duration of hexobarbital narcosis was significantly greater in exposed rats than in controls, 62.0 ± 5.2 minutes versus 37.4 ± 0.7 minutes. The authors attributed this change to the effect of cresol on the liver. A slight decrease in the reactivity of the pituitary-adrenal system of rats exposed to o-cresol was observed, but it was not stated how this was measured.

In guinea pigs, inhalation of o-cresol had no effect on the leukoid-to-erythroid ratio in the bone marrow [24]. Some unspecified changes in the hemoglobin concentration were mentioned. The R wave component of the ECG was slightly decreased in exposed guinea pigs, but it was not indicated when these measurements were taken.

In addition to noting a threshold concentration for irritation of the nasal mucosa in humans (see (b) in Effects on Humans), Uzhdavini et al [24] interpreted respiratory irritation in five cats by measuring secretions from fistulas of the salivary parotoid glands. The threshold concentration was stated to be 5-9 mg/cu m.

This report [24] is difficult to evaluate, because the data presented are incomplete. For example, in the description of exposure conditions, neither the type of chamber employed nor the method used for generating

vapor-aerosols was given. The number of animals employed for various experimental procedures generally was not specified, and control conditions were not detailed adequately. Despite these shortcomings, the agreement of the findings of Uzhdavini et al with those reported by other investigators, such as Deichmann and Witherup [31], suggests that satisfactory test and control procedures were used. Therefore, NIOSH believes that the adverse effects found by Uzhdavini et al [24] are meaningful.

In 1975, Kurlyandskiy et al [35] reported the effects on rats exposed to tricresol vapor. Three groups of six rats each (sex and age unspecified) were exposed to tricresol vapor at concentrations of 2.4, 0.1, and 0.01 mg/cu m for 24 hours. Three other groups of six rats served as controls. No description was given of the exposure method or of the system used to generate the vapor. After the rats had been exposed for 24 hours, the amount of neutral red dye absorbed by the lung tissue was measured. The experimental procedure used in determining the absorption of dye was not described. The authors regarded dye absorption as an indication of protein denaturation, which, they reported, was one of the toxic actions of tricresol. An increase in the absorption of dye or decrease in the excretion of dye would indicate a denaturation of protein. The absorption of the dye, expressed in extinction units, was measured spectrophotometrically. In rats exposed to tricresol at a concentration of 2.4 mg/cu m, absorption was significantly higher than it was in the controls ($P<0.001$). This was also the case at 0.1 mg/cu m ($P<0.05$), but, at 0.01 mg/cu m, the effect was not significant ($P>0.05$). Dye absorption at the 0.01 mg/cu m level was greater than that seen at 0.1 mg/cu m, indicating that there was no direct dose-response relationship. The value

for the control animals used in the group exposed at 2.4 mg/cu m was markedly different from control values for the 0.1 and 0.01 mg/cu m groups; however, the authors offered no explanation for the differences observed.

Kurlyandskiy et al [35] also exposed two groups of rats (unstated number) to tricresol vapor at concentrations of 0.05 and 0.0052 mg/cu m for 3 months. It is unclear how many hours/day the animals were exposed and whether the exposure was daily. A third group of rats served as controls. The variables observed during the experiment were body weight, CNS effects, oxygen and carbon dioxide metabolism, total protein content in the blood, tertiary structure of an unspecified protein molecule, cardiovascular effects, and the activity of an unnamed liver transaminase.

Compared with controls, the rats exposed to tricresol at 0.05 mg/cu m showed less weight gain, increased excitability of the CNS (method of measurement not given), higher oxygen consumption and carbon dioxide excretion, and lower concentrations of the gamma globulins in the blood [35]. The tertiary structure of the globular and aglobular portions of the protein molecule was altered, and an increased absorption of dye in the lungs was noted. The observed changes were reversible after exposure ended. No changes were seen in rats exposed to tricresol at a concentration of 0.0052 mg/cu m, and the authors recommended this value as the mean daily maximum permissible concentration. It is difficult to assess these findings because of some unexplained differences noted in the experimental results, the difficulty in evaluating toxicity from a colorimetric determination of protein denaturation, and unanswered questions concerning the procedures used to measure central nervous system function.

Uzhdavini et al [25], as part of their study of various cresol and xylenol isomers (see also (a) and (c) in Animal Toxicity), reported the effects of inhalation of o-cresol and of five xylenol isomers on mice exposed to a vapor-aerosol formed by warming the compounds. They determined that the LC50 for o-cresol in mice was 0.179 mg/liter (179 mg/cu m), but the duration of exposure was not specified. It was noted that o-cresol precipitated on the walls of the exposure chamber and on the fur of the mice, so there was possible exposure by the dermal and oral routes, as well as by inhalation. Toxic signs of exposure to o-cresol as a heated vapor-aerosol included irritation of the mucous linings, dilation of the vessels of the ears and extremities, excitation, hematuria, and convulsions. No inhalation results for the other materials were given. The authors concluded that the danger of poisoning from cresol exists when vapor-aerosol mixtures are present that may lead to skin penetration.

(c) Other Routes of Administration

In 1944, Deichmann and Witherup [31] published their study comparing the toxicities of phenol and o-, m-, and p-cresol. They exposed rats, rabbits, and cats by various routes of administration to determine the minimum lethal doses of each compound. In one experiment, single subcutaneous injections of phenol or one of the cresol isomers, as 10% solutions in olive oil, were given to one cat in each of 10 dose groups. The doses ranged from 0.024 to 0.94 g/kg. The minimum lethal doses were 0.080, 0.055, 0.180, and 0.080 g/kg for phenol and o-, m-, and p-cresol, respectively. The authors concluded that "o-cresol was slightly more toxic than phenol and p-cresol, and that m-cresol was the least toxic following subcutaneous injection."

Rabbits were also given oral doses of phenol or of each of the cresol isomers as 20% aqueous emulsions [31]. The compounds were given by stomach tube at doses ranging from 0.18 to 2.10 g/kg to one rabbit in each of seven groups. Phenol and p-cresol each appeared to be somewhat more toxic than o-cresol. Again, m-cresol was the least toxic. Minimum lethal doses were 0.42, 0.94, 1.40, and 0.62 g/kg for phenol and o-, m-, and p-cresol, respectively.

Single iv injections of 0.5% aqueous solutions of the compounds were given to rabbits in the marginal ear vein at the rate of 1 ml/minute [31]. The doses, ranging from 0.08 to 0.42 g/kg, were administered to one rabbit in each dose group. Given iv, phenol, o-cresol, and p-cresol were equally toxic, with a minimum lethal dose of 0.18 g/kg. The minimum lethal dose for m-cresol was 0.28 g/kg.

Single oral doses of 10% solutions of phenol or cresol in olive oil were given to rats by stomach tube, and the LD50 of each compound was determined [31]. The LD50 values were 1.35 g/kg for o-cresol, 1.5 g/kg for phenol, 1.8 g/kg for p-cresol, and 2.02 g/kg for m-cresol.

Deichmann and Witherup [31] also reported that the signs of poisoning were quite similar for phenol and for the cresol isomers by all of the routes of administration they tested. One of the first apparent effects was a twitching in the muscles of the eyes, eyelids, and ears, which later occurred in isolated muscles throughout the body. The pupils were contracted in the early stages of poisoning but later became dilated. Labored breathing was marked, and pulse and respiration became slow, irregular, and weak after initial increases. Cats and rabbits convulsed

before they became lethargic and comatose, and rabbits exhibited asphyxial convulsions just before death. Convulsions were generally less severe after cresol exposure than after exposure to phenol, although signs of weakness, collapse, and the depth of coma were greater with cresol.

Oral LD50 values for phenol, cresols, and xylenols were also determined by Uzhdavini et al [25]. The compounds were administered as 10% solutions in oil into the stomachs of mice and rats. The LD50 values are listed in Table III-3.

Oral toxicity determinations on the three cresol isomers were included as part of a commercial laboratory study [30] previously discussed (see (a) and (b) in Animal Toxicity). In one study, male albino rats, weighing approximately 180 g, were each given single oral doses by stomach tube of one isomer in undiluted form. Five animals were used at each dose level for each of the three compounds administered. Signs of intoxication, including mortality, were recorded for 14 days, at which time all survivors were killed. Autopsies were performed on all rats. The LD50 values were 121, 242, and 207 mg/kg for o-, m-, and p-cresol, respectively. Signs of intoxication observed in the rats exposed to any one of the isomers included hypoactivity, tremors, convulsions, salivation, prostration, and death. Dyspnea and cyanosis were also observed in rats given p-cresol. Autopsies on exposed rats that died revealed inflammation or hemorrhage of the gastrointestinal tract and hyperemia of the lungs, liver, and kidneys. The only gross change observed in rats that survived exposure was inflammation of the gastrointestinal tract in those given p-cresol.

TABLE III-3

LD50'S OF PHENOL, CRESOL, AND XYLENOL IN MICE AND RATS

Substance*	LD50 with Confidence Intervals (mg/kg)	
	Mice	Rats
Phenol	436 (311-610)	-
o-Cresol	344 (270-436)	1,470 (1,170-1,830)
m-Cresol	828 (695-985)	2,010 (1,240-3,200)
p-Cresol	344 (266-443)	1,460 (1,260-1,670)
2,4-Xylenol	809 (724-914)	3,200 (2,780-3,680)
2,5-Xylenol	1,140 (797-1,530)	1,270**
2,6-Xylenol	980 (823-1,166)	1,750 (1,420-2,150)
3,4-Xylenol	948 (658-1,365)	1,620**
3,5-Xylenol	836 (773-906)	1,915**

*Administered in 10% oil solution by stomach tube
**No confidence intervals available

Adapted from reference 25

(d) Metabolism

In 1950, Bray and associates [36] published a study on the metabolism of the cresol isomers in rabbits. They administered each isomer, in sodium bicarbonate solution, by stomach tube to rabbits weighing 2-3 kg each. Doses of 500-600 mg of o- or m-cresol were given, but no more than 200-300 mg of p-cresol could be tolerated unless the rabbits had been fed 1-2 hours

beforehand. Ethereal sulfates, ether glucuronides, and free and total cresol were measured in the urine during the 24 hours after each dose was given. Conjugated compounds accounted for most of the cresol excreted, an average of 87% of the total dose of o-cresol, 70% of that of m-cresol, and 76% of that of p-cresol. Of the amount of cresol excreted as conjugated products, most was the ether glucuronides. The average percentages of o-, m-, and p-cresol excreted as the glucuronides were 72%, 60%, and 61%, respectively. Additional metabolites were detected by paper chromatography. About 7% of p-cresol was excreted as free hydroxybenzoic acid and about 3% as conjugated hydroxybenzoic acid. o-Cresol and m-cresol each yielded about 3% of 2,5-dihydroxytoluene. The urinary metabolites of the three isomers are summarized in Figure XI-1.

Correlation of Exposure and Effect

The ability of cresols to be absorbed through the skin and produce local and systemic effects has been demonstrated in humans [14,16(p 36),17-21]. The skin, considered to be the primary route of occupational exposure, is the site of most of the worker injuries reported from cresols [16(pp 3,28,36)]. Skin contact with cresols has resulted in skin peeling on the hands [18], facial peripheral neuritis [18], severe facial burns [14], and damage to internal organs, including loss of kidney function [17] and necrosis of the liver and kidneys [21]. Cresols have also caused sensitization of the skin [19,20]. Dermatitis developed on the fingers of workers who had been using a solution containing cresol and cresylic acid [19]. Of 30 workers in a synthetic plastics plant, 6 developed dermatitis

on the hands and face resulting from exposure to cresol and phenol [20]. Although the information in these reports was insufficient to allow determination of dose-response relationships, industrial experience indicated that only small quantities of cresols were needed to produce chemical burns of the skin [16(p 3)].

Animal studies have also indicated that cresols can cause local irritation and be absorbed after skin contact [28,30,33]. Discoloration of the skin, convulsions, and death occurred in rats given dermal appplications of 1 ml/kg of various coal tar-derived cresylic acids [28]. In rabbits that had any of the three cresol isomers applied dermally in doses of 1 ml/kg for 24 hours, severe edema, erythema, or subdermal hemorrhaging developed [30]. Other effects included salivation, lacrimation, hypoactivity, tremors, convulsions, sedation, and death [30]. Shelley [33] reported that repeated dermal application of 0.5% p-cresol caused depigmentation of the hair and epidermis and local corrosion of the skin in mice.

Appreciable concentrations of cresol vapors are rarely generated in industry because all three cresol isomers have low vapor pressures [16(pp 21,25)]. However, a hazardous concentration of vapor may be generated at elevated temperatures, and there have been a few reports in the literature [22,24] describing effects from inhalation of cresol vapor. Corcos [22] reported that seven workers exposed to airborne cresol at an unspecified concentration developed headaches and nausea. Some workers also had hypertension, muscular irritability, convulsions, and decreased kidney function [22]. Interviews with workers exposed to cresol and phenol at concentrations of 0.02-10 ppm (0.08-38 mg/cu m) in air did not delineate

effects on the eyes, nose, and throat [23]. The airborne concentration was reported as total phenols, so the actual exposure to cresol was not known. However, Uzhdavini et al [24] found that 8 of 10 subjects experimentally exposed to o-cresol vapor at a concentration of 6 mg/cu m complained of dryness of the respiratory mucosa, nasal constriction, irritation of the throat, and the sensation of an unspecified taste. In spite of the lack of specific details regarding methodology, this is the only reference of human inhalation exposure to a pure cresol and should not be ignored.

Inhalation experiments on mice [24,25,28], rats [24,30,35], and guinea pigs [24] have produced some varying results, especially with regard to the concentrations of cresol necessary to produce irritation of the eyes and respiratory tract and to cause death. No deaths were reported [30] in rats exposed for 1 hour to o-cresol vapor at a concentration of 1.22 mg/liter (1,220 mg/cu m) or to m- or p-cresol vapor at a concentration of 0.71 mg/liter (710 mg/cu m). The only toxic effects seen were inactivity and lacrimation in rats exposed to o-cresol. Uzhdavini et al [25] reported that the LC50 of warmed o-cresol administered for an indeterminate exposure period to mice as a vapor-aerosol was 179 mg/cu m. Mice inhaling coal tar- or petroleum-derived cresylic acid vapors at "saturated" concentrations for a single 5-hour period showed no effects.

Although no reports of effects in humans from long-term exposure to cresols were found, toxic effects have been observed in animals repeatedly exposed by inhalation [24,28,35]. Campbell [28] reported irritation of the nose and eyes and some deaths in mice that inhaled coal tar- or petroleum-derived cresylic acid vapors at "saturated" air concentrations for 1 hour/day on 10 consecutive days. Uzhdavini et al [24] observed some

microscopic changes in mice exposed to o-cresol vapor-aerosol at an average concentration of 50 mg/cu m for 2 hours/day, 6 days/week, for 1 month, and in rats and guinea pigs exposed to o-cresol vapor at a concentration of 9 mg/cu m for 6 hours/day, 5 days/week, for 2 months, and 4 hours/day, 5 days/week, for another 2 months. These authors also reported irritation of the upper respiratory tract in humans exposed to airborne o-cresol at 6 mg/cu m and in cats exposed at 5-9 mg/cu m. They did not comment on whether similar effects were found in rats and guinea pigs. Kurlyandskiy et al [35] found that 0.05 mg/cu m of tricresol vapor was the lowest concentration at which effects, including CNS excitability and protein denaturation, were noted in rats exposed for 3 months.

Several cases of cresol ingestion and its intravaginal application have shown cresol to be corrosive to body tissues and to cause toxic effects on the vascular system, liver, kidneys, and pancreas. Cresol introduced into the uteri of pregnant women has produced abortion [15,26], extensive hemolysis [26], erosion of blood vessels [15], damage to the kidney tubules [26], necrosis of the liver [26], and death [26].

Most cases of cresol ingestion have been the result of attempted [11,12,27] or successful [11,13] suicides. The smallest amount of cresol that produced death was 4 ml of a 25-50% cresol solution in an 11-month-old child [11]. Systemic effects observed after cresol ingestion reflected those observed after its use as an abortifacient and included elevated blood pressure [27], damage to the vascular system [27] and kidneys [11-13,27], and acute pancreatitis [13,27].

Mice [25], rats [25,30], and rabbits [31] that were exposed to cresol by the oral route have shown toxic effects similar to the effects on

humans. Reported effects included labored breathing, cyanosis, inactivity, and convulsions [30,31], inflammation and hemorrhage of the gastrointestinal tract [30], and hyperemia of the lungs, liver, and kidneys [30].

Although no data were found that compared the effects of o-, m-, and p-cresol in humans, several animal studies [25,30,31,36] suggest that their biologic actions are similar. Mortality studies using dermal, oral, subcutaneous, or iv administration have generally shown that o- and p-cresol are about equal in toxicity, but that m-cresol is less toxic. The only inhalation study [30] that compared the three isomers showed no difference in effect between m- and p-cresol at identical concentrations; o-cresol was given at a somewhat higher concentration. The toxic effects other than mortality observed in these studies [25,30,31] were qualitatively similar for the three isomers, and included skin irritation, CNS disturbances, and liver and kidney damage. The urinary metabolites of the three isomers have also been found to be similar [36]. Compounds conjugated at the hydroxyl group accounted for the majority of the metabolites.

In summary, the most frequently observed effects resulting from occupational exposure to cresols are burns of the skin and eyes. In addition to being strong tissue irritants, cresols may cause impairment of kidney and liver function and CNS and cardiovascular disturbances. The effects of exposure to cresols on humans and animals are summarized in Tables III-4 and III-5, respectively.

Carcinogenicity, Mutagenicity, Teratogenicity, and Effects on Reproduction

No investigations of the mutagenic or teratogenic potential of cresol were found in the literature. Boutwell and Bosch [34] presented data on the role of phenol and its derivatives, including cresol, in promoting the formation of both papillomas and carcinomas. They found that each of the cresol isomers promoted DMBA-induced papillomas in mice, but no carcinomas were produced. Administration of several of the tested xylenols resulted in increased numbers of papillomas and carcinomas in mice. In addition, some of the xylenols were found to be weak carcinogens. This report suggests that the cresol and xylenol isomers may promote the action of DMBA resulting in the production of benign tumors.

TABLE III-4

EFFECTS OF EXPOSURE TO CRESOLS IN HUMANS

Route of Exposure	Subjects			Exposure		Observed Effects	Reference
	No.	Age (yr)	Sex	Description	Duration		
Dermal	1	47	M	Total body immersion in vat of cresylic acid derivative	-	Burns, anuria, high BUN, coma, heart failure, death	17
"	1	<1	"	20 ml of 90% cresol poured on head	-	Burns, edema, internal hemorrhage, kidney damage, death	21
"	1	16	F	Anesthetic mask soaked in 10% cresol on face	2 hr	Erythema, blisters, scars	14
"	1	41	M	Hands in 6% cresylic acid	5-6 hr	Skin dry and peeling, erythema, tearing, facial peripheral neuritis	18
"	-	-	-	-	-	Burns	11, 16(p 36)
"	-	-	-	Work in plastics or cable and rubber plant	-	Eczema	20
"	1	21	M	Contact with antimildew solution with cresol and cresylic acid	8 mon	Dermatitis	19
Inhalation	34	23-32	-	Cresol vapor	-	Headache, vomiting, hypertension, tremors, spasms, elevated Ambard's constant, enlarged heart	22
"	10	-	-	o-Cresol at 6 mg/cu m	-	Respiratory tract irritation	24
"	-	-	-	Degreasers with cresol and phenol at up to 10 ppm	-	None	23

TABLE III-4 (CONTINUED)

EFFECTS OF EXPOSURE TO CRESOLS IN HUMANS

Route of Exposure	Subjects			Exposure		Observed Effects	Reference
	No.	Age (yr)	Sex	Description	Duration		
Ocular	-	-	-	-	-	Eye irritation	11
Oral	1	49	F	250 ml of Lysol (50% cresol) plus 250 ml of ethyl alcohol	-	Unconsciousness, kidney failure, pancreatitis, pneumonia	27
"	-	-	-	4-120 ml of Lysol (25-50% cresol)	-	Abdominal pain, vomiting, unconsciousness, death	11
"	1	24	F	25 ml of Lysol	-	Unconsciousness, pneumonia	12
"	1	31	"	Unknown amount of Lysol	-	Pancreatitis, fat necrosis, kidney congestion, death	13
Vaginal	1	26	"	"	-	Low blood pressure, breathing difficulty, hemolysis, pulmonary oil embolism, blood vessel erosion, death	15
"	4	18-35	"	"	-	Vaginal bleeding; elevated temperature, pulse, WBC; hemolysis; pulmonary edema; liver and kidney damage; death	26

TABLE III-5

EFFECTS OF EXPOSURE TO CRESOLS IN ANIMALS

Route of Exposure	Species	Isomer/ Compound	Exposure: Concentration	Exposure: Duration	Effects	Reference
Dermal	Rat	Coal tar cresylic acid	1-2 ml/kg	1-2 hr	Skin discoloration, convulsions, death	28
"	"	Coal tar cresylic disinfectants	1-3.5 ml/kg	"	"	28
"	"	Coal tar cresol	1.0-1.7 ml/kg	"	Skin discoloration, death	28
"	"	Petroleum cresylic acid	1.0 ml/kg	"	Skin irritation, discoloration	28
"	"	m-Cresol	1,100 mg/kg	Single dose	LD50	25
"	"	p-Cresol	750 mg/kg	"	"	25
"	"	o-Cresol	620 mg/kg	"	"	25
"	Mouse z	o- or m-Cresol	0.5%	6 wk	No effects	33
"	"	p-Cresol	"	"	Skin corrosion, depigmentation	33
"	Rabbit	m-Cresol	1,000-3,160 mg/kg	24 hr	Skin irritation, convulsions, death, hyperemia	30
"	"	o-Cresol	681-2,150 mg/kg	"	Erythema, tremors, death	30
"	"	p-Cresol	215-681 mg/kg	"	Skin irritation, tremors, sedation, death, kidney inflammation	30
Inhalation	Rat	o-Cresol	1,220 mg/cu m	1 hr	Inactivity, lacrimation	30
"	"	m-Cresol	710 mg/cu m	"	No effects	30
"	"	p-Cresol	"	"	"	30

TABLE III-5 (CONTINUED)

EFFECTS OF EXPOSURE TO CRESOLS IN ANIMALS

Route of Exposure	Species	Isomer/ Compound	Exposure: Concentration	Exposure: Duration	Effects	Reference
Inhalation	Rat	o-Cresol	9.0 mg/cu m	4 mon	CNS effects, blood changes	24
"	"	Tricresol	2.4 mg/cu m	24 hr	Protein denaturation in lungs	35
"	"	"	0.1 mg/cu m	"	"	35
"	"	"	0.01 mg/cu m	"	No effects	35
"	"	"	0.05 mg/cu m	3 mon	CNS excitation, protein denaturation in lungs	35
"	"	"	0.052 mg/cu m	"	No effects	35
"	Mouse	Cresylic acid	Saturated air	10 d	Mucosal irritation, death	28
"	"	"	"	5 hr	No effects	28
"	"	o-Cresol	26-76 mg/cu m	1 mon	Vascular congestion, changes in CNS, inflammation of airways	24
"	Guinea pig	o-Cresol	9.0 mg/cu m	4 mon	Changes in ECG	24
Oral	Rat	m-Cresol	1,700-2,700 mg/kg	Single dose	Twitching, coma, death	31
"	"	p-Cresol	1,300-2,700 mg/kg	"	"	31
"	"	o-Cresol	1,000-2,200 mg/kg	"	"	31
"	"	m-Cresol	215-464 mg/kg	"	Hypoactivity, convulsions, GI tract inflammation, hyperemia, death	30
"	"	p-Cresol	215-316 mg/kg	"	"	30
"	"	o-Cresol	100-215 mg/kg	"	"	30

TABLE III-5 (CONTINUED)

EFFECTS OF EXPOSURE TO CRESOLS IN ANIMALS

Route of Exposure	Species	Isomer/ Compound	Exposure		Effects	Reference
			Concentration	Duration		
Oral	Rat	m-Cresol	147 mg/kg	Single dose	Hypoactivity, convulsions, GI tract inflammation, hyperemia	30
"	"	p-Cresol	100-147 mg/kg	"	"	30
"	"	o-Cresol	68 mg/kg	"	"	30
"	Rabbit	m-Cresol	1,400-2,100 mg/kg	"	Convulsions, coma, death	31
"	"	o-Cresol	940-1,400 mg/kg	"	"	31
"	"	p-Cresol	620-1,400 mg/kg	"	"	31
iv	"	m-Cresol	280-420 mg/kg	"	"	31
"	"	o-Cresol	180-280 mg/kg	"	"	31
"	"	p-Cresol	"	"	"	31
"	Mouse	m-Cresol	2,010 mg/kg	"	LD50	25
"	"	o-Cresol	1,470 mg/kg	"	"	25
"	"	p-Cresol	1,460 mg/kg	"	"	25
Subcutaneous	Cat	m-Cresol	180-940 mg/kg	"	"	31
"	"	p-Cresol	80-940 mg/kg	"	"	31
"	"	o-Cresol	55-940 mg/kg	"	"	31

IV. ENVIRONMENTAL DATA

Sampling and Analytical Methods

Few reports of methods for the sampling of airborne cresol [37-39] were found, and these provided inadequate descriptions so that the precision of the sampling techniques and their suitability for personal air monitoring could not be assessed. Majewskaja [37] and Manita [38] suggested using 0.1 N sodium hydroxide solution as a collecting medium contained in an absorber. Ethyl alcohol and isopropanol in midget impingers have also been used to collect o-cresol from the air [39]. These methods, however, can pose problems in taking field measurements because liquid spills can occur during sampling and handling.

NIOSH investigated the suitability of a solid sorbent for sampling airborne cresol [40]. The tested and validated sampling method involves drawing a known volume of air through a silica gel tube. This sampling device has an advantage over the midget impinger in personal air monitoring because it does not involve the use of liquid and because its precision in collecting cresol is known. The silica gel tube is the recommended sampling method; details of the method are presented in Appendix I.

Numerous analytical methods are available for separating and analyzing the cresol isomers and for separating them from other phenolic compounds, particularly phenol and xylenols. Most of these have been used to determine cresol in liquid mixtures, and their usefulness in analyzing air samples has not been established. Suggested methods have included gas-liquid [41-48], paper [49,50] and thin-layer [49] chromatography,

ultraviolet [38,39,51-54] and infrared [55,56] spectrophotometry, colorimetry [57,58], and analysis by crystallization point [59,60].

Ultraviolet spectrophotometry has been used to determine cresol in air samples [38,39]. Cresol was measured by detecting particular absorption bands, but interference from other air contaminants with absorption bands in the same range reduced the sensitivity and precision of the ultraviolet spectrophotometric method. For instance, one method [38] involved determination of total phenol and cresol because the absorption bands were not separable.

Ultraviolet methods have also been used in the analysis of liquid mixtures containing cresol [52-54,61,62]. However, since most were concerned with quantitative analysis of a mixture of only the three cresol isomers, their usefulness in determining the amount of cresol in an air sample that may contain a variety of similar compounds is not known. In one method [54], phenol was successfully separated from o- and p-cresol, but m-cresol had an absorption band similar to that of phenol.

Paper and thin-layer chromatography have been suggested as methods for the separation and analysis of cresol and structurally similar compounds [49,50]. One paper chromatographic method involved separating the compounds as the sodium salts of phenyl azo dyes [50], but interference from other compounds, such as phenol, could not be prevented. Another study showed that paper chromatography was effective in separating m- and p-cresol but that quantitative analysis of phenol and cresol could not be accomplished [49]. Phenol and total cresol could be successfully analyzed by thin layer chromatography [49]. These methods have not been tested for their suitability in analyzing air samples.

The concentrations of phenol and cresol in alkaline solutions were determined quantitatively using a colorimetric procedure [57]. When reacted with Folin-Denis reagent, the compounds yielded distinct colors whose intensities could be measured. The concentration of the cresol isomers was determined as total cresol. This method has been applied to analysis of cresol and phenol in biologic fluids, such as blood and urine [57].

The meta and para isomers of cresol have been detected in a cresylic acid mixture on the basis of the crystallization points of cresol complexes [59,60]. However, the accuracy of this method varied according to the concentration of the individual isomers and of phenol in the cresylic acid mixture.

Infrared spectrophotometry was shown to be effective in separating cresol from other structurally related substances [55,56]. Separation and quantitative analyses of the cresol isomers, phenol, and xylenols were possible when either cyclohexane or carbon disulfide was used as the solvent. In the direct-reading infrared analyzers, cresol reportedly absorbs at the 8.6 μm wavelength, with a sensitivity of 0.3 ppm [63].

The photoionization detectors are claimed to be capable of detecting cresol vapor concentrations below 1 ppm. One manufacturer has estimated that 0.1 ppm of cresol can be detected by analogy to phenol [82].

Colorimetric tubes for phenol can be used to measure cresol, but their accuracy, precision, and sensitivity have not been validated by NIOSH [64].

Gas-liquid chromatographic (GLC) techniques are available that provide a specific quantitative analytical method for cresol [41,45,46,65]. Resolution of interferences from various compounds, such as phenol and xylenols, has been accomplished by selection of the appropriate stationary phase. Some stationary phases that have been used successfully to quantitatively analyze cresol, phenol, and xylenols include tri-o-cresyl phosphate [41,45,65], 2,4-xylenyl phosphate [41,45], dimethyl phthalate [46], and free fatty acid polymer [40].

A GLC method using free fatty acid polymer [40] is recommended for analysis of samples of cresol collected from the workplace environment because of its ability to separate and quantitatively determine cresol from a mixture containing structurally similar compounds and because of its known precision, accuracy, and sensitivity. This method, which is described in detail in Appendix I, has been tested and validated by NIOSH. Although the chromatographic conditions of the recommended method do not permit separation of m- and p-cresol, such separation is not necessary, since the recommended environmental limit is for total cresol.

Environmental Levels

Only one report that gave measured concentrations of airborne cresol in the workplace was found in the literature [23]. It concerned a survey of a maintenance shop to assess exposure to degreasing agents containing cresol and phenol. Air samples taken from the general room air adjacent to the degreaser vats were collected in a midget impinger. The author did not analyze cresol and phenol separately but expressed the concentration as

total phenols. Therefore, the exact concentrations of cresol in the air are not known. Three room-air samples were taken in 1 day, two in the morning and one in the afternoon. The levels of airborne phenol were 0.05 and 0.02 ppm (0.22 and 0.08 mg/cu m) in the morning and 10 ppm (44.2 mg/cu m) in the afternoon. This large variation was attributed to changes in work practices. The degreasing vat had been covered in the morning except for brief periods when engine parts were immersed or removed from the liquid. However, it was left open in the afternoon, and a high vapor concentration resulted.

Engineering Controls

Engineering controls must be instituted in areas where the concentrations of airborne cresol exceed the recommended environmental limit to reduce the concentrations to levels as low as possible. Industrial experience indicates that closed systems under negative pressure, when properly operated and maintained, are the best method of preventing exposure. When closed systems are not feasible, well-designed local exhaust ventilation should prevent the accumulation of airborne cresol at levels in excess of the environmental limit. Since cresol vapor can be flammable at high temperatures, the National Fire Protection Association Codes for handling flammable vapors (NFPA N. 70-1971) and for blower and exhaust systems (MFPA N. 91-1973) should be followed. Recommendations for appropriate ventilation systems can also be found in NIOSH Recommended Industrial Ventilation Guidelines [66], in Industrial Ventilation--A Manual of Recommended Practice [67], published by the

American Conference of Government Industrial Hygienists, and in Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2-1971 [68], published by the American National Standards Institute. Any operation where cresol is transferred, charged, or discharged into otherwise closed systems should have local exhaust ventilation at the transfer point. Ventilation systems should be inspected and maintained regularly to ensure effective operation. Changes in process that may affect the ventilation system should be assessed promptly to make certain that workers are adequately protected.

V. WORK PRACTICES

Occupational exposure to cresol can occur by inhalation, skin and eye contact, and ingestion. In order to reduce the likelihood of adverse health effects developing in employees, work practices must be implemented that will minimize exposure by these routes.

Industrial experience has shown that skin burns and irritation occur from contact with small quantities of liquid cresol [16(p 3)]. Therefore, protective clothing and equipment must be worn by workers who handle this compound. The degree of protection required depends on the severity of the potential exposure. Operations in which an aerosol is generated may require coveralls and face shields (8-inch minimum) with goggles to prevent contact of particulate cresol with the body, including the eyes. For jobs that involve handling the materials and in which there is a possibility of the body being soaked, the use of full-body suits for adequate protection of the skin and eyes is required. Employees involved in operations in which splashes or sprays to the face or body may occur can be adequately protected with face shields (8-inch minimum) with goggles, aprons, and gloves. When exposure is limited to handling contaminated equipment or to handling small amounts of liquid that are unlikely to be splashed, gloves should afford adequate protection.

Rubber gloves have been reported to be effective in protecting the hands of workers handling cresol [16(p 29)]. To provide additional protection, they should have cotton liners making a tight seal with the hands. Protective clothing and equipment should be decontaminated before

reuse, and any protective apparel showing signs of deterioration should be discarded in clearly labeled, closed containers.

Emergency showers and eyewash fountains must be available near work areas where cresol is manufactured, processed, stored, or otherwise used. Cresol can produce chemical burns on contact, and the most effective method of preventing serious injury is quickly removing the compound from the affected area with copious amounts of water [16(pp 22,24)]. Severe eye injury can be prevented by immediately flushing the eyes with water for at least 15 minutes.

Compliance with the recommended exposure limit should protect workers against the adverse health effects of inhaling cresol. However, during certain operations when the environmental limit is temporarily exceeded respiratory devices may be permitted. Any devices provided must meet the specifications of Table I-1.

Because the vapors of cresol may cause skin irritation and be absorbed through the skin, protective clothing should be provided and worn whenever respiratory protective devices are required. Any respiratory protective device that does not provide adequate eye protection, such as half-mask facepiece respirators, should not be used because of the possibility of eye injury.

A respiratory protective program in accordance with 29 CFR 1910.134 must be followed to ensure that respirators are routinely inspected and properly cleaned, maintained, and stored.

Ingested cresols can be fatal [11-13], but a good sanitation program, safe work practices, and good personal hygiene practices will reduce the risk of exposure by this route. If eating areas are provided they should

be separate from all areas where cresol is manufactured, processed, used, or stored. Food and beverage consumption and smoking must be prohibited in these latter areas to eliminate possible sources of lip or mouth burns, as well as ingestion.

Cresol should be stored in tightly closed, well-labeled iron or steel containers (avoid the use of aluminum, copper, and brass alloys) in cool, well-ventilated areas away from heat and strong oxidizers. Damaged drums or other containers for storage or transportation should be repaired only after they have been thoroughly purged with steam, flushed with water, and air-dried.

Spilled cresol must be cleaned up immediately. Only properly trained and adequately protected employees should take part in cleanup operations. The area of a spill should be posted and secured to prevent entry by unauthorized personnel. Liquid cresol can be sorbed with vermiculite, dry sand, earth, or other suitable material. If sufficient drainage to a suitable collection basin is available, spilled liquid can be hosed away with large quantities of water. Spilled solid material should be collected by vacuuming (provided it does not cause a dust hazard) and deposited in a sealed container, and the area of a spill should be ventilated to remove any vapor or aerosol. Methods of waste disposal must comply with federal, state, and local regulations.

Cresol vapor at elevated temperatures is flammable [1]. However, cresol can be handled at temperatures below its flashpoint (178-187 F or 81-86 C) with little direct danger of fire [1]. Because fire or explosion is possible, ignition sources should be controlled in areas where cresol is

manufactured, processed, stored, or otherwise used. In the event of a fire, foam, dry-chemical, or carbon dioxide extinguishers should be used.

Whenever feasible, operations, processes, and materials should be enclosed to minimize occupational exposure to cresol. These systems should be inspected frequently for leaks or damage, and any needed repairs should be made promptly. Several incidents involving skin contact with cresols that occurred as a result of leaks [16(p 37)] have clearly shown the importance of frequent inspection of equipment.

Maintenance and repair workers, especially those working on ventilation systems or in enclosed environments, have a high risk of exposure because of the nature of their work. To minimize or prevent exposure, they must be familiar with the hazards of the materials that may be encountered and with proper work practices, as well as have adequate supervisory control. Special precautions must be taken when work is to be performed in confined spaces. Entry into confined spaces should be controlled by a permit system. Prior to entry, the confined space must be purged and tested for oxygen deficiency and for the presence of flammable vapors and toxic gases. Purging should be done with steam and followed by flushing with water. Personnel entering confined spaces must wear protective clothing, be equipped with a safety harness and lifeline, and use either a self-contained, pressure-demand mode breathing apparatus or a combination supplied-air suit with an auxiliary self-contained air supply. Anyone entering a confined space should be observed by a properly trained and equipped standby worker familiar with emergency procedures, in case rescue is necessary. A communication system should be set up between the workers involved in the operation.

Employee education on the safe handling of cresol and its hazards is essential if adverse health effects are to be reduced. It is particularly important that employees be informed of the danger of skin and eye contact with these materials and of possible toxic effects from inhalation of airborne cresol. The importance of immediately removing contaminated clothing and of washing with liberal amounts of water to remove the materials from the skin or eyes must be stressed. Industrial experience has shown that serious chemical burns and systemic injuries from cresol are usually prevented if the materials are immediately washed from the skin [16(p 16)].

In all workplaces where there is occupational exposure to cresol, written instructions informing employees of the particular hazards of these chemicals, proper handling methods, procedures for cleaning up spilled material, personal protective equipment, and procedures to be used in emergencies must be kept on file and available to employees. The Material Safety Data Sheet shown in Appendix II may be used as a guide for employers in providing the required information.

VI. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The American Conference of Governmental Industrial Hygienists (ACGIH) first recommended a Threshold Limit Value (TLV) for cresol in 1952 [69]. The recommended level of 5 ppm, which, beginning in 1956 [70], was also expressed as 22 mg/cu m, represented a TWA for an 8-hour workday and 40-hour workweek. A "Skin" notation was added in 1961 to acknowledge that the cutaneous route of exposure was important because cresol was rapidly absorbed through the skin [71]. The initial recommendation has not changed in 25 years and is the current ACGIH TLV [72].

The ACGIH 1974 Documentation of Threshold Limit Values for Substances in Workroom Air [73] cited three reports in support of the ACGIH recommended TLV. Elkins [74] reported that cresol should not present an inhalation hazard under normal conditions because of its low vapor pressure. He noted that cresol was a strong irritant that frequently caused dermatitis and that fatal poisoning could result from dermal contact. Reference was also made to Fairhall [75] and to Hamilton and Hardy [76], who had compared the toxicity of cresol with that of phenol. Fairhall [75] concluded that cresol was somewhat less toxic than phenol and noted some differences in degree of toxicity among the three cresol isomers. The meta isomer was said to be the least toxic, while the para isomer was considered the most toxic. The differences, however, were deemed too slight to warrant the ACGIH [73] recommending separate TLV's. In a review of cresol, Hamilton and Hardy [76], making statements similar

to those of Fairhall [75], thought that the toxic action of cresol was similar to that of phenol. Based on the literature and on experience with phenol, the ACGIH [73] stated that a limit of 5 ppm (approximately 22 mg/cu m) is "believed sufficiently low to prevent any serious degree of irritation from cresol vapor."

The ACGIH [72] proposed the addition of a Threshold Limit Value-Short Term Exposure Limit (TLV-STEL) for cresol of 22 mg/cu m (5 ppm). The TLV-STEL was defined as the "maximal concentration to which workers can be exposed for a period up to 15 minutes continuously without suffering from (1) irritation, (2) chronic or irreversible tissue change, or (3) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency, provided that no more than four excursions per day are permitted, with at least 60 minutes between exposure periods, and provided that the daily TLV-TWA also is not exceeded."

The present federal standard (29 CFR 1910.1000) for workplace exposure to cresol is an 8-hour TWA concentration limit of 22 mg/cu m (5 ppm) with a "Skin" notation, based on the 1968 ACGIH TLV for workplace exposure [77].

Several other countries have standards for cresol expressed as Maximum Allowable or Acceptable Concentrations (MAC's) [78,79]. Finland and Yugoslavia each have adopted an MAC of 22 mg/cu m. Hungary has set a limit of 5 mg/cu m but allows a single 30-minute exposure at up to twice the MAC. Poland and West Germany each have a limit of 5 mg/cu m, while Rumania has an MAC of 15 mg/cu m. No justification was found for any of these standards. In a 1969 Documentation of MAC in Czechoslovakia [80], an MAC-TWA of 20 mg/cu m with a peak exposure limit of 40 mg/cu m was

recommended. It was noted that the irritating effect of cresol was greater than that of phenol but that its vapor pressure was lower.

Basis for the Recommended Standard

(a) Permissible Exposure Limits

Exposure to cresols has produced effects on the CNS [18,21,22], respiratory system [12,15,24,26], liver [21,26], kidneys [13,17,21,22, 26,27], pancreas [13,27], vascular system [15,26], skin [11,14,18-21], and eyes [16(p 3)]. Although occupational exposure to cresol has involved skin and eye contact [16 (p 3),17-20] and inhalation of vapor [22,23], past industrial experience and the low vapor pressure of cresol indicate that the greatest hazard from exposure to this material results from skin and eye contact [16(pp 3,36)].

The effects on humans and animals from inhalation of airborne cresol have been reported. Seven workers, exposed to cresol vapor at an unspecified concentration, had headaches, which were often accompanied by vomiting [22]. Four workers also had elevated blood pressure, signs of impaired kidney function and blood calcium imbalance, and marked tremors. An additional 27 workers complained of headache, nausea, and vomiting. Six persons from this group were hypertensive, and one had signs of blood calcium imbalance [22].

A survey of a maintenance shop indicated that workers were being exposed to cresol and phenol vapors [23]. The total concentration of phenol and cresol, expressed as total phenols, ranged from 0.02 to 10 ppm (0.08-38 mg/cu m). None of the workers examined had any signs or symptoms

of intoxication, but one worker was bothered by the odor of cresol and phenol. The specific exposure to cresol could not be ascertained because no attempt was made to separate the phenol and cresol in the sampling and analytical procedure.

The current federal standard for occupational exposure to cresol is similar to that of phenol, a compound for which NIOSH has recommended a TWA concentration limit of 20 mg/cu m [81]. The ACGIH-recommended TLV for cresol appeared to be based, to a great extent, on comparison to phenol. Cresol and phenol are derived from similar sources and usually occur in the same working environments.

The data presented in Chapter III suggest that the toxic effects of cresol are similar to those produced by phenol. Deichman and Witherup [31] reported that phenol and o- and p-cresol were similar in toxicity when given to animals by iv or subcutaneous injection or by stomach tube. m-Cresol was somewhat less toxic. Qualitatively, the signs and symptoms of intoxication were also similar. Like that of cresol, the primary route of occupational exposure to phenol is skin contact. Both compounds are rapidly absorbed through the skin, cause skin and eye burns, and produce effects on the liver, kidneys, pancreas, lungs, and vascular system. Uzhdavini et al [25] reported that the oral LD50 values in mice were similar for phenol and o- and p-cresol, while m-cresol had a higher LD50.

Although the data indiciate similarities in toxicity between cresol and phenol when they are given by several routes of exposure, some evidence suggests that cresol is more toxic by the inhalation route [24].

Uzhdavini et al [24] exposed 10 subjects to o-cresol vapor at a concentration of 6 mg/cu m and reported that 8 of them experienced upper

respiratory tract irritation, including dryness, constriction in the nose, irritation of the throat, and the sensation of an unspecified taste.

Animals were also used by Uzhdavini et al [24] to study the effects of inhalation of cresol at concentrations near or below the present workplace exposure limit of 22 mg/cu m (5 ppm). Mice exposed to o-cresol vapor-aerosol at concentrations that varied from 26 to 76 mg/cu m (average, 50 mg/cu m) for 2 hours/day, six times/week, for 1 month showed signs of irritation, lack of activity, and eventual mummification of tail tissues. Microscopic examination showed vascular congestion and degenerative changes in the nerve cells and glial elements of the CNS, hemorrhaging in the lungs, inflammation of the airways, and degeneration of the myocardial fibers.

The closest approximation to chronic poisoning available involved rats exposed to o-cresol vapor at 9 ± 0.9 mg/cu m, 5 days/week, for 4 months (6 hours/day for 2 months, then 4 hours/day for 2 months) [24]. The exposed rats lost the elementary conditioned defensive reflex more rapidly than controls. Other observed changes included an elevated leukocyte count in the peripheral blood (22,000/cu mm vs 14,000 for controls) during the exposure period and a statistically significant lowering of the leukoid-to-erythroid ratio (1.3:1 vs 2.1:1 for controls) in the bone marrow.

Difficulties exist in the evaluation of both reports of Uzhdavini et al [24,25], because of incomplete information in presentation of the data. For example, the description of the exposure conditions specified neither the type of chamber nor the method used for generating vapor-aerosols. The number of animals used for various experimental procedures generally was not specified, and control conditions were not adequately detailed.

Despite such shortcomings, however, there is sufficient agreement between the findings of Uzhdavini et al and those reported by other independent investigators, such as Deichmann and Witherup [31], that the findings of Uzhdavini et al of adverse effects on humans and animals exposed to cresol at concentrations below 20 mg/cu m should be considered in recommending an environmental workplace exposure limit. Therefore, NIOSH recommends that an environmental limit for cresol of 10 mg/cu m as a TWA concentration be established. It is believed that a TWA concentration of 10 mg/cu m will protect the worker from the occupational health hazards associated with cresol, considering the limited information available, and, in addition, it will reduce the probability of cresol acting as a promoter.

The workplace environmental limit recommended for cresol applies to the individual cresol isomers when they occur alone or to any mixture of the isomers.

(b) Sampling and Analysis

NIOSH recommends that sampling and analysis for cresol be accomplished by the procedures outlined in Appendix I or by any other methods shown to be equivalent or superior in precision, accuracy, and sensitivity. The sampling procedure involves adsorption on silica gel followed by desorption with acetone. The analytical procedure recommended is gas-liquid chromatography. This sampling and analytical method has been validated over a range of 10.5-42.2 mg/cu m at an atmospheric temperature and pressure of 22 C and 760 mmHg, respectively [40].

(c) Medical Surveillance and Recordkeeping

Medical surveillance, including preplacement and periodic medical examinations, should be made available to all workers who are

occupationally exposed to cresol. Because percutaneous absorption, inhalation, and ingestion of cresols have resulted in impairment of the liver, kidneys, pancreas, cardiovascular system, CNS, skin, and eyes [11,13,16(p 36),17-22,24], special attention should be given to identifying individuals with any disorders of these organs and systems. Such individuals should be informed of the possible increased risk of health impairment from cresol and be counseled by the medical personnel on the appropriate measures to take. Blood tests, urinalyses, and other tests considered necessary by the attending physician should also be included. The interval between periodic medical examinations should be no longer than 1 year.

Medical and other pertinent records should be retained for all employees exposed to cresol for at least 30 years after termination of employment.

(d) Personal Protective Equipment and Clothing

The evidence gathered from the available literature indicates that the greatest danger to employees from exposure to cresols, under most conditions, is from skin contact.

Only one report [17] of a death from occupational exposure to cresol or cresylic acid was found in the literature. A man fell into a vat containing a derivative of cresylic acid, and burns developed on 15% of his body. Anuria developed within 36 hours, and he died 11 days after the exposure. A second occupational incident involved a man who, during one workday, had repeatedly immersed his hands in a solvent containing 6% cresylic acid [18]. His hands became severely irritated, and facial peripheral neuritis developed 1 day after the exposure.

Dermatitis developed in 10 workers at a silkmill who were using a solution containing cresols for 4-8 months [19]. Their fingers became reddened, and itching was reported. Of 30 workers in a synthetic plastics plant, 6 had dermatitis of the hands and face that was attributed to contact with cresol and phenol [20].

Several deaths and many injuries have resulted from dermal exposure to cresol in nonoccupational settings [11,14,21], confirming its toxicity by this route. An infant died after accidental skin contact with about 20 ml of a solution containing 90% cresol [21]. Necrosis of the liver and kidneys resulted. Severe burning of the skin was also produced after contact with cresol [11,14,21].

Because cresols are readily absorbed through the skin and are irritating to the skin and eyes [11,14,16(pp 3,36),17-21], protective equipment and clothing, including aprons, trousers, gloves, shoes, and safety goggles, should be provided. Respirators and protective clothing should be made available and used in accordance with the specifications in Section 4 and Table I-1 of Chapter I.

(e) Informing Employees of Hazards

A comprehensive educational program on safety procedures should effectively reduce occupational injuries from exposure to cresols. Therefore, all employees assigned to work in operations involving possible exposure to cresols must be informed of the hazards and possible injuries resulting from such exposure at the start of employment. Instructions should be given on the proper procedures for handling and using cresols and for using appropriate safety equipment. Employees should also be instructed on appropriate emergency procedures. Periodic retraining and

instruction should be provided to maintain employee awareness of the current safety and maintenance procedures.

Since the major source of occupational injury is skin contact with cresol [16 (pp 3,28,36)], employees must be informed that cresols are readily absorbed through the skin and can cause both local and systemic effects if they are not removed from the skin immediately.

(f) Work Practices

The likelihood of exposure to cresols can best be reduced by implementing engineering controls and appropriate work practices. Since toxic effects from exposure to cresols have been produced by skin and eye contact [11,14,16(pp 3,36),17-21], inhalation [22,24], and ingestion [11,13,27], work practices must protect against exposure by these routes. The effects produced by exposure to cresols by skin and eye contact and by inhalation have been discussed in Sections (a) and (d) of this chapter. Enclosure of operations to the extent that is feasible and adherence to the recommendations in these sections should prevent or minimize adverse health effects.

In areas where there is potential occupational exposure to cresol safety showers and eyewash fountains must be available for immediate use should contact of cresol with the body occur.

Data in the published literature also indicate that cresol is rapidly absorbed from the gastrointestinal tract and can be injurious or fatal when ingested even in small amounts [11,13,27]. An infant died after ingesting 4 ml of a 25-50% cresol solution [11]. Toxic effects from ingestion included cyanosis, vomiting, irritation of the mucous membranes that came in contact with cresol, necrosis of the liver and kidneys, and

pancreatitis. Because of the known hazards of ingesting cresol [11,13,27], smoking, eating, and drinking must be prohibited in any area containing cresol.

Cresol that has spilled or leaked must be cleaned up immediately to prevent accidental exposure. All personnel involved in cleanup operations must be provided with suitable protective equipment and clothing.

At temperatures below its flashpoint (178-187 F or 81-86 C), cresol can be handled with little direct danger of fire. However, at higher temperatures, flammable vapor can be given off [1,5]; thus extra precautions should be taken. Smoking and open flames should be prohibited in any area where cresol is found.

(g) Monitoring and Recordkeeping Requirements

Industrial hygiene surveys should be conducted as soon as practicable after the promulgation of a standard based on these recommendations and within 30 days of any process change.

If the concentration of airborne cresol in a work area exceeds the action level, personal monitoring should be performed every 3 months to ensure the adequacy of control procedures. If the concentration exceeds the recommended workplace environmental limit, personal monitoring should be performed at least weekly until two consecutive determinations, at least 1 week apart, indicate that workplace air levels no longer exceed the recommended limit. Monitoring every 3 months should then be resumed.

VII. RESEARCH NEEDS

Although cresol is manufactured in large quantities and has widespread application, the available toxicologic information is minimal. The following research needs have been identified during the development of this document.

Investigations, including epidemiologic studies, of the health effects from long-term exposure to airborne cresol at levels at or below the recommended environmental limit are needed. These should include an examination of the effects on the skin, eyes, respiratory and cardiovascular systems, CNS, liver, kidneys, and pancreas, all of which have been adversely affected by exposure to cresol [16(pp 3,36),17-20,22, 24,27]. Possible carcinogenic effects should also be included. Attempts should be made to correlate the degree of exposure to cresol with effects. Workers that have been dermally exposed to cresol should be monitored for an extended period to see if any systemic effects are produced.

Only a few investigations of the effects of inhalation of cresols on animals were found in the literature. Further research is needed to examine fully the biologic effects of long-term low-level exposure to cresol and to delineate dose-response relationships. Behavioral changes and changes in blood cell counts and hemoglobin content were observed in rats subacutely exposed to o-cresol vapor [24]. Research to determine the importance of these changes and their relationship, if any, to possible health impairment in exposed workers would permit better understanding of the toxic action of cresol.

No studies of the carcinogenic, mutagenic, teratogenic, and reproductive effects of cresol were found, although one study [34] showed that cresol promoted DMBA-induced papillomas. Carefully planned experiments in these areas are therefore needed to help determine the risks of long-term exposure to cresol. The TSCA Interagency Testing Committee has recommended to the administrator of the Environmental Protection Agency that cresol be a priority substance to be tested for carcinogenicity, mutagenicity, and teratogenicity (Federal Register 42:24-5, October 12, 1977).

Although the urinary metabolites of cresol have been reported in the rabbit [36], the rate of metabolism, the biologic half-lives of the metabolites, and the metabolic pathways in humans have not been determined. Since some of these metabolites are probably derived from epoxide intermediates that may covalently bind to cellular macromolecules, including DNA, the existence of a carcinogenic risk must be considered. Experiments, both short and long term, designed to evaluate the magnitude of this potential risk are urgently needed.

VIII. REFERENCES

1. Properties and Essential Information for Safe Handling and Use of Cresol, Chemical Safety Data Sheet SD-48. Washington, DC, Manufacturing Chemists' Association, 1952, 16 pp

2. Deichmann WB, Keplinger ML: Phenols and phenolic compounds, in Patty FA (ed): Industrial Hygiene and Toxicology, ed 2 rev; Toxicology (Fassett DW, Irish DD, eds). New York, Interscience Publishers, 1963, vol 2, pp 1363-1408

3. Cresol (cresylic acid)--(Mixture of ortho-, meta-, and para-isomers). Am Ind Hyg Assoc J 19:441-43, 1958

4. Weast RC (ed): Handbook of Chemistry and Physics--A Ready-Reference Book of Chemical and Physical Data, ed 55. Cleveland, Chemical Rubber Co, 1974, pp 518-19

5. NIOSH/OSHA Draft Technical Standard and Supporting Documentation for Cresol. Standards Completion Program. US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, 1976, 29 pp (unpublished)

6. Leo A, Hansch C, Elkins D: Partition coefficients and their uses. Chem Rev 71:525-616, 1971

7. Oelert HH, Florian TH: Odor threshold values. Staub Reinhalt Luft 32:28, 1972

8. Klapproth EM: Cresols and cresylic acid, in Chemical Economics Handbook. Menlo Park, Calif, Stanford Research Institute, 1976, pp 637.5030A to 637.5530E

9. Folkins HO: Cresols, in Kirk-Othmer Encyclopedia of Chemical Technology, ed 2 rev. New York, Interscience Publishers, 1964, vol 6, pp 434-44

10. Cresol, in Gafafer WM (ed): Occupational Diseases--A Guide to Their Recognition, PHS publication No. 1097. US Dept of Health, Education, and Welfare, Public Health Service, Division of Occupational Health, 1964, pp 126-27

11. Isaacs R: Phenol and cresol poisoning. Ohio State Med J 18:558-61, 1922

12. Burg K: [Double central pneumonia in a case of Lysol poisoning.] Med Klin 23:1134-36, 1929 (Ger)

13. Dellal V: Acute pancreatitis following lysol poisoning. Lancet 1:407, 1931

14. Herwick RP, Treweek DN: Burns from anesthesia mask sterilized in compound solution of cresol. JAMA 100:407-08, 1933

15. Vance BM: Intrauterine injection of Lysol as an abortifacient--Report of a fatal case complicated by oil embolism and Lysol poisoning. Arch Pathol 40:395-98, 1945

16. Plant observation reports and evaluation. Menlo Park, Calif Stanford Research Institute, Oct 1977, 146 pp (submitted to NIOSH under Contract No. CDC-99-74-31)

17. Cason JS: Report on three extensive industrial chemical burns. Br Med J 1:827-29, 1959

18. Klinger ME, Norton JF: Toxicity of cresylic acid-containing solvent. US Nav Med Bull, pp 438-39, 1945

19. Goodman H: Silk handler's disease of the skin--Dermatitis venenata due to isomers of cresol. Med J Rec 138:349-50, 1933

20. Zalecki M: [The results of examination of Cracow plant employees for detection of occupational skin diseases.] Med Pr 16:385-93, 1965 (Pol)

21. Green MA: A household remedy misused--Fatal cresol poisoning following cutaneous absorption--(A case report). Med Sci Law 15:65-66, 1975

22. Corcos A: [Contribution to the Study of Occupational Poisoning by Cresols], dissertation. Paris, Vigot Freres Editeurs, 1939, 62 pp (Fre)

23. Cummins Northeastern Incorporated--Dedham, Massachusetts, Health Hazard Evaluation/Toxicity Determination report No. 73-5-110. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Hazard Evaluation Services Branch, 1974, 7 pp

24. Uzhdavini ER, Astafyeva IK, Mamayeva AA, Bakhtizina GZ: [Inhalation toxicity of o-cresol.] Tr Ufim Nauchno-Issled Inst Gig Profzabol 7:115-19, 1972 (Rus)

25. Uzhdavini ER, Astafyeva NK, Mamayeva AA: [The acute toxicity of lower phenols.] Gig Tr Prof Zabol 18:58-59, 1974 (Rus)

26. Presley JA, Brown WE: Lysol-induced criminal abortion. Obstet Gynecol 8:368-70, 1956

27. Klimkiewicz E, Klinger M, Kurbiel A, Soltys W: [A case of liquid phenol poisoning complicated by acute pancreatitis and acute renal failure.] Wiad Lek 27:1211-14, 1974 (Pol)

28. Campbell J: Petroleum cresylic acids--A study of their toxicity and the toxicity of cresylic disinfectants. Soap Sanit Chem 17:103-11, 121, 1941

29. Back KC, Thomas AA, MacEwen JD: Reclassification of Materials Listed as Transportation Health Hazards--Supplement. Springfield, Va, US Dept of Commerce, National Technical Information Service, 1973, 21 pp (NTIS PB 225 283)

30. Bio Fax Techniques--Methods Used in Determining Biological Activity of Chemicals. Northbrook, Ill, Industrial Bio-Test Laboratories Inc, 1969, vols 3-5,4-5,5-5

31. Deichmann WB, Witherup S: Phenol studies--VI. The acute and comparative toxicity of phenol and o-, m- and p-cresols for experimental animals. J Pharmacol Exp Ther 80:233-40, 1944

32. Shelley WB, Raque CJ: Delayed patterned hair depigmentation in CBA mice following application of laundry ink. J Invest Dermatol 59:202-05, 1972

33. Shelley WB: p-Cresol--Cause of ink-induced hair depigmentation in mice. Br J Dermatol 90:169-74, 1974

34. Boutwell RK, Bosch DK: The tumor-promoting action of phenol and related compounds for mouse skin. Cancer Res 19:413-24, 1959

35. Kurlyandskiy BA, Partsef DP, Chernomorskiy AR: [Methods for determination of mean daily MPC of tricresol in the atmosphere.] Gig Sanit 5:85-87, 1975 (Rus)

36. Bray HG, Thorpe WV, White K: Metabolism of derivatives of toluene--4. Cresols. Biochem J 46:275-78, 1950

37. Majewskaja WP: [Determination of phenol and cresols in the atmosphere.] Chem Zentralbl 1:2423, 1941 (Ger)

38. Manita MD: Determination of the vapors of monohydric phenols (phenol and o-, m-, p-cresols) in the atmosphere by ultraviolet spectrophotometry. Hyg Sanit 31:260-64, 1966

39. o-, m-, and p-Cresol, Analytical Abstracts. Akron, Ohio, American Industrial Hygiene Association, 1965, 5 pp

40. Cresol, all isomers, method No. S167, in Documentation of the NIOSH Validation Tests, HEW publication No. (NIOSH) 77-185. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Division of Physical Sciences and Engineering, 1977, pp S167-1 to S167-7

41. Brooks VT: Gas-liquid chromatography--Separation of close-boiling phenol isomers. Chem Ind 1317-18, 1959

42. Hughes MA, White D, Roberts AL: Separation of the meta- and para-isomers of the xylenes, cresols and toluidines by gas solid chromatography. Nature 184:1796-97, 1959

43. Grant DW, Vaughan, GA: The analysis of complex phenolic mixtures by capillary column GLC after silylation, in Van Swaay M (ed): Gas Chromatography. London, Butterworth and Co Ltd, 1962, pp 305-14

44. Alderweireldt F: An improved technique for recording chromatograms--Analysis of cresol mixtures. J Chromatogr 5:98-102, 1961

45. Hrivnak J, Macak J: Gas chromatographic analysis of phenol and substituted methyl phenols using open tubular columns. Anal Chem 43:1039-42, 1971

46. Rudol'fi TA, Sharapova RI, Lushchik VI: [Gas chromatography of cresol isomers.] Zh Anal Khim 19:903-05, 1964 (Rus)

47. Cohen IC, Norcup J, Ruzicka JHA, Wheals BB: Trace determination of phenols by gas chromatography as their 2,4-dinitrophenyl ethers. J Chromatogr 44:251-55, 1969

48. Anwar MM, Hanson C, Pratt MWT: Gas chromatographic separation of cresol, xylenol and chloroaniline isomers. J Chromatogr 46:200-01, 1970

49. Dyatlovitskaya FG, Gladenko EF: Separate determination of volatile phenols by paper chromatography. Hyg Sanit 30:77-80, 1965

50. Hossfeld RL: Paper partition chromatography of simple phenols. J Am Chem Soc 73:852-54, 1951

51. Belova IM: [Determination of monohydric phenols by partition chromatography and ultraviolet spectrophotometry.] Zh Anal Khim 16:229-36, 1961 (Rus)

52. Subrahmanyam VS: Ultraviolet spectrophotometric studies of isomeric cresols--Part I. Ferric cresolate complexes, in Proceedings of the Symposium on Low-Temperature Carbonization of Non-Caking Coals, Hyderabad, India, 1964, pp 181-83

53. Carney GE, Sanford JK: Ultraviolet analysis of isomeric cresol mixtures. Anal Chem 25:1417-18, 1953

54. Robertson WW, Ginsberg N, Matsen FA: Quantitative analysis of isomeric cresols and cresol-phenol mixtures by ultraviolet absorption spectra of vapors. Ind Eng Chem, Anal Ed 18:746-50, 1946

55. Whiffen DH, Thompson HW: The infra-red spectra of cresols and xylenols and the analysis of cresylic acid. J Chem Soc X:268-73, 1945

56. Liedmann R: The quantitative analysis of technical cresols with the infrared spectrophotometer UR 10. Jenaer Rundsch 5:3-7, 1960

57. Chapin RM: The determination of cresol by the phenol reagent of Folin and Denis. J Biol Chem 47:309-14, 1921

58. Feigl F, Anger V: Detection of p-cresol in spot test analysis. Anal Chem 33:89-90, 1961

59. Ortho-cresol in cresylic acid, serial No. PC 17-62, in Watkins PV (ed): Standard Methods for Testing Tar and Its Products, ed 5. London, Standardization of Tar Products Tests Committee, 1962, pp 320-23

60. Meta-cresol in cresylic acid, serial No. PC 18-62, in Watkins PV (ed): Standard Methods for Testing Tar and Its Products, ed 5. London, Standardization of Tar Products Tests Committee, 1962, pp 324-29

61. Rao PR: Spectroscopic studies of the cresols--III. Emission and absorption spectra of meta-cresol in the near ultra-violet region. Proc Indian Acad Sci Sect A 53:300-10, 1962

62. Rao PR: Spectroscopic studies of the cresols--I. Emission and absorption spectra of para-cresol in the near ultra-violet region. Proc Indian Acad Sci Sect A 55:232-46, 1962

63. 1977 OSHA Concentration Limits for Gases--Incorporating Infrared Analytical Data for Compliance Testing and Other Applications, rev. Norwalk, Conn, Wilks Scientific Corp, 1977, 1p

64. Leichnitz K (ed): Detector Tube Handbook--Air Investigations and Technical Gas Analysis with Grager Tubes, ed 2 rev. Lubeck, Federal Republic of Germany, Dragerwerk AG Lubeck, 1976, p 118

65. Oydvin K: The constituents of cresol--Separation of close-boiling phenol isomers by gas liquid chromatography. Medd Nor Farm Selsk 28:116-20, 1966

66. Hagopian JH, Bastress EK: Recommended Industrial Ventilation Guidelines, HEW publication No. (NIOSH) 76-162. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Divison of Physcial Sciences and Engineering, 1976, 330 pp

67. American Conference of Governmental Industrial Hygienists, Committee on Industrial Ventilation: Industrial Ventilation--A Manual of Recommended Practice, ed 14. Lansing, Mich, ACGIH, 1976, pp 1-1 to 14-8

68. American National Standards Institute Inc: Fundamentals Governing the Design and Operation of Local Exhaust Systems, ANSI Z9.2-1971. New York, ANSI, 1971, 63 pp

69. American Conference of Governmental Industrial Hygienists: Threshold Limit Values for 1952. AMA Arch Ind Hyg Occup Med 6:178-80, 1952

70. American Conference of Governmental Industrial Hygienists: Threshold Limit Values for 1956. AMA Arch Ind Health 14:186-89, 1956

71. American Conference of Governmental Industrial Hygienists: Threshold Limit Values for 1961. Cincinnati, ACGIH, 1961, p 4

72. American Conference of Governmental Industrial Hygienists: TLVs--Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1977. Cincinnati, ACGIH, 1977, p 13

73. American Conference of Governmental Industrial Hygienists: Documentation of the Threshold Limit Values for Substances in Workroom Air, ed 3, 1971. Cincinnati, ACGIH, 2nd printing, 1974, pp 61,93

74. Elkins HB: The Chemistry of Industrial Toxicology, ed 2. New York, Wiley and Sons, 1958, pp 116-17

75. Cresols--Cresylic acid, in Fairhall LT: Industrial Toxicology ed 2. Baltimore, Williams and Wilkins Co, 1957, pp 198-99

76. Hamilton A, Hardy HL: Industrial Toxicology, ed 2. New York, Hoeber Inc, 1949, p 288

77. Conference of Governmental Industrial Hygienists: Threshold Limit Values of Air-borne Contaminents [sic] for 1968--Recommended and Intended Values. Cincinnati, ACGIH, 1968, p 7

78. Senate Commission for the Study of Harmful Work Substances: [Maximum Workplace Concentrations--1976, communication No. 12.] Bonn, Bundesrepublik, Deustchland, German Research Assoc, 1976, vol 28, pp 3,12,22-23,25-26 (Ger)

79. Permissible Levels of Toxic Substances in the Working Environment--Sixth Session of the Joint ILO/WHO Committee on Occupational Health, Geneva, June 4-10, 1968. Geneva, International Labour Office, 1970, pp 190,197,200,205,213,223-24,231,233,347-48

80. Bardodej Z: Cresol, in Documentation of MAC in Czechoslovakia. Praha, Czechoslovak Committee of MAC, 1969, pp 61-62

81. National Institute for Occupational Safety and Health: Criteria for a Recommended Standard....Occupational Exposure to Phenol, HEW publication No. (NIOSH) 76-196. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, NIOSH, 1976, 167 pp

82. Driscoll JN, Staziani F: Trace Gas Analysis by Photoionization. Unpublished report submitted to NIOSH by HNU Systems Inc, Newton Upper Falls, Mass, Dec 1977, 9 pp

IX. APPENDIX I

SAMPLING AND ANALYTICAL METHOD FOR CRESOL

This method for sampling and analysis is adopted from NIOSH Method No. S167 [40].

Principle of the Method

(a) A known volume of air is drawn through a silica gel tube to trap the organic vapors present.

(b) The silica gel in the tube is transferred to a small, stoppered sample container, and the analyte is desorbed with acetone.

(c) An aliquot of the desorbed sample is injected into a gas chromatograph.

(d) The combined areas of the resulting two peaks are determined and compared with areas obtained for standards.

Range and Sensitivity

(a) This method was validated over the range of 10.54-42.2 mg/cu m at an atmospheric temperature and pressure of 22 C and 760 mmHg, using a 20-liter sample. Under the conditions of sample size (20 liters), the probable useful range of this method is 5-60 mg/cu m at a detector sensitivity that gives nearly full deflection on the strip chart recorder for a 1-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.

(b) The upper limit of the range of the method is dependent on the adsorptive capacity of the silica gel tube. This capacity varies with the concentrations of the analyte and other substances in the air. The first section of the silica gel tube was found to hold at least 1.87 mg of analyte when a test atmosphere containing 42.2 mg/cu m of analyte in air was sampled at 0.185 liter/minute for 240 minutes. (The silica gel tube consists of two sections of silica gel separated by a section of urethane foam.) If a particular atmosphere is suspected of containing a large amount of contaminant, a smaller sampling volume should be taken.

Interferences

(a) Silica gel has a high affinity for water, so organic vapors will not be trapped efficiently in the presence of a high relative humidity. This effect may be important even though there is no visual evidence of condensed water in the silica gel tube.

(b) When compounds other than the isomers of cresol are known or suspected to be present in the air, such information, including their suspected identities, should be transmitted with the sample. Since acetone is used to desorb the analyte from the silica gel, it is not possible to measure acetone in the sample.

(c) It must be emphasized that any compound which has the same retention time as the analyte at the operating conditions described in this method is an interference. Retention time data on a single column cannot be considered proof of chemical identity.

(d) If the possibility of interference exists, separation conditions (column packing, temperature, etc.) must be changed to circumvent the problem.

Precision and Accuracy

(a) The Coefficient of Variation for the total analytical and sampling method in the range of 10.54-42.2 mg/cu m was 0.068. This value corresponds to a 1.5 mg/cu m standard deviation at the OSHA standard level.

(b) On the average, the concentrations obtained at the OSHA standard level using the overall sampling and analytical method were 4.2% lower than the "true" concentrations for a limited number of laboratory experiments. Any difference between the "found" and "true" concentrations may not represent a bias in the sampling and analytical method, but rather a random variation from the experimentally determined "true" concentration. Therefore, no recovery correction should be applied to the final result.

Advantages and Disadvantages of the Method

(a) The sampling device is small, portable, and involves no liquids. Interferences are minimal, and most of those which do occur can be eliminated by altering chromatographic conditions. The tubes are analyzed by means of a quick, instrumental method. The method can also be used for the simultaneous analysis of two or more substances suspected to be present in the same sample by simply changing gas chromatographic conditions from isothermal to a temperature-programmed mode of operation.

(b) One disadvantage of the method is that the amount of sample that can be taken is limited by the number of milligrams that the tube will hold before overloading. When the sample value obtained for the backup section of the silica gel tube exceeds 25% of that found on the front section, the possibility of sample loss exists.

(c) Furthermore, the precision of the method is limited by the reproducibility of the pressure drop across the tubes. This drop will affect the flowrate and cause the volume to be imprecise, because the pump is usually calibrated for one tube only.

Apparatus

(a) A calibrated personal sampling pump whose flow can be determined within ±5% at the recommended flowrate.

(b) Silica gel tubes: glass tube with both ends flame sealed, 7 cm long with a 6-mm OD and a 4-mm ID, containing two sections of 20/40 mesh silica gel separated by a 2-mm portion of urethane foam. The adsorbing section contains approximately 150 mg of silica gel, the backup section, approximately 75 mg. A 3-mm portion of urethane foam is placed between the outlet end of the tube and the backup section. A plug of silylated glass wool is placed in front of the adsorbing section. The pressure drop across the tube must be less than 1 inch of mercury at a flowrate of 1 liter/minute.

(c) Gas chromatograph equipped with a flame ionization detector.

(d) Column (10-ft x 1/8-in stainless steel) packed with 10% FFAP in 80/100 mesh, acid washed DMCS Chromosorb W.

(e) An electronic integrator or some other suitable method for measuring peak areas.

(f) Two-milliliter sample containers with glass stoppers or Teflon-lined caps. If an automatic sample injector is used, the associated vials may be used.

(g) Microliter syringes: 10 μl and other convenient sizes for making standards.

(h) Pipets: 1.0-ml delivery pipets.

(i) Volumetric flasks: convenient sizes for making standard solutions.

Reagents

(a) Chromatographic quality acetone.

(b) Cresol (all isomers): Prepare a standard mixture of the isomers by adding together 20 g of the ortho, 40 g of the meta, and 30 g of the para isomers and mix.

(c) Prepurified hydrogen.

(d) Filtered compressed air.

(e) Purified nitrogen.

(f) n-Hexane, reagent grade.

Procedure

(a) Cleaning of Equipment. All glassware used for the laboratory analysis should be detergent washed and thoroughly rinsed with tapwater and distilled water.

(b) Calibration of Personal Pumps. Each personal pump must be calibrated with a representative silica gel tube in the line. This will minimize errors associated with uncertainties in the sample volume collected.

(c) Collection and Shipping of Samples

(1) Immediately before sampling, break the ends of the tube to provide an opening at least one-half the internal diameter of the tube (2 mm).

(2) The smaller section of silica gel is used as a backup and should be positioned nearest the sampling pump.

(3) The silica gel tube should be placed in a vertical direction during sampling to minimize channeling through the silica gel.

(4) Air being sampled should not be passed through any hose or tubing before entering the silica gel tube.

(5) A sample size of 20 liters is recommended. Sample at a flow of 0.20 liter/minute or less. The flowrate should be known with an accuracy of at least ±5%.

(6) The temperature and pressure of the atmosphere being sampled should be recorded. If pressure reading is not available, record the elevation.

(7) The silica gel tubes should be capped with the supplied plastic caps immediately after sampling. Under no circumstances should rubber caps be used.

(8) One tube should be handled in the same manner as the sample tube (break, seal, and transport), except that no air is sampled through this tube. This tube should be labeled as a blank.

(9) Capped tubes should be packed tightly and padded before they are shipped to minimize tube breakage during shipping.

(10) A sample of the bulk material should be submitted to the laboratory in a glass container with a Teflon-lined cap. This sample should not be transported in the same container as the silica gel tubes.

(d) Analysis of Samples

(1) Preparation of Samples. In preparation for analysis, each silica gel tube is scored with a file in front of the first section of silica gel and broken open. The glass wool and the silica gel in the first (larger) section are transferred to a 2-ml stoppered sample container. The separating section of foam is removed and discarded; the second section is transferred to another stoppered container. These two sections are analyzed separately.

(2) Desorption of Samples. Prior to analysis, 1.0 ml of acetone is pipetted into each sample container. Desorption should be done for 30 minutes. Tests indicate that this is adequate if the sample is agitated occasionally during this period. If an automatic sample injector is used, the sample vials should be capped as soon as the solvent is added to minimize volatilization.

(3) GC Conditions. The typical operating conditions for the gas chromatograph are:

50 ml/min (60 psig) nitrogen carrier gas flow

65 ml/min (24 psig) hydrogen gas flow to detector

500 ml/min (50 psig) airflow to detector

230 C injector temperature

250 C manifold temperature (detector)

200 C column temperature

(4) Injection. The first step in the analysis is the injection of the sample into the gas chromatograph. To eliminate difficulties arising from blowback or distillation within the syringe needle, one should employ the solvent flush injection technique. The 10-μl syringe is first flushed with solvent several times to wet the barrel and plunger. Then 3 μl of solvent are drawn into the syringe to increase the accuracy and reproducibility of the injected sample volume. The needle is removed from the solvent, and the plunger is pulled back about 0.2 μl to separate the solvent flush from the sample with a pocket of air to be used as a marker. The needle is then immersed in the sample, and a 5-μl aliquot is withdrawn, taking into consideration the volume of the needle, since the sample in the needle will be completely injected. After the needle is removed from the sample and prior to injection, the plunger is pulled back 1.2 μl to minimize evaporation of the sample from the tip of the needle. Observe that the sample occupies 4.9-5.0 μl in the barrel of the syringe. Duplicate injections of each sample and standard should be made. No more than a 3% difference in area is to be expected. An automatic sample injector can be used if it is shown to give reproducibility at least as good as the solvent flush method.

(5) Measurement of area. Although there are three isomers of cresol, there are only two peaks on the gas chromatogram, because the meta and para isomers have the same retention time. The total area of the two sample peaks is measured by an electronic integrator or some other suitable form of area measurement, and preliminary results are read from a standard curve prepared as discussed below.

(e) Determination of Desorption Efficiency

(1) Importance of determination. The desorption efficiency of a particular compound can vary from one laboratory to another and also from one batch of silica gel to another. Thus, it is necessary to determine, at least once, the percentage of the specific compound that is removed in the desorption process, provided the same batch of silica gel is used.

(2) Procedure for determing desorption efficiency. Silica gel equivalent to the amount in the first section of the sampling tube (approximately 150 mg) is measured into a 2.5-inch, 4-mm ID glass tube, flame sealed at one end. This silica gel must be from the same batch as that used in obtaining the samples and can be obtained from unused silica gel tubes. The open end is capped with Parafilm.

A standard solution is prepared by placing 1,100 mg of the mixture of the isomers of cresol in a 10-ml volumetric flask and making it up to volume with n-hexane. A known amount of the standard solution is injected directly into the silica gel with a microliter syringe, and the tube is capped with more Parafilm. When an automatic sample injector is used, the sample injector vials, capped with Teflon-faced septa, may be used in place of the glass tubes.

The amount injected is equivalent to that present in a 20-liter air sample at the selected level. Six tubes at each of the three levels are prepared in this manner and allowed to stand for at least overnight to assure complete adsorption of the analyte onto the silica gel. These tubes are referred to as the samples. A parallel blank tube should be treated in the same manner except that no sample is added to it. The sample and blank

tubes are desorbed and analyzed in exactly the same manner as the sampling tube described in (d).

Two or three standards are prepared by injecting the same volume of compound into 1.0 ml of acetone with the same syringe used in the preparation of the samples. These are analyzed with the samples.

The desorption efficiency (DE) is dependent on the amount of analyte collected on the silica gel. The desorption efficiency equals the average weight in mg recovered from the tube divided by the weight in mg added to the tube, or

$$DE = \frac{\text{Average weight recovered (mg)}}{\text{Weight added (mg)}}$$

The desorption efficiency is dependent on the amount of analyte collected on the silica gel. Plot the desorption efficiency versus weight of analyte found. This curve is used to correct for adsorption losses.

Calibration and Standards

It is convenient to express concentration of standards in terms of mg/1.0 ml acetone, because samples are desorbed in this amount of acetone. A series of standards, varying in concentration over the range of interest, are prepared and analyzed under the same GC conditions and during the same time period as the unknown samples. Curves are established by plotting concentration in mg/1.0 ml versus total peak area. Note: Since no internal standard is used in the method, standard solutions must be analyzed at the same time that the sample analysis is done. This will minimize the effect of known day-to-day variations and variations during the same day of the flame-ionization detector response.

Calculations

(a) Read the weight, in mg, corresponding to each combined peak area from the standard curve. No volume corrections are needed, because the standard curve is based on mg/1.0 ml acetone and the volume of sample injected is identical to the volume of the standard injected.

(b) Corrections for the blank must be made for each sample.

$$\text{mg} = \text{mg sample} - \text{blank}$$

where:

mg sample = mg found in front section of sample tube
mg blank = mg found in front section of blank tube

A similar procedure is followed for the backup sections.

(c) Add the weights found in the front and backup sections to get the total weight in the sample.

(d) Read the desorption efficiency from the curve for the amount found in the front section. Divide the total weight by this desorption efficiency to obtain the corrected mg/sample.

$$\text{Corrected mg/sample} = \frac{\text{Total weight}}{\text{DE}}$$

(e) The concentration of the analyte in the air sampled can be expressed in mg/cu m.

$$\text{mg/cu m} = \frac{\text{Corrected mg} \times 1{,}000 \text{ (liters/cu m)}}{\text{Air volume sampled (liters)}}$$

(f) Another method of expressing concentration is ppm.

$$\text{ppm} = \text{mg/cu m} \times \frac{24.45}{\text{MW}} \times \frac{760}{\text{P}} \times \frac{\text{T} + 273}{298}$$

where:

P	= pressure (mmHg) of air sampled
T	= temperature (C) of air sampled
24.45	= molar volume (liter/mole) at 25 C and 760 mmHg
MW	= molecular weight (g/mole) of analyte
760	= standard pressure (mmHg)
298	= standard temperature (K)

X. APPENDIX II

MATERIAL SAFETY DATA SHEET

The following items of information which are applicable to a specific product or material shall be provided in the appropriate block of the Material Safety Data Sheet (MSDS).

The product designation is inserted in the block in the upper left corner of the first page to facilitate filing and retrieval. Print in upper case letters as large as possible. It should be printed to read upright with the sheet turned sideways. The product designation is that name or code designation which appears on the label, or by which the product is sold or known by employees. The relative numerical hazard ratings and key statements are those determined by the rules in Chapter V, Part B, of the NIOSH publication, An Identification System for Occupationally Hazardous Materials. The company identification may be printed in the upper right corner if desired.

(a) Section I. Product Identification

zThe manufacturer's name, address, and regular and emergency telephone numbers (including area code) are inserted in the appropriate blocks of Section I. The company listed should be a source of detailed backup information on the hazards of the material(s) covered by the MSDS. The listing of suppliers or wholesale distributors is discouraged. The trade name should be the product designation or common name associated with the material. The synonyms are those commonly used for the product, especially formal chemical nomenclature. Every known chemical designation or

competitor's trade name need not be listed.

(b) Section II. Hazardous Ingredients

The "materials" listed in Section II shall be those substances which are part of the hazardous product covered by the MSDS and individually meet any of the criteria defining a hazardous material. Thus, one component of a multicomponent product might be listed because of its toxicity, another component because of its flammability, while a third component could be included both for its toxicity and its reactivity. Note that a MSDS for a single component product must have the name of the material repeated in this section to avoid giving the impression that there are no hazardous ingredients.

Chemical substances should be listed according to their complete name derived from a recognized system of nomenclature. Where possible, avoid using common names and general class names such as "aromatic amine," "safety solvent," or "aliphatic hydrocarbon" when the specific name is known.

The "%" may be the approximate percentage by weight or volume (indicate basis) which each hazardous ingredient of the mixture bears to the whole mixture. This may be indicated as a range or maximum amount, ie, "10-40% vol" or "10% max wt" to avoid disclosure of trade secrets.

Toxic hazard data shall be stated in terms of concentration, mode of exposure or test, and animal used, eg, "100 ppm LC50-rat," "25 mg/kg LD50-skin-rabbit," "75 ppm LC man," or "permissible exposure from 29 CFR 1910.1000," or, if not available, from other sources of publications such as the American Conference of Governmental Industrial Hygienists or the American National Standards Institute Inc. Flashpoint, shock sensitivity,

or similar descriptive data may be used to indicate flammability, reactivity, or similar hazardous properties of the material.

(c) Section III. Physical Data

The data in Section III should be for the total mixture and should include the boiling point and melting point in degrees Fahrenheit (Celsius in parentheses); vapor pressure, in conventional millimeters of mercury (mmHg); vapor density of gas or vapor (air = 1); solubility in water, in parts/hundred parts of water by weight; specific gravity (water = 1); percent volatiles (indicated if by weight or volume) at 70 degrees Fahrenheit (21.1 degrees Celsius); evaporation rate for liquids or sublimable solids, relative to butyl acetate; and appearance and odor. These data are useful for the control of toxic substances. Boiling point, vapor density, percent volatiles, vapor pressure, and evaporation are useful for designing proper ventilation equipment. This information is also useful for design and deployment of adequate fire and spill containment equipment. The appearance and odor may facilitate identification of substances stored in improperly marked containers, or when spilled.

(d) Section IV. Fire and Explosion Data

Section IV should contain complete fire and explosion data for the product, including flashpoint and autoignition temperature in degrees Fahrenheit (Celsius in parentheses); flammable limits, in percent by volume in air; suitable extinguishing media or materials; special firefighting procedures; and unusual fire and explosion hazard information. If the product presents no fire hazard, insert "NO FIRE HAZARD" on the line labeled "Extinguishing Media."

(e) Section V. Health Hazard Information

The "Health Hazard Data" should be a combined estimate of the hazard of the total product. This can be expressed as a TWA concentration, as a permissible exposure, or by some other indication of an acceptable standard. Other data are acceptable, such as lowest LD50 if multiple components are involved.

Under "Routes of Exposure," comments in each category should reflect the potential hazard from absorption by the route in question. Comments should indicate the severity of the effect and the basis for the statement if possible. The basis might be animal studies, analogy with similar products, or human experiences. Comments such as "yes" or "possible" are not helpful. Typical comments for cresol might be:

> Skin Contact--single short contact, irritation, erythema; prolonged or repeated contact, chemical burn, skin discoloration, possible systemic effects.
>
> Eye Contact--some pain and mild transient irritation; possible burning and conjunctivitis.

"Emergency and First Aid Procedures" should be written in lay language and should primarily represent first-aid treatment that could be provided by paramedical personnel or individuals trained in first aid.

Information in the "Notes to Physician" section should include any special medical information which would be of assistance to an attending physician including required or recommended preplacement and periodic medical examinations, diagnostic procedures, and medical management of overexposed employees.

(f) Section VI. Reactivity Data

The comments in Section VI relate to safe storage and handling of hazardous, unstable substances. It is particularly important to highlight instability or incompatibility to common substances or circumstances, such as water, direct sunlight, steel or copper piping, acids, alkalies, etc. "Hazardous Decomposition Products" shall include those products released under fire conditions. It must also include dangerous products produced by aging, such as peroxides in the case of some ethers. Where applicable, shelf life should also be indicated.

(g) Section VII. Spill or Leak Procedures

Detailed procedures for cleanup and disposal should be listed with emphasis on precautions to be taken to protect employees assigned to cleanup detail. Specific neutralizing chemicals or procedures should be described in detail. Disposal methods should be explicit including proper labeling of containers holding residues and ultimate disposal methods such as "sanitary landfill" or "incineration." Warnings such as "comply with local, state, and federal antipollution ordinances" are proper but not sufficient. Specific procedures shall be identified.

(h) Section VIII. Special Protection Information

Section VIII requires specific information. Statements such as "Yes," "No," or "If necessary" are not informative. Ventilation requirements should be specific as to type and preferred methods. Respirators shall be specified as to type and NIOSH or US Bureau of Mines approval class, ie, "Supplied air," "Organic vapor canister," etc. Protective equipment must be specified as to type and materials of construction.

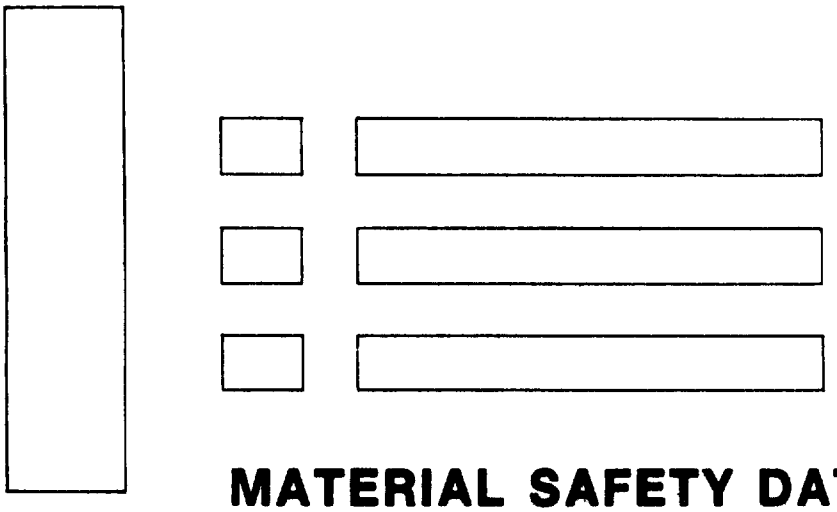
(i) Section IX. Special Precautions

"Precautionary Statements" shall consist of the label statements selected for use on the container or placard. Additional information on any aspect of safety or health not covered in other sections should be inserted in Section IX. The lower bloc can contain references to published guides or in-house procedures for handling and storage. Department of Transportation markings and classifications and other freight, handling, or storage requirements and environmental controls can be noted.

(j) Signature and Filing

Finally, the name and address of the responsible person who completed the MSDS and the date of completion are entered. This will facilitate correction of errors and identify a source of additional information.

The MSDS shall be filed in a location readily accessible to employees exposed to the hazardous substance. The MSDS can be used as a training aid and basis for discussion during safety meetings and training of new employees. It should assist management by directing attention to the need for specific control engineering, work practices, and protective measures to ensure safe handling and use of the material. It will aid the safety and health staff in planning a safe and healthful work environment and in suggesting appropriate emergency procedures and sources of help in the event of harmful exposure of employees.



MATERIAL SAFETY DATA SHEET

I PRODUCT IDENTIFICATION			
MANUFACTURER'S NAME		REGULAR TELEPHONE NO. EMERGENCY TELEPHONE NO.	
ADDRESS			
TRADE NAME			
SYNONYMS			
II HAZARDOUS INGREDIENTS			
MATERIAL OR COMPONENT		%	HAZARD DATA
III PHYSICAL DATA			
BOILING POINT, 760 MM HG		MELTING POINT	
SPECIFIC GRAVITY (H_2O=1)		VAPOR PRESSURE	
VAPOR DENSITY (AIR=1)		SOLUBILITY IN H_2O, % BY WT	
% VOLATILES BY VOL		EVAPORATION RATE (BUTYL ACETATE 1)	
APPEARANCE AND ODOR			

IV FIRE AND EXPLOSION DATA

FLASH POINT (TEST METHOD)		AUTOIGNITION TEMPERATURE	
FLAMMABLE LIMITS IN AIR, % BY VOL.	LOWER		UPPER	
EXTINGUISHING MEDIA			
SPECIAL FIRE FIGHTING PROCEDURES			
UNUSUAL FIRE AND EXPLOSION HAZARD			

V HEALTH HAZARD INFORMATION

HEALTH HAZARD DATA

ROUTES OF EXPOSURE

INHALATION

SKIN CONTACT

SKIN ABSORPTION

EYE CONTACT

INGESTION

EFFECTS OF OVEREXPOSURE

ACUTE OVEREXPOSURE

CHRONIC OVEREXPOSURE

EMERGENCY AND FIRST AID PROCEDURES

EYES

SKIN

INHALATION

INGESTION

NOTES TO PHYSICIAN

VI REACTIVITY DATA

CONDITIONS CONTRIBUTING TO INSTABILITY

INCOMPATIBILITY

HAZARDOUS DECOMPOSITION PRODUCTS

CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION

VII SPILL OR LEAK PROCEDURES

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED

NEUTRALIZING CHEMICALS

WASTE DISPOSAL METHOD

VIII SPECIAL PROTECTION INFORMATION

VENTILATION REQUIREMENTS

SPECIFIC PERSONAL PROTECTIVE EQUIPMENT

RESPIRATORY (SPECIFY IN DETAIL)

EYE

GLOVES

OTHER CLOTHING AND EQUIPMENT

IX SPECIAL PRECAUTIONS

PRECAUTIONARY
STATEMENTS

OTHER HANDLING AND
STORAGE REQUIREMENTS

PREPARED BY _____

ADDRESS _____

DATE _____

XI. TABLES AND FIGURES

TABLE XI-1

PHYSICAL AND CHEMICAL PROPERTIES OF CRESOL

	o-Cresol	m-Cresol	p-Cresol
Molecular formula	$CH_3C_6H_4OH$	$CH_3C_6H_4OH$	$CH_3C_6H_4OH$
Formula weight	108.13	108.13	108.13
Appearance	Colorless crystals or liquid	Colorless liquid	Colorless crystals
Boiling point	191.0 C	202.7 C	201.9 C
Melting point	30.9 C	12.0 C	34.8 C
Vapor pressure (at 25 C)	0.25 mmHg	0.15 mmHg	0.11 mmHg
Specific gravity at 20 C (water = 1.000 at 4 C)	1.048	1.034	1.035
Saturated concentration (at 20 C)	1,428 mg/cu m (323 ppm)	888 mg/cu m (201 ppm)	628 mg/cu m (142 ppm)
Flashpoint (closed cup)	81.1 C	86.1 C	86.1 C
Autoignition temperature	559 C	626 C	559 C
Vapor density (air = 1)	3.72	3.72	3.72
Odor threshold	0.0028 mg/cu m (0.00063 ppm)	0.034 mg/cu m (0.0076 ppm)	0.0021 mg/cu m (0.00047 ppm)
Oil/water partition coefficient	1.34	1.21	1.21
Solubility in water (by weight at 25 C)	2.5%	2.2%	1.9%
Solubility in other substances	Soluble in alcohol and caustic alkalies; miscible with benzene, ether, and petroleum ether		
Conversion factors (760 mmHg and 25 C)	1 ppm = 4.42 mg/cu m; 1 mg/cu m = 0.226 ppm		

Adapted from references 1-7

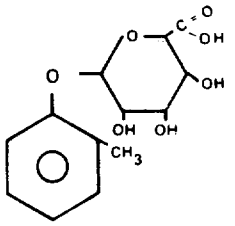
TABLE XI-2

OCCUPATIONS WITH POTENTIAL EXPOSURE TO CRESOL

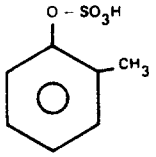
Antioxidant producers	Paint remover makers
Coal tar workers	Paint removers
Cresol soap makers	Perfume makers
Cresol workers	Phenolic resin producers
Cresylic acid makers	Phosphate ester producers
Deodorant workers	Photographic developer workers
Disinfectant makers	Pitch workers
Disinfectors	Resin makers
DNOC producers	Roofers
Dyemakers	Rubber makers
Enamel makers	Scouring compound makers
Explosive workers	Stainers
Flotation agent makers	Stain makers
Flotation workers	Surfactant makers
Foundry workers	Tanning agent makers
Glue workers	Tar distillery workers
Ink makers	Textile sizers
Ink remover makers	Varnish remover makers
Ink removers	Varnish removers
Insecticide workers	Veterinarians
Insulation enamel workers	Wool scourers
Oil additive makers	

Adapted from references 8-10

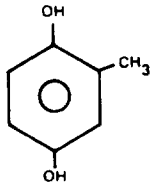
o–Cresol
(500–600 mg)



2-methyl phenyl glucuronide (72%)

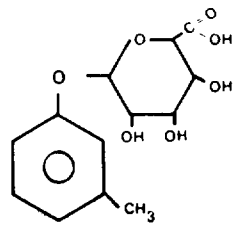


2-methyl phenyl sulfuric acid (15%)

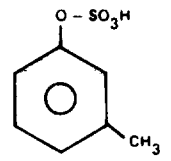


2, 5-dihydroxytoluene (3%)

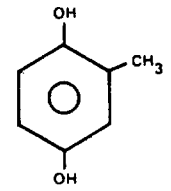
m–Cresol
(500–600 mg)



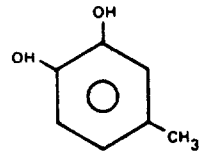
3-methyl phenyl glucuronide (60%)



3-methyl phenyl sulfuric acid (10%)

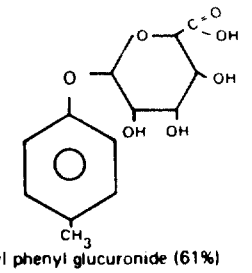


2, 5-dihydroxytoluene (3%)

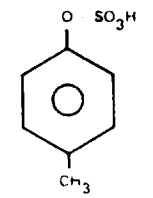


3, 4-dihydroxytoluene (traces)

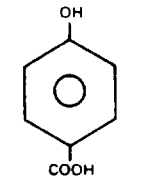
p–Cresol
(200–300 mg)



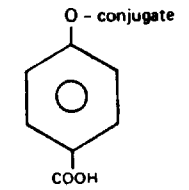
4-methyl phenyl glucuronide (61%)



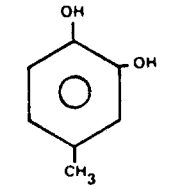
4-methyl phenyl sulfuric acid (15%)



hydroxybenzoic acid (7%)



conjugated hydroxybenzoic acid (3%)



3, 4-dihydroxytoluene (traces)

FIGURE XI–1

URINARY PRODUCTS OF CRESOL ADMINISTERED BY STOMACH TUBE TO RABBITS

Adapted from Bray et al [36]

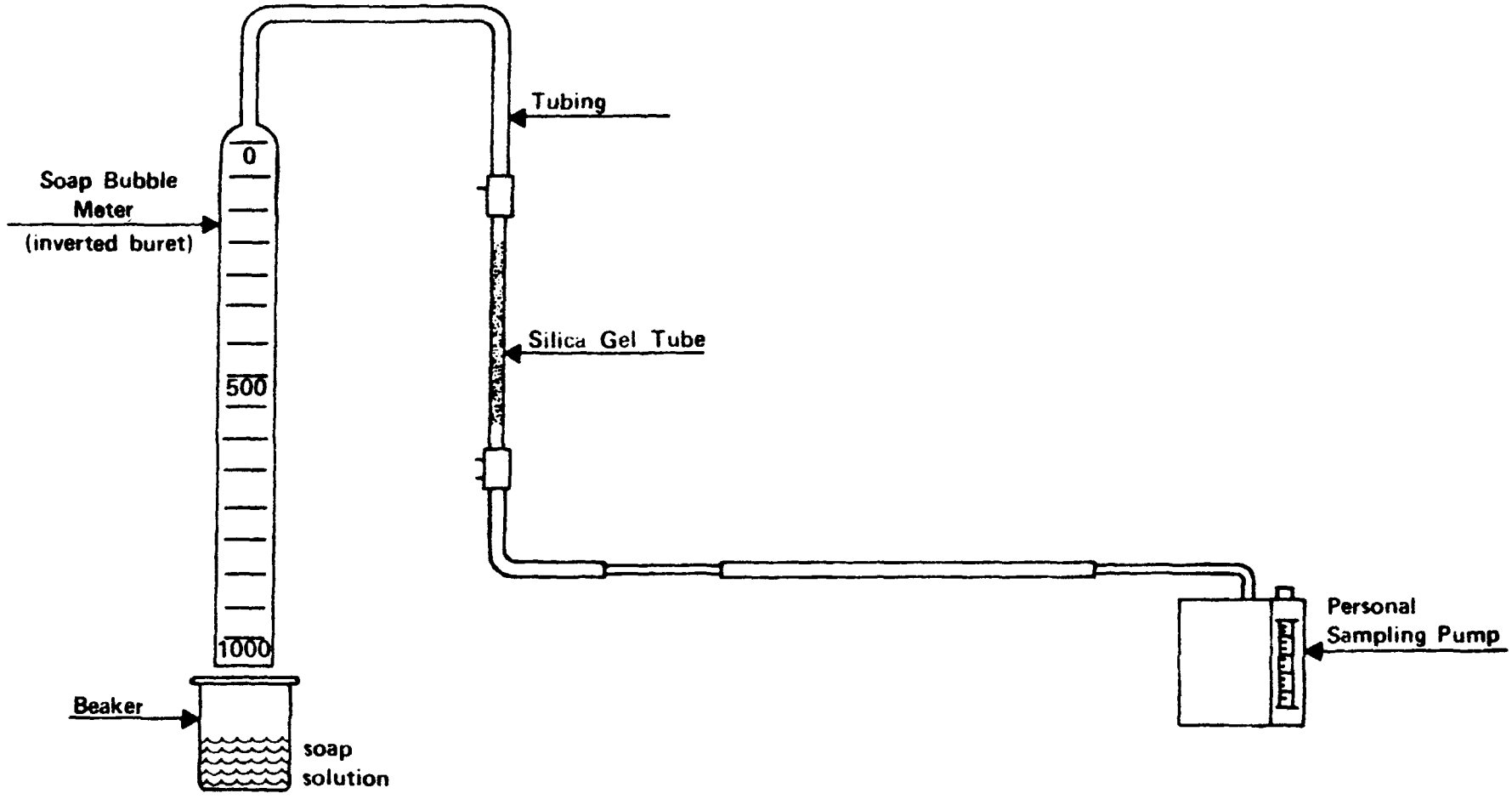


FIGURE XI–2

CALIBRATION SETUP FOR PERSONAL SAMPLING WITH SILICA GEL TUBE

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