criteria for a recommended standard . . . .
occupational exposure to
ALKANES (C5–C8)
criteria for a recommended standard.

OCCUPATIONAL EXPOSURE
TO
ALKANES
(C5–C8)

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

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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 alkanes (C5-C8) by members of the NIOSH staff and the valuable constructive comments by the Review Consultants on Alkanes (C5-C8), by the ad hoc committees of the American Industrial Hygiene Association and the American Occupational Medical Association 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 alkanes. A list of Review Consultants appears on page vi.

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The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for development of the criteria and recommended standard for alkanes (C5-C8). The division review staff for this document consisted of Richard A. Rhoden, Ph.D., Chairman, Keith H. Jacobson, Ph.D., and Victor E. Archer, M.D. (Division of Surveillance, Hazard Evaluations, and Field Studies), with Charles C. Hassett, Ph.D., and Seymour D. Silver, Ph.D. Stanford Research Institute (SRI) developed the basic information for consideration by NIOSH staff and consultants under contract No. CDC-99-74-31. Patricia G. Heitman served as criteria manager.

The views expressed and conclusions reached in this document, together with the recommendations for a standard, are those of NIOSH, after review of the evidence and considering the comments of reviewers; these views and conclusions are not necessarily those of the consultants, other federal agencies, and professional societies, or of the contractor.
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I. RECOMMENDATIONS FOR AN ALKANES (C5-C8) STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to pentane, hexane, heptane, and octane in the workplace be controlled by adherence to the following sections. The standard is designed to protect the health and safety of employees for up to a 10-hour work shift in a 40-hour workweek over a working lifetime. Compliance with all sections of the standard should prevent adverse effects of pentane, hexane, heptane, and octane on the health and safety of employees. Sufficient technology exists to permit compliance with the recommended standard. Although the workplace environmental limits are considered to be safe levels based on current information, they should be regarded as the upper boundaries of permissible exposure and every effort should be made to maintain the exposure as low as is technically feasible. The criteria and standard will be subject to review and revision as necessary.

These criteria and the recommended standard apply to exposure of workers to alkanes which are aliphatic hydrocarbons with the empirical formula C(n) H(2n+2) where n = 5, 6, 7, or 8. These alkanes are hereinafter referred to as pentane, hexane, heptane, and octane, respectively. The prefix "n-" will be used to refer to the straight chain isomeric form of an alkane, eg, n-pentane. An alkane without the "n-" prefix is a mixture of isomeric forms, unless otherwise designated.

"Action level" is defined as an airborne time-weighted average (TWA) concentration of 200 milligrams per cubic meter of air (mg/cu m) of these alkanes for up to a 10-hour work shift in a 40-hour workweek.
"Occupational exposure" to alkanes is defined as exposure above the action level. Exposure at lower concentrations will not require adherence to the following sections of the standard except sections 3a, 4a, 4b, 5a, 6, and 7a.

Section 1 - Environmental (Workplace Air)

(a) Workplace Environmental Limits

Occupational exposure to airborne C5-C8 alkanes shall be controlled so that no employee is exposed at concentrations greater than 350 mg/cu m as a TWA concentration for up to a 10-hour work shift in a 40-hour workweek. This concentration is equivalent to about 120 parts of pentane per million parts of air (ppm), 100 ppm of hexane, 85 ppm of heptane, or 75 ppm of octane. If an employee is exposed to a mixture of C5-C8 alkanes, total alkane exposure shall not be greater than 350 mg/cu m. In addition, no employee shall be exposed to individual C5-C8 alkanes or mixtures of these alkanes at ceiling concentrations greater than 1,800 mg/cu m as determined over a sampling time of 15 minutes. This concentration is equivalent to about 610 ppm pentane, 510 ppm hexane, 440 ppm heptane, or 385 ppm octane.

(b) Sampling and Analysis

Procedures for the collection of workplace environmental samples shall be as provided in Appendix I, or by any method shown to be at least as efficient. Analysis of samples shall be performed as provided in Appendix II or by any methods shown to be at least equivalent in precision, sensitivity, and accuracy.
Section 2 - Medical

Medical surveillance shall be made available as outlined below to all workers subject to occupational exposure to alkanes (C5-C8).

(a) Preplacement examinations shall include at least:

(1) Comprehensive medical and work histories with special emphasis toward conditions affecting the peripheral and central nervous systems and skin.

(2) Physical examination giving particular attention to general tests of nervous system function and evidence of skin conditions.

(3) 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) Physical examination as outlined in (a)(2) and (3) above.

(c) During examinations, applicants or employees having medical conditions which would be directly or indirectly aggravated by exposure to alkanes shall be counseled on the increased risk of impairment of their health from working with these substances.

(d) Initial medical examinations shall be made available to all workers within 6 months after the promulgation of a standard based on these recommendations.

(e) Pertinent medical records shall be maintained for all employees exposed to alkanes in the workplace. Such records shall be kept for at least 30 years after termination of employment. 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

(a) Containers of substances which comprise 10% or more alkanes shall bear the following label in addition to, or in combination with, labels required by other statutes, regulations, or ordinances:

CONTAINS ALKANES

WARNING! HIGHLY FLAMMABLE

Keep away from sparks and open flame.
In case of fire, use foam, dry chemical, or carbon dioxide fire extinguisher.
In case of spill, flush area with water spray.
Use with adequate ventilation.
Avoid prolonged or repeated breathing of vapor.
Repeated exposure may produce nerve damage.
Avoid contact with eyes.
Do not take internally.

First Aid: In case of eye contact, flush with plenty of water. Call a physician.

(b) Areas where there is occupational exposure to pentane, hexane, heptane, octane, or mixtures of these, and areas where there is bulk storage of alkanes shall be posted with signs reading:

ALKANE NAME (eg, PENTANE)

WARNING! HIGHLY FLAMMABLE

Avoid heat, sparks, and open flames.
No smoking permitted.
In case of fire, use fire extinguishers located at (location).
Avoid breathing vapor.
Avoid contact with skin, eyes, and clothing.
These warning signs shall be printed both in English and in the predominant language of non-English-reading employees. All employees shall be trained and informed of the hazardous areas, with special instructions given to illiterate employees and to those reading only languages other than those used on labels and posted signs.

Section 4 - Personal Protective Equipment and Clothing

(a) Eye Protection

Full-facepiece respirators, safety glasses, or chemical safety goggles shall be provided and worn by workers during those operations in which pentane, hexane, heptane, or octane may splash into the eyes. Face shields may be used to augment chemical safety goggles and safety glasses where full facial protection is needed, but face shields are not adequate for eye protection when used alone. Eye protective equipment shall be selected and used in accordance with 29 CFR 1910.133.

(b) Respiratory Protection

Engineering controls shall be used wherever feasible to maintain alkane concentrations below the recommended environmental limits. Compliance with the permissible exposure limit by the use of respirators is allowed only while required engineering controls are being installed or tested, when nonroutine maintenance or repair is being accomplished, or during emergencies. When a respirator is thus permitted, it shall be selected and used in accordance with the following requirements:

(1) For the purpose of determining the type of respirator to be used, the employer shall measure, when possible, the concentration of the airborne alkane or mixture of alkanes in the workplace both initially
and thereafter whenever process, worksite, or control changes occur which are likely to result in increases in the alkane concentrations; this requirement does not apply when only atmosphere-supplying positive pressure respirators are used.

(2) The employer shall ensure that no worker is exposed to alkanes at concentrations in excess of the workplace environmental limits because of improper respirator selection, fit, use, or maintenance.

(3) A respiratory protection program meeting the requirements of 29 CFR 1910.134 shall be established and enforced by the employer.

(4) The employer shall provide respirators in accordance with Table I-1 and shall ensure that the employees use the respirators provided.

(5) Respiratory protective devices described in Table I-1 shall be those approved under the provisions of 30 CFR 11.

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

(7) The employer shall ensure that respirators are cleaned, maintained, and stored in accordance with 29 CFR 1910.134.

(8) The employer shall ensure that employees are instructed on the use of respirators assigned to them and on how to test for leaks.

(9) Each area where posting is required in accordance with Section 3(b) shall have emergency respiratory protective devices readily available in nearby locations which do not require entry into a contaminated atmosphere for access. Respiratory protective devices provided shall consist of at least two self-contained breathing apparatus.
TABLE I-1

RESPIRATOR SELECTION GUIDE FOR ALKANES (C5-C8)

<table>
<thead>
<tr>
<th>Concentration of Alkanes</th>
<th>Respirator Type Approved Under Provisions of 30 CFR 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than or equal to 3,500 mg/cu m</td>
<td>Chemical cartridge respirator with half-mask or full facepiece and organic vapor cartridge</td>
</tr>
</tbody>
</table>
| Less than or equal to 12,500 mg/cu m | (1) Gas mask with chin-style or front- or back-mounted organic vapor canister and full facepiece  
(2) Supplied-air respirator with full facepiece, helmet, hood, or suit operated in continuous-flow, demand (negative pressure), or pressure-demand mode (positive pressure) |
| Less than or equal to 17,500 mg/cu m | Self-contained breathing apparatus operated in demand mode (negative pressure) with full facepiece |
| Greater than 17,500 mg/cu m | (1) Self-contained breathing apparatus with full facepiece operated in pressure-demand or other positive pressure mode  
(2) Combination Type C supplied-air respirator with full facepiece operated in the pressure-demand or other positive pressure mode and an auxiliary self-contained air supply operated in the pressure-demand or other positive pressure mode |
| Emergency (entry into an area of unknown concentration for emergency purposes) | (1) Self-contained breathing apparatus with full facepiece operated in the pressure-demand or other positive pressure mode  
(2) Combination Type C supplied-air respirator with full facepiece operated in the pressure-demand or other positive pressure mode and an auxiliary self-contained air supply operated in the pressure-demand or other positive pressure mode |
| Escape (from an area of unknown concentration) | (1) Any gas mask providing protection against organic vapors  
(2) Any self-contained breathing apparatus |
as described in Table I-1. Well-ventilated outdoor locations where egress and escape are unhindered may be exempted from this requirement.

(c) Skin Protection

The employer shall provide protective apparel, including gloves, aprons, suits, boots, or face shields (8-inch minimum) with goggles, and ensure that they are worn where needed to prevent skin contact with liquid alkanes. Protective apparel shall be made of materials which most effectively prevent skin contact under the conditions for which it is deemed necessary. Rubber articles may be used provided care is taken to ensure that permeation does not occur during usage. Protective apparel should be discarded at the first sign of deterioration.

Section 5 - Informing Employees of Hazards from Alkanes

(a) At the beginning of employment, employees shall be informed of the presence of alkanes in the workplace, including the trade-name substances, if any, that contain alkanes, the hazards, signs and symptoms of overexposure, emergency procedures including first aid, and precautions to take to ensure safe use and to minimize exposure. This information shall also be posted in the workplace and kept on file, readily accessible to all employees.

(b) The employer shall institute a continuing education program, conducted by persons qualified by experience or special training, to ensure that all employees occupationally exposed to alkanes shall have current knowledge of job hazards, proper maintenance procedures, cleanup methods, and proper use of protective clothing and equipment, including respirators. In addition, employees and members of emergency teams who work adjacent to
alkane systems or containers where a potential for emergencies exists shall participate in periodic drills simulating emergencies appropriate to the work situation. Drills shall be held at intervals not greater than 6 months. Drills should cover, but should not be limited to:

Evacuation procedures.
Handling of spills and leaks, including decontamination.
Location and use of emergency firefighting equipment, and handling of alkane systems and containers in case of fire.
First-aid and rescue procedures, including prearranged procedures for obtaining emergency medical care.
Location, use, and care of protective apparel and respiratory protective equipment.
Location of shutoff valves or switches.
Location, purpose, and use of safety showers, eyewash fountains, and other sources of water for emergency use.
Operating procedures, including communication procedures.
Entry procedures for confined spaces.

Deficiencies noted during drills shall be included in a continuing educational program, together with the required remedial actions. Records of drills and training conducted shall be kept for 1 year and made available for inspection by authorized personnel. Information as required shall be recorded on the "Material Safety Data Sheet" shown in Appendix III or on a similar form approved by the Occupational Safety and Health Administration, US Department of Labor, and shall be filed in a location readily accessible to employees.

Section 6 - Work Practices

Alkanes present significant fire hazards. Therefore, appropriate regulations for Class IA or Class IB flammable liquids as provided in 29 CFR 1910.106 shall be followed.
(a) Control of Airborne Alkanes

Engineering controls, such as process enclosure or local exhaust ventilation, shall be used to maintain airborne alkane concentrations at or below the recommended environmental limits. All such control equipment shall meet the requirements of subpart S of 29 CFR 1910 for hazardous locations. Ventilation systems, if used, shall be designed and operated to minimize the accumulation or recirculation of airborne alkanes in the workplace and to effectively decrease the concentrations of airborne alkanes to safe levels in the breathing zones of employees. Exhaust ventilation systems discharging into outside air must conform with applicable local, state, and federal air pollution regulations and must not constitute a hazard. Ventilation systems shall be subject to regular preventive maintenance and cleaning to ensure effectiveness, which shall be verified by airflow measurements taken at least quarterly.

(b) Sources of Ignition

(1) Precautions shall be taken to prevent the ignition of alkanes or, in the case of engines, torches, or other devices fueled by alkanes, to control their ignition.

(2) Workplaces in which explosive concentrations of alkane vapors may develop shall meet provisions for Class I, Division 2, of the National Electric Code as required by 29 CFR 1910.309.

(3) Where spark- and flame-generating operations are necessary, they shall be started only after an authorized representative of the employer signs a permit declaring the operation to be safe. This should be done only after a calibrated combustible-gas meter or other suitable instrument indicates that the concentration of alkane vapors is
less than 10% of the lower explosive limit.

(4) Alkanes in bulk quantities may not be dispensed into metal containers unless the nozzle and the container are electrically bonded. The container and the nozzle shall be grounded properly as required by 29 CFR 1910.106.

(5) Smoking shall be prohibited in alkane work and storage areas.

(c) Loading and Unloading

(1) Safety showers and eyewash fountains, as well as fire extinguishers containing chemicals approved for Class B fires, shall be installed in bulk loading and unloading areas. Safety showers, eyewash fountains, and fire extinguishers shall be checked to ensure that they are in working order before alkanes are loaded or unloaded.

(2) If a leak in an alkane container occurs during the loading or unloading process, the operation shall be stopped and resumed only after necessary repair or replacement has been completed.

(3) Bonding facilities for protection against sparks from discharge of static charge during the loading of tank vehicles shall be provided as required by 29 CFR 1910.106.

(d) Storage

Containers shall be stored in accordance with the applicable provisions of 29 CFR 1910.106 and shall be protected from heat, mechanical damage, and sources of ignition.

(e) Disposal

Spills shall be flushed with water. Where it is not possible to flush a spill with water, the area should be cordoned off and ventilated
until it is cleaned by other means, such as a venturi-type vacuum system.

(f) **Vessel Entry**

(1) Entry into confined spaces, such as tanks, pits, tank cars, and process vessels which have contained alkanes, shall be controlled by a permit system. Permits shall be signed by an authorized employer representative, certifying that preparation of the confined space, precautionary measures, and personal protective equipment are adequate, and that prescribed procedures will be followed.

(2) Confined spaces which have contained alkanes shall be thoroughly ventilated, cleaned, washed, inspected, and tested for oxygen deficiency and for the presence of alkanes and other contaminants prior to entry.

(3) All efforts shall be made to prevent inadvertent release of alkanes into the confined space while work is in progress. Alkane supply lines shall be disconnected and blocked off while such work is in progress.

(4) Confined spaces shall be ventilated while work is in progress to keep airborne alkane concentrations at or below the recommended environmental limits and to prevent oxygen deficiency.

(5) Individuals entering confined spaces where they may be exposed to alkanes shall wear respirators as outlined in Section 4(b) and lifelines tended by another worker outside the space who shall also be equipped with the necessary protective equipment.

(g) **Emergency Procedures**

For all work areas where a reasonable potential for emergencies exists, procedures as specified below, as well as any other procedures
appropriate for a specific operation or process, shall be formulated in advance and employees shall be instructed in their implementation:

(1) Procedures shall include prearranged plans for obtaining emergency medical care, for necessary transportation of injured employees, and for general evacuation.

(2) Firefighting procedures shall be established. These shall include procedures for emergencies involving release of alkane vapors. In case of fire, alkane sources shall be shut off or removed. Alkane containers shall be removed or cooled with water spray. Chemical foam, carbon dioxide, or dry chemicals shall be used for fighting alkane fires, and proper respiratory protective devices and protective attire shall be worn.

(3) Approved eye, skin, and respiratory protective devices, as specified in Section 4, shall be used by personnel involved in the emergency operations.

(4) Employees not essential for emergency operations shall be evacuated from exposure areas during emergencies. The perimeters of hazardous exposure areas shall be delineated, posted, and secured.

(5) Only personnel properly trained in the relevant procedures and adequately protected against the attendant hazards shall shut off sources of alkanes, clean up spills, and repair leaks.

(6) Eyewash fountains and emergency showers shall be provided in accordance with 29 CFR 1910.151.

(7) Warning or alarm systems shall be considered to warn workers of possible hazardous exposures to alkanes during emergencies involving release of alkane vapors.
Section 7 - Monitoring and Recordkeeping Requirements

(a) Survey Requirements

Workers are not considered to have occupational exposure to alkanes if environmental concentrations, as determined on the basis of an industrial hygiene survey, do not exceed the action level. Surveys shall be repeated at least once a year and within 30 days after any process change likely to result in increases of airborne alkane concentrations. Records of these surveys, including the basis for concluding that airborne concentrations of alkanes are at or below the action level, shall be maintained. If there is occupational exposure to alkanes, then the following requirements apply:

(b) Personal Monitoring

(1) A program of personal monitoring shall be instituted to identify and measure, or permit calculation of, the exposures of all employees who are occupationally exposed to alkanes. Monitoring of employee exposures to airborne alkanes shall be conducted at least every 6 months. If monitoring of an employee's exposure to an alkane or a mixture of alkanes reveals that he is exposed at concentrations in excess of either recommended environmental limit, control measures shall be initiated, the employee shall be notified of his exposure and the control measures being implemented to correct the situation, and the exposure of that employee shall be measured at least once every 30 days. Such monitoring shall continue until two consecutive samplings, at least a week apart, indicate that the employee's exposure no longer exceeds the environmental limit stated in Section 1(a). Semiannual monitoring may then be resumed.
(2) In all personal monitoring, samples of airborne alkanes shall be collected which, when analyzed, will provide an accurate representation of the concentration of an alkane or a mixture of alkanes in the air breathed by the worker. Procedures for sampling and analysis of alkanes shall be as provided in Appendices I and II, or by any method shown to be at least equivalent in precision, accuracy, and sensitivity to the methods specified.

(3) For each TWA determination, a sufficiently large number of samples shall be taken to characterize every employee's exposure during each work shift. Variations in work and production schedules shall be considered in deciding when and how many samples are to be collected. The number of representative TWA determinations for an operation or process shall be based on the variations in location and job functions of employees in relation to that operation or process.

(c) Recordkeeping

Records of environmental monitoring shall be kept by the employer for at least 30 years. These records shall include the dates of measurements, job function and location of the employees at 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, and exposed employees' names. Each employee shall have access to information on his or her own environmental exposures. Environmental records shall be made available to designated representatives of the Secretary of Labor, and of the Secretary of Health, Education, and Welfare. Pertinent medical records shall be retained by the employer for 30 years after termination of employment. Records of environmental
exposures applicable to an employee should be included in that employee's medical records. These medical records shall be made available to the designated medical 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 and injury arising from workplace exposure to pentane, hexane, heptane, or octane. 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 on which standards can be established to protect the health of employees from exposure to hazardous chemical and physical agents. Criteria and recommended standards should enable management and labor to develop better engineering controls resulting in more healthful work environments. Mere compliance with the recommended standard should not be used as a final goal.

These criteria for a standard for alkanes are part of a continuing series of criteria developed by NIOSH. The recommended standard applies to the processing, manufacture, and handling of these alkanes in products 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 occupational exposures is not warranted. It is
intended to (1) protect against the development of acute and chronic alkane (C5-C8) poisoning, (2) be measurable by techniques that are available to industry and official agencies, and (3) be attainable with existing technology.

Although the neurologic effects of exposure to airborne hexane have been documented and some experimental and epidemiologic studies have been conducted to determine the effects of exposure to hexane at various concentrations, at the present time, limited data exist to present a definitive correlation between hexane exposure concentrations and acute and chronic effects observed in humans or animals. There are even fewer data concerning the relationships between concentrations of pentane, heptane, or octane and the observed effects. Further research is needed to determine (1) the nature of these relationships, (2) the mechanisms of toxic action of these alkanes, (3) if additive or synergistic effects occur when humans or animals are exposed to mixtures of these alkanes, (4) how the toxicities of the normal forms of the alkanes and the toxicities of their isomeric forms are related, and (5) whether or not any of these alkanes produce carcinogenic, mutagenic, or teratogenic effects.

The alkanes reviewed in this criteria document and included in the recommended standard are the straight- or branched-chain saturated aliphatic hydrocarbons containing from five to eight carbon atoms. In practice, alkanes are available as mixtures of two or more isomers; the data reviewed in this criteria document are based on human and animal exposures to such mixtures, often incompletely characterized as to their components. The recommended standard is based on the conclusion that acute intoxication by these alkanes involves a transient central nervous system
depression and that chronic intoxication may involve a more persistent effect, polyneuropathy. Polyneuropathy has usually been attributed to n-hexane, but exposures to n-hexane alone have not been described, and the recommended standard is based on the belief that this neuropathy can be caused by other alkanes and their isomers as well. It might be reasoned, by analogy with the metabolism of straight-chain fatty acids or with the biologic degradation of straight-chain versus branched-chain alkyl benzene sulfonates (detergents), that only straight-chain or straight-chain alkanes with even numbers of carbon atoms could cause polyneuropathy. It might also be interpreted, from the limited evidence on metabolism of n-hexane presented in Chapter III, that only n-hexane among the C5-C8 alkanes could cause polyneuropathy. Should sufficient evidence be developed that this is the case, the TWA limit of 350 mg/cu m of total alkanes recommended in this document might be considered for revision in the case of those substances not causing polyneuropathy.