#### 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 gasliquid [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  $\mu$ m 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 to reduce the concentrations to levels as low as possible. limit 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 exhaust systems (MFPA N. 91-1973) should be followed. blower and 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 <u>Fundamentals Governing the Design and Operation of Local Exhaust Systems</u>, 29.2-1971 [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 Operations in which an aerosol is generated may potential exposure. 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 When exposure is limited to handling contaminated equipment or to gloves. 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.

workers, especially those working on Maintenance and repair 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 with water. Personnel entering confined spaces must wear flushing 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 40hour 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 Elkins [74] reported that cresol should not present an recommended TLV. 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(p 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  $9 \pm 0.9$  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-toerythroid 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, ot 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.

the carcinogenic, mutagenic, teratogenic, and No studies of reproductive effects of cresol were found, although one study [34] showed promoted DMBA-induced papillomas. Carefully planned that cresol 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, Occober 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

- 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
- 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
- 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
- Oelert HH, Florian TH: Odor threshold values. Staub Reinhalt Luft 32:28, 1972
- 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
- 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
- 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)
- Cason JS: Report on three extensive industrial chemical burns. Br Med J 1:827-29, 1959
- 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
- 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)
- 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)
- 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 Zentralb1 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 paraisomers 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