CRITERIA FOR A RECOMMENDED STANDARD

Occupational Exposure to Metalworking Fluids

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FOREWORD

In the Occupational Safety and Health Act of 1970 (Public Law 91-596), Congress declared that its purpose was to assure, insofar as possible, safe and healthful working conditions for every working man and woman and to preserve our human resources. In this Act, the National Institute for Occupational Safety and Health (NIOSH) is charged with recommending occupational safety and health standards and describing exposure concentrations that are safe for various periods of employment—including but not limited to concentrations at which no worker will suffer diminished health, functional capacity, or life expectancy as a result of his or her work experience. By means of criteria documents, NIOSH communicates these recommended standards to regulatory agencies (including the Occupational Safety and Health Administration [OSHA]) and to others in the occupational safety and health community.

Criteria documents provide the scientific basis for new occupational safety and health standards. These documents generally contain a critical review of the scientific and technical information available on the prevalence of hazards, the existence of safety and health risks, and the adequacy of control methods. In addition to transmitting these documents to the Department of Labor, NIOSH also distributes them to health professionals in academic institutions, industry, organized labor, public interest groups, and other government agencies.

This criteria document reviews available information about the adverse health effects associated with occupational exposure to metalworking fluids (MWFs) and MWF aerosols. Substantial evidence indicates that workers currently exposed to MWF aerosols have an increased risk of nonmalignant respiratory disease and skin diseases. To prevent or greatly reduce the risk of adverse health effects in exposed workers, NIOSH recommends that exposures to MWF aerosols be limited to 0.4 mg/m^3 of air for thoracic particulate mass (or 0.5 mg/m^3 for total particulate mass) as a time-weighted average (TWA) concentration for up to 10 hr/day during a 40-hr workweek. Total particulate mass is an acceptable substitute for thoracic particulate mass until thoracic samplers are widely available. This recommended exposure limit (REL) is based on evaluation of health effects data, sampling and analytical feasibility, and technological feasibility. The NIOSH recommendation for reducing MWF aerosol exposures is supported by substantial evidence associating some MWFs used before the mid-1970s with cancer at several organ sites, and by the potential for current MWFs to pose a similar carcinogenic hazard. However, the primary basis of the NIOSH recommendation is the risk that MWFs pose for nonmalignant respiratory disease.

In addition to the REL, NIOSH recommends that a comprehensive safety and health program be developed and implemented as part of the employer's management system. This program should include safety and health training, worksite analysis, hazard prevention and control, and medical monitoring of exposed workers.

Future research may provide new and more effective methods for minimizing occupational health risks among workers exposed to MWFs. If future developments permit a lower exposure limit that is technologically feasible and prudent for the public health, NIOSH will revise its recommended standard. Until then, adherence to the REL of 0.4 mg/m^3 will minimize the risk that workers exposed to MWFs will suffer adverse health effects.

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ABSTRACT

This criteria document reviews available information about the adverse health effects associated with occupational exposure to metalworking fluids (MWFs) and MWF aerosols. Substantial evidence indicates that workers currently exposed to MWF aerosols have an increased risk of nonmalignant respiratory disease and skin diseases. To prevent or greatly reduce the risk of adverse health effects in exposed workers, NIOSH recommends that exposures to MWF aerosols be limited to 0.4 mg/m^3 of air for thoracic particulate mass (or 0.5 mg/m^3 for total particulate mass) as a time-weighted average (TWA) concentration for up to 10 hr/day during a 40-hr workweek. Total particulate mass is an acceptable substitute for thoracic particulate mass until thoracic samplers are widely available. This recommended exposure limit (REL) is based on evaluation of health effects data, sampling and analytical feasibility, and technological feasibility. The NIOSH recommendation for reducing MWF aerosol exposures is supported by substantial evidence associating some MWFs used before the mid-1970s with cancer at several organ sites, and by the potential for current MWFs to pose a similar carcinogenic hazard. However, the primary basis of the NIOSH recommendation is the risk that MWFs pose for nonmalignant respiratory disease.

In addition to the REL, NIOSH recommends that a comprehensive safety and health program be developed and implemented as part of the employer's management system. This program should include safety and health training, worksite analysis, hazard prevention and control, and medical monitoring of exposed workers.

CONTENTS

ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
ANSI	American National Standards Institute
APF	Assigned protection factor
ASTM	American Society for Testing and Materials
Ca	NIOSH potential occupational carcinogen
cc	Cubic centimeter
CFR	*Code of Federal Regulations*
CI	Confidence interval
CMA	Chemical Manufacturers Association
CPC	Chemical protective clothing
DEA	Diethanolamine
EPA	U.S. Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
°F	Degrees Fahrenheit
Fed. Reg.	*Federal Register*
FEF	Forced expiratory flow
FEV_1	Forced expiratory volume in 1 sec
ft	Feet or foot
FVC	Forced vital capacity
HEPA filter	High-efficiency particulate air filter
HHE	Health Hazard Evaluation
HP	Hypersensitivity pneumonitis
Hr	Hour(s)
IARC	International Agency for Research on Cancer
lb	Pound(s)
ILMA	Independent Lubricant Manufacturers Association
IMIS	Integrated Management Information System

ISO	International Standards Organization
L/min	Liters/minute
LOQ	Limit of quantitation
m^3	Cubic meter
MEA	Monoethanolamine
mg	Milligram
min	Minute(s)
ml	Milliliter
MOR	Mortality odds ratio
MSDS	Material safety data sheet
MSHA	Mine Safety and Health Administration
MWF	Metalworking fluid
NCI	National Cancer Institute
NCMS	National Center for Manufacturing Sciences
NDBA	N-nitrosodibutylamine
NDELA	N-nitrosodiethanolamine
NDEA	N-nitrosodiethylamine
NDMA	N-nitrosodimethylamine
ng	Nanogram
NIOSH	National Institute for Occupational Safety and Health
NMOR	N-nitrosomorpholine
NO	Nitrous oxide
NOES	National Occupational Exposure Survey
NTP	National Toxicology Program
OHAB	Occupational Health Advisory Board of the UAW–GM
OR	Odds ratio
OSHA	Occupational Safety and Health Administration
P	Probability
PAH	Polyaromatic hydrocarbons
PEL	Permissible exposure limit

PMR	Proportionate mortality ratio
ppm	Parts per million
psi	Pounds per square inch
PTFE	Polytetrafluoroethylene
RD_{50}	Exposure concentration resulting in a 50% reduction in respiratory frequency
REL	Recommended exposure limit
RR	Relative risk, rate ratio
RSD	Relative standard deviation
SD	Standard deviation
sec	Second(s)
SENSOR	Sentinel Event Notification System for Occupational Risks
SIC	Standard Industrial Classification
SIR	Standardized incidence ratio
SMR	Standardized mortality ratio
spp.	Species
STEL	Short-term exposure limit
TEA	Triethanolamine
TLV	Threshold limit value
TWA	Time-weighted average
UAW	International Union, United Automobile, Aerospace and Agricultural Implement Workers of America
µg	Microgram
µm	Micrometer

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CHAPTER 1

Recommendation for a Metalworking Fluids Standard

The National Institute for Occupational Safety and Health (NIOSH) recommends that exposure to metalworking fluid (MWF) aerosols be controlled in the workplace by complying with the recommendations presented in this chapter. These recommendations are designed to protect the safety and health of workers for up to a 10-hr work shift during a 40-hr workweek over a working lifetime. Compliance with all sections of the recommended standard should prevent or greatly reduce the risk of adverse health effects in exposed workers.

1.1 Recommended Exposure Limits

1.1.1 Exposure

NIOSH recommends that occupational exposures to MWF aerosols be limited to 0.4 mg/m^3 of air (thoracic particulate mass*) as a time-weighted average (TWA) concentration for up to 10 hr/day during a 40-hr workweek, measured according to NIOSH Method 0500 [NIOSH 1984]. The 0.4-mg/m^3 concentration corresponds to approximately 0.5 mg/m^3 for total particulate mass.†

This recommended exposure limit (REL) is intended to prevent the respiratory disorders associated with MWF exposure in the workplace. However, concentrations of MWF aerosols should be kept below the REL where possible because some workers have developed work-related asthma, hypersensitivity pneumonitis (HP), or other adverse respiratory effects when exposed to MWFs at lower concentrations. Limiting exposure to MWF aerosols is also prudent because certain MWF exposures have been associated with various cancers. In addition, limiting dermal (skin) exposures is critical to preventing allergic and irritant skin disorders related to MWF exposure. In most metalworking operations, it is technologically feasible to limit MWF aerosol exposures to 0.4 mg/m^3 or less.

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*Thoracic particulate mass is the portion of MWF aerosol that penetrates beyond the larynx.

†Total particulate mass has no precise mathematical definition. For the purposes of this criteria document, total particulate mass is that portion of the aerosol spectrum that would be sampled by a 37-mm, closed-face filter cassette that is worn by a worker and connected to a portable sampling pump operated at 2.0 L/min.

1.1.2 Safety and Health Program

In addition to the REL of 0.4 mg/m^3 (thoracic particulate mass), NIOSH recommends that a comprehensive safety and health program be developed and implemented as part of the employer's management system. Such a program must have strong management commitment and worker involvement. The major elements for a comprehensive, effective safety and health program are (1) safety and health training, (2) worksite analysis, (3) hazard prevention and control, and (4) medical monitoring of exposed workers.

1.2 Definitions

1.2.1 MWF Aerosol

MWF aerosol refers to the mist and all contaminants in the mist generated during grinding and machining operations involving products from metal and metal substitutes. MWF aerosols result from the combination of many factors, including MWF type, application pressure, nozzle (size, type, and position), temperature, tool type and speed, use of chip drags, lack of splash-guarding, ventilation, or air cleaners, and other factors [ANSI 1997].

MWF aerosol may contain a mixture of substances, including any of the chemical components of MWFs or additives to MWFs, chemical contaminants of MWFs that are in service (such as tramp oils or leached metals), metal particles, biological contaminants (such as bacterial and fungal cells or cell components and their related biological by-products such as endotoxins, exotoxins, and mycotoxins), and other material aerosolized when MWF is used in grinding and machining processes.

1.2.2 The Metalworking Environment

The *metalworking environment* refers to any environment in which workers are exposed to the following: metals, metal alloys being machined, chemical residues from preceding operations, MWF additives, MWF contamination from housekeeping and cleaning processes, biological contaminants (bacterial toxins and metabolic products), or physical contaminants (e.g, chips and fines) from MWFs.

1.2.3 MWF Classes

MWFs are grouped into four major classes:

Straight oil (neat oil) MWFs are severely solvent-refined petroleum oils (lubricant-base oils) or other animal, marine, vegetable, or synthetic oils used singly or in combination and with or without additives. Straight oils are not designed to be diluted with water.

2. *Soluble oil (emulsifiable oil) MWFs* are combinations of 30% to 85% severely refined lubricant-base oils and emulsifiers that may include other performance additives. Soluble oils are diluted with water at ratios of 1 part concentrate to 5–40 parts water.

3. *Semisynthetic MWFs* contain a lower amount of severely refined lubricant-base oil in the concentrate (5% to 30%), a higher proportion of emulsifiers, and 30% to 50% water. The transparent concentrate is diluted with 10 to 40 parts water.

4. *Synthetic MWFs* contain no petroleum oils and may be water soluble or water dispersible. The synthetic concentrate is diluted with 10 to 40 parts water.

1.3 Sampling and Analysis

Until thoracic samplers are more widely available and adopted, an acceptable substitute for the thoracic particulate mass is the total particulate mass sample. To translate the thoracic particulate measurement into an equivalent total particulate measurement, divide the total concentration by a correction factor of 1.25[‡] (or other factor experimentally measured for that operation). Thus the REL of 0.4 mg/m^3 for thoracic particulate mass is equivalent to 0.5 mg/m^3 for total particulate mass.

The recommendation for the thoracic particulate REL and sampler is based on the importance of adverse respiratory health effects and the ability of size-selective sampling to measure the particulates that reach the pulmonary airways [ACGIH 1996; ISO 1995]. NIOSH recommends that samples collected by either thoracic or total particulate samplers be analyzed gravimetrically by NIOSH Method 0500. The methods for sampling thoracic particulates are discussed in Chapter 7, Sampling and Analytical Methods.

1.4 Exposure Monitoring

An effective workplace monitoring program should include routine environmental monitoring of dermal and inhalation exposures. Such monitoring provides a means of assessing the effectiveness of engineering controls, work practices, and personal protective equipment.

The goal of the environmental sampling strategy is to ensure a more healthful work environment where worker exposure (measured by full-shift samples) does not exceed the REL. Since adverse respiratory health effects can occur at the REL, lower exposures are desirable where feasible. In work where airborne MWF exposures may occur, the initial environmental sampling survey should collect representative personal samples for the entire work shift. Surveys should be repeated at least annually and whenever any

[‡]Conversion factor from the data of Woskie et al. [1994].

major process change takes place. Surveys should also qualitatively evaluate the workers' potential skin exposures. All routine personal samples should be collected in the breathing zones of the workers. For workers exposed to concentrations above the REL, more frequent monitoring should be undertaken until at least two samples indicate that the worker's exposure no longer exceeds the REL. All workers should be notified of monitoring results and of any control actions taken to reduce their exposures. An environmental sampling strategy should consider variations in work and production schedules and the inherent variability in most environmental sampling [NIOSH 1995].

When the goal of sampling is to determine whether worker exposures are below the REL, random sampling (without a systematic bias excluding high or low exposures for workers or sampling periods) is usually not included in the sampling strategy. Instead, sampling efforts are focused on workers with the highest exposures (i.e., or the maximum-risk workers discussed by Leidel and Busch [1994]). Such targeted strategies are most efficient for identifying exposures above the REL if maximum-risk workers and time periods are accurately identified. However, all workers or worker groups should be periodically sampled to ensure that the targeted sampling includes all workers exposed to MWF aerosols at concentrations above the REL.

Area sampling may be a useful supplement to personal monitoring when determining the source of MWF aerosol exposures and assessing the effectiveness of engineering controls.

1.5 Informing Workers About the Hazards

1.5.1 Safety and Health Training

Employers should establish a safety and health training program for all workers with MWF exposures. Both employees and contract workers should be informed about hazardous chemicals in their work areas and the availability of information from material safety data sheets (MSDSs) or other sources. Workers should also be instructed about the adverse health effects associated with MWF exposures.

Workers should be trained to detect hazardous situations (e.g., the appearance of bacterial overgrowth and degradation of MWFs). Instruction should include information about how workers can protect themselves (e.g., the use of appropriate work practices, emergency procedures, and personal protective equipment).

1.5.2 Hazard Prevention and Control

Workers should be informed that exposures to MWFs during metalworking operations can occur through inhalation of MWF aerosols and through contamination of the skin by settled mists, splashes, dipping of hands and arms into MWFs, or handling of parts coated with MWF. Workers should also know that most exposures can be controlled by

a combination of proper MWF use and application, MWF maintenance, isolation of the operation(s), ventilation, and other operational procedures. Workers should be aware that dermal exposures may be reduced by the use of machine guarding and protective equipment such as gloves, face guards, aprons, or other protective work clothes.

1.6 Engineering Controls and Work Practices

Engineering controls and work practices should be used to reduce MWF inhalation and skin exposures in the workplace. A comprehensive control strategy includes guidelines for selecting and using fluids, properly maintaining the fluid, applying the fluids in a manner that avoids unnecessary skin contact and mist generation, containing any generated mist, and exhausting or removing the contained mist.

1.6.1 MWF Selection

The MWFs selected should be as nonirritating and nonsensitizing as possible while remaining consistent with their operational requirements. Petroleum-containing MWFs should be evaluated for potential carcinogenicity using American Society for Testing and Materials (ASTM) Standard D1687–95, *Determining Carcinogenic Potential of Virgin Base Oils in Metalworking Fluids* [ASTM 1997b]. If soluble oils or synthetic fluids are used, ASTM Standard E1497–94 (*Safe Use of Water-Miscible Metalworking Fluids* [ASTM 1997a]) should be consulted for safe-use guidelines, including product selection, storage, dispensing, and maintenance. To minimize the potential for nitrosamine formation, nitrite-containing materials should not be added to MWFs containing ethanolamines.

1.6.2 Fluid Use and Delivery

Many factors influence the generation of MWF mists, which can be minimized through the proper design and operation of the MWF delivery system. American National Standards Institute (ANSI) Technical Report B11 TR 2–1997 (*Mist Control Considerations for the Design, Installation and Use of Machine Tools Using Metalworking Fluids* [ANSI 1997]) provides directives for minimizing mist and vapor generation. These include minimizing fluid delivery pressure, matching the fluid to the application, using MWF formulations with low oil concentrations, avoiding contamination with tramp oils, minimizing the MWF flow rate, covering fluid reservoirs and return systems where possible, and maintaining control of the MWF chemistry.

1.6.3 Fluid Maintenance

A key element in controlling worker exposure to MWFs is the development of a written MWF management plan [ORC 1997]. Components of this plan should include maintenance of the fluid chemistry as well as the fluid filtration and delivery systems.

The machine(s) should be kept clean and free of debris. Parts washing before machining can be an important part of maintaining cleaner MWFs [Joseph 1991].

MWFs should be maintained within the pH and concentration ranges recommended by the formulator or supplier. In addition, they should be maintained at the lowest practical temperature to slow the growth of microorganisms, reduce water losses and change in viscosity, and (in the case of straight oils) reduce the risk of fire.

Drums, tanks, and other containers of MWF concentrates and additives should be stored according to the manufacturers' recommendations. Personal protective clothing and equipment should be used when removing concentrates from the original container, mixing and diluting MWF concentrate, preparing additives (including biocides), and adding MWF emulsions, biocides, or other hazardous ingredients to the coolant reservoir.

Biocides maintain the functionality and efficacy of MWFs by preventing microbial overgrowth. Biocides with a wide spectrum of biocidal activity should be used to suppress the growth of the widely diverse contaminant population. Only the concentration of biocide needed to meet fluid specifications should be used, since overdosing could lead to skin or respiratory irritation in workers, and under-dosing could lead to an inadequate level of microbial control.

MWFs should be routinely monitored and a record should be kept of fluid level in the sump or coolant tank. MWF concentration should be measured by a refractometer or by titration. The fluid pH and the degree of tramp oil contamination should be inspected visually. More frequent testing should be undertaken during hot weather or during periods of increased work output—both of which may result in increased fluid losses [HSE 1994; ORC 1997].

1.6.4 Ventilation Systems

The ventilation system should be designed and operated to prevent the accumulation or recirculation of airborne contaminants in the workplace. General principles for the design and operation of ventilation systems are presented in the following publications:

Industrial Ventilation: A Manual of Recommended Practice [ACGIH 1995];
American National Standard: Fundamentals Governing the Design and Operation of Local Exhaust Systems [ANSI 1979]; and
Recommended Industrial Ventilation Guidelines [Hagopian and Bastress 1976].

Exhaust ventilation systems function through suction openings placed near a source of contamination. The suction opening or exhaust hood creates an air motion sufficient to overcome room air currents and any airflow generated by the process. This airflow

captures the contaminants and conveys them to a point where they can either be discharged or removed from the airstream. Exhaust hoods are classified by their position relative to the process as *canopy, side draft, down draft* or *enclosure*. ANSI Technical Report B11 TR 2–1997 [ANSI 1997] contains guidelines for exhaust ventilation of machining and grinding operations. Enclosures are the only type of exhaust hood recommended by the ANSI committee. They consist of physical barriers between the process and the worker's environment. Enclosures can be further classified by the extent of enclosure: close capture (enclosure of the point of operation), total enclosure (enclosure of the entire machine), or tunnel enclosure (continuous enclosure over several machines).

If no fresh make-up air is introduced into the plant, air will enter the building through open doors and windows, potentially causing cross contamination of all process areas. Ideally, all air exhausted from the building should be replaced by tempered air from an uncontaminated location. By providing a slight excess of make-up air in relatively clean areas and a slight deficit of make-up air in dirty areas, cross contamination can be reduced. In addition, this air can be channeled directly to operator work areas, providing the cleanest possible work environment. Ideally, this fresh air should be supplied in the form of a low-velocity air shower (<100 ft/min to prevent interference with the exhaust hoods) directly above the worker.

Some commercial air cleaners recirculate exhaust in the workplace. The filters on these units should be inspected for physical integrity and filter loading, and airflow should be measured. Detailed recommendations for air recirculation are contained in *Industrial Ventilation: A Manual of Recommended Practice* [ACGIH 1995]. A better practice might be to connect such machines into a duct system discharging outdoors through a single, larger mist collection unit (see Section 9.4.4, Ventilation Systems).

1.6.5 Protective Clothing and Equipment

Engineering controls are used to reduce worker exposure to MWF aerosols. But in some situations, the added protection of chemical protective clothing (CPC) and equipment (e.g., respirators) should be provided in the event of dermal contact with the MWFs or airborne exposures that exceed the NIOSH REL. Maintenance staff may also need CPC because the nature of the work requires contact with MWFs during certain operations. All workers should be trained in the proper use and care of CPC. After any item of CPC has been in routine use, it should be examined to ensure that its effectiveness has not been compromised. The following recommendations should be used as a guide to the selection of CPC.

When evaluating the performance of CPC materials, three factors should be considered: the chemical resistance of the materials, the physical properties of the materials, and the human factors associated with the materials. Chemical resistance testing of CPC

evaluates the interaction between challenge chemicals and the garment material. When feasible, selection of CPC must be based on specific permeation data. Furthermore, the chemical permeation properties of chemical mixtures must be determined by testing—not inferred from the permeation characteristics of the individual constituents of mixtures. Physical properties of CPC are important to barrier performance. Key physical properties for gloves are resistance to flexing, tearing, abrasions, cuts, and punctures. Evaluations of ergonomic factors such as dexterity and grip involve physical properties that are governed by glove thickness. Surface texture is another important property; grip is enhanced by a rough surface. The physical requirements of the task must be balanced against the chemical resistance requirements and the human factors. CPC must protect the worker but must not unduly restrict worker performance.

The physical and chemical properties of CPC may sometimes be derived from tables, charts, and general references used to select the CPC. Chemical resistance data specific to a brand of CPC and physical properties of these materials may be available from the manufacturer. Because few references are available on CPC material for MWFs, selection is based on limited data collected for one cutting oil and one emulsifiable cutting fluid. According to the available data, nitrile affords the most chemical resistance [Forsberg and Mansdorf 1993]. The physical properties of nitrile are rated as excellent for abrasion, tear and puncture resistance, and flexibility. In addition, Silvershield™ and 4H™ material are believed to afford protection similar to that of nitrile. Approximate service life is 4 hr for these materials.

CPC for MWFs should protect the wearer from chemicals as well as punctures, cuts, and abrasions. The use of gloves may increase the risk of injury from possible entanglement in moving tool or workpiece parts. If gloves are required, special attention should be given to guarding the equipment and ensuring that the glove will tear easily if entangled. Workers should also wear safety shoes with slip-resistant soles. Workers should wear faceshields or goggles, protective sleeves, aprons, trousers, and caps as needed to protect the skin from contact with MWFs.

1.7 Respiratory Protection

Respirators should not be used as the primary means of controlling worker exposures. Instead, effective engineering controls (such as machine enclosures or local exhaust ventilation) should be implemented to minimize routine exposures to MWF aerosol. However, workers may use respirators when engineering controls are being implemented and intermittent tasks expose them to concentrations that cannot be kept below the REL by engineering controls alone.

If respiratory protection is needed, the employer should establish a comprehensive respiratory protection program as outlined in the *NIOSH Respirator Decision Logic* [NIOSH 1987b] and the *NIOSH Guide to Industrial Respiratory Protection* [NIOSH

1987a] and as required in the Occupational Safety and Health Administration (OSHA) respiratory protection standard [29 CFR[§] 1910.134]. Respirators should be selected by the person who is in charge of the program and knowledgeable about the workplace and the limitations associated with each type of respirator.

Selection of the appropriate respirator depends on the operation, MWF chemical components, and airborne concentrations of MWFs in the worker's breathing zone (see Chapter 9, Table 9–1). Additional guidance on the selection of respirators can be found in the *NIOSH Respirator Decision Logic* [NIOSH 1987b].

1.8 Sanitation and Hygiene

Workers should be encouraged to maintain good personal hygiene and housekeeping practices to reduce their exposures and to prevent MWF contamination of the environment.

Employees should be encouraged to clean MWF-contaminated skin periodically with gentle soaps, clean water, and clean towels. Workers should not need to place their unprotected hands and arms repeatedly into MWFs. Barrier creams may be useful for some workers, but their protective effects are controversial. The use of nonbarrier cream moisturizers may also be protective.

1.9 Medical Monitoring

Medical monitoring (together with any intervention based on results of medical monitoring) represents secondary prevention and should not supplant primary prevention efforts to control inhalation and skin exposures to MWF aerosol. However, as indicated by evidence reviewed in this document, the 0.4-mg/m^3 (thoracic particulate mass) REL for MWF aerosol does not remove all risk for the development of skin or respiratory disease among exposed workers. Medical monitoring is therefore needed for early identification of workers who develop symptoms of MWF-related conditions such as asthma, HP, and dermatitis. If identified early, affected workers can control their exposures and minimize their risks of acute or chronic effects. Another important objective of medical monitoring is to provide standardized data on exposed workers to identify work areas in need of additional primary prevention efforts.

All exposed workers may benefit by inclusion in an occupational medical monitoring program. However, priority should be given to those at highest risk. All workers exposed to MWF aerosol concentrations above a designated level (e.g., half of the REL) should be included. Medical monitoring should be conducted regardless of exposure

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[§]*Code of Rederal Regulations*. See CFR in references.

concentration in work areas where one or more workers have recently developed asthma, HP, or other serious conditions apparently related to MWF exposure. Medical monitoring should be more intense in work areas where exposures are higher or where more workers have more numerous or more severe adverse health effects.

All exposed workers should be provided with appropriate education and training—particularly in the area of self-referral for further medical evaluation if they develop symptoms suggestive of asthma, HP, other respiratory conditions, or dermatitis.

1.9.1 Supervision of the Medical Monitoring Program

The employer should assign responsibility for the medical direction and supervision of the program to a qualified physician or other qualified health care provider (as determined by appropriate State laws and regulations) who is informed and knowledgeable about the following:

- The respiratory protection program
- The identification and management of occupational asthma and other work-related respiratory effects or illnesses
- The identification and management of occupational skin diseases

The employer should provide the necessary information for each worker covered by the medical monitoring program, including the following:

- Current and previous job descriptions
- Hazardous exposures
- Actual exposure measurements
- Personal protective equipment
- Relevant MSDSs
- Applicable occupational safety and health standards

Anyone who administers spirometric tests as part of an occupational medical monitoring program should have completed a NIOSH-approved training course in spirometry or other equivalent training. All spirometry equipment and procedures should comply with American Thoracic Society guidelines that are current at the time of the testing (e.g., ATS [1995]).

1.9.2 Initial or Preplacement Examinations

Newly hired workers and workers transferred from unexposed work areas should receive the initial medical examination before they are assigned to jobs involving exposure to MWF or MWF aerosol. At a minimum, the initial examination should consist of

a standardized questionnaire about symptoms, a medical history (of asthma, other serious respiratory conditions, and skin diseases), and an examination of the skin. Baseline spirometric testing may also be useful for comparing results from subsequent tests.

1.9.3 Periodic Examinations

All workers included in the medical monitoring program should receive periodic screening examinations that include a brief standardized questionnaire. The frequency of these examinations for a specific worksite should be dictated by the frequency and severity of health effects in the worker population. They may be semiannual, annual, or biannual. In the absence of a case of disease associated with MWF, an annual examination would be reasonable.

1.9.4 Detailed Medical Examinations for Selected Workers

A worker should undergo additional or more frequent detailed medical evaluations if he or she

- has respiratory symptoms (or physiologic effects) suggestive of asthma or another respiratory condition possibly related to MWF aerosol exposure, or
- has recurrent or chronic dermatitis, or
- is judged by the program director or supervisor to have a medically significant reason for more detailed assessment (see Section 9.8.4, Detailed Medical Examination for Selected Workers).

1.9.5 Physician's Reports to the Worker

Following each examination (initial, periodic, or detailed), the physician should provide a written report to the worker that includes (1) the results of any medical tests performed on the worker, (2) the physician's opinion about any medical conditions that would increase the worker's risk of impairment from exposure to MWF or MWF aerosols (or any other agents in the workplace), (3) the physician's recommended restrictions on the worker's exposure to MWF or MWF aerosols (or any other agents in the workplace) and on the worker's use of respiratory protective devices and/or protective clothing, and (4) the physician's recommendations about further evaluation and treatment of any detected medical conditions.

1.9.6 Physician's Reports to the Employer

Following each examination (initial, periodic, or detailed), the physician should provide a written report to the employer that includes (1) the physician's recommended restrictions on the worker's exposure to MWF or MWF aerosols (or any other agents in the workplace) and on the worker's use of personal respiratory protective devices and/or protective clothing, (2) a statement that the worker has been informed about the results of the medical examination and of any medical conditions that should have further

evaluation and treatment, and (3) a signed authorization from the worker permitting the employer to receive the report if it reveals specific findings or diagnoses.

1.9.7 Employer Actions

Medical monitoring and followup medical evaluations should be provided without cost to workers. The employer should assure that the physician's recommended restrictions on exposures and on the use of personal protective equipment are not exceeded. The employer should ensure that the program director or supervisor regularly collaborates with the employer's safety and health personnel (e.g., industrial hygienists) to identify and control work exposures and activities that might place workers at risk.

1.9.8 Followup Medical Evaluations

Workers who are transferred as a result of the physician's opinion should be re-evaluated later to document that the intended benefit (e.g., reduced symptoms and/or reduced physiologic effects) has been achieved. Transferred workers should continue to be monitored periodically until they have been asymptomatic for at least 2 years. If symptoms persist, the responsible physician should carefully consider any continuing (e.g., irritant) exposures that may be exacerbating the worker's condition.

In addition, workers who have negative physiologic test results despite symptoms suggestive of asthma should be carefully followed and should receive another medical evaluation during an episode of acute symptoms.

1.10 Labeling and Posting

Warning labels and signs should be posted on or near hazardous metalworking processes. Depending on the process and MWF exposure concentration, warning signs should state the need to wear protective clothing or an appropriate respirator for exposure to MWF aerosol concentrations exceeding the REL.

If respiratory protection is required, the following statement should be posted:

RESPIRATORY PROTECTION REQUIRED IN THIS AREA

All labels and warning signs should be printed in both English and the predominant language of workers who do not read English. Workers unable to read the labels and signs should be informed verbally about the hazards and instructions printed on the labels and signs.

CHAPTER 2

Production, Formulation, Application, and Deterioration

The term *metalworking fluids (MWFs)* is commonly used in the lubricant production and compounding industries and in the manufacturing industries that perform machining, grinding, forming, or treating operations. This generic term encompasses coolants and lubricants used during the fabrication of products from metals and metal substitutes to prolong the life of machine tools, carry away metal chips, and protect or treat the surfaces of the material being processed. The discussions presented in this document pertain to MWFs formulated and manufactured for grinding and machining operations. Manufacturers and formulators have identified four MWF subgroups: metal-removal fluids, metal-forming fluids, metal-protecting fluids, and metal-treating fluids [Howell 1996]. See Sections 1.2.1 and 1.2.2 for definitions of MWF aerosol and the metalworking environment.

A variety of factors must be examined to evaluate worker exposures to MWFs thoroughly. Inhalation and skin exposures in the metalworking environment include those resulting from aerosolization and splashing of MWFs from fluid application, machining processes, and other operations. Workers may be exposed to the metals being machined, residues from preceding operations, MWF additives, MWF contaminants from housekeeping and cleaning processes, biological contaminants (e.g., bacterial toxins and metabolic products), and physical contaminants (e.g., chips and fines). Excessive exposure may be caused by inadequate machine enclosures, poorly designed ventilation systems, high-pressure or excessive fluid application, contamination of the MWFs with tramp oils, improper selection of the MWFs, and lack of maintenance.

2.1 Production and Use

MWFs were first used in the early 1900s to prolong the tool life of metalworking equipment [Newhouse 1982]. The Independent Lubricant Manufacturers Association (ILMA) reported that 71.5 million gallons of MWFs were produced in the United States in 1992 [ILMA 1993]. These fluids (i.e., cutting oils, machining fluids, lubricants, and coolants) reduce friction between the cutting tool and the work surface, reduce wear and galling, protect surface characteristics, reduce surface adhesion or welding, carry away generated heat, and flush away swarf, chips, fines, and residues [Nachtman and Kalpakjian 1985]. MWFs are designed for use in various machining operations such as turning,

grinding, boring, tapping, threading, gear shaping, reaming, milling, broaching, drilling, hobbing, and band and hack sawing [Weindel 1982].

2.2 Formulation

MWFs are grouped into four major classes: straight oil, soluble oil, semisynthetic, and synthetic MWFs (see Section 1.2.3 and Table 2–1).

2.2.1 Straight Oil MWFs

Straight oils (cutting oils) function as lubricants, improve the finish on the metal cut, and prevent rusting [Frazier 1982; CRC 1985]. Depending on the application, petroleum oils used in straight oil MWFs are usually mineral oils from highly refined naphthenic (generally saturated, ring-type structures) or paraffinic oils (straight or branched-chain saturated hydrocarbons) [Bigda and Associates 1980]. The lubricant base oils may also be reprocessed oils from various sources.

Mineral oils may serve as a blending medium or as an additive carrier in straight oils. Mineral oils may be derived from highly refined petroleum stocks or from reprocessed oils of unknown origin. Animal, marine, or vegetable oils may be used singly or in combination with straight oils to increase the wetting action and lubricity [Cookson 1971]. Straight oils containing both fatty oil and sulfur additives provide greater lubricity, whereas those containing sulfochlorinated mineral oils have improved antiweld properties* over a wide temperature range. Sulfochlorinated mineral oils with fatty oils added are good for heavy-duty, slow-speed operations [CRC 1985]. ILMA [1996] reports that current formulations have reduced or eliminated the addition of both sulfur and chlorine compounds.

2.2.2 Soluble Oil MWFs

Soluble MWFs (emulsions and water soluble oils) cool and lubricate to prevent welding of the cutting tool to the work surface, reduce abrasive wear of the tool at high temperatures, and prevent distortion caused by residual heat [Frazier 1982]. The mineral oils (paraffinic or naphthenic base oils) of soluble MWFs are blended from highly refined, high-viscosity oil bases. Soluble MWF concentrates are diluted with water before use [ILMA 1996]. They contain surface-active emulsifying agents to maintain the oil-water mix as an emulsion [Cookson 1971; Menter et al. 1975]. Superfatted emulsions of soluble MWFs are produced by the addition of fatty oils, fatty acids, or esters; extreme-pressure emulsions for very heavy-duty operations are produced with the addition of sulfur, chlorine, or phosphorus derivatives [CRC 1985].

*That is, properties that prevent the welding of the tool with the workpiece or chips.

Table 2–1. Components of the four MWF classes (undiluted)*

Component	Function	Amount			
		Straight oils	Soluble oils	Semi-synthetics	Synthetics
Water	Acts as coolant solvent, diluent	Dissolved 10–500 ppm/ wt†	5–40 parts/ 1 part concentrate	10–40 parts/ 1 part concentrate	10–40 parts/ 1 part concentrate
Mineral oil	Carries lubrication	60%–100%	30%–85%	5%–30%	‡
Emulsifier	Emulsifies	‡	5%–20%	5%–10%	5%–10%
Chelating agents	Tie up ions in solution	‡	0%–1%	0%–1%	0%–1%
Coupling agents	Stabilize	‡	1%–3%	1%–3%	1%–3%
Viscosity index improvers	Maintain viscosity	§	‡	‡	‡
Detergent	Prevents deposit formation	§	§	§	§
Plasticizer	Reduces tackiness	‡	§	§	§
Antimist agent	Reduces misting	§	§	‡	‡
Antiweld agent	Prevents welding	0%–20%	0%–20%	0%–10%	0%–10%
Oiliness agent	Increases film strength	§	‡	‡	‡
Surfactant wetting agent	Reduces surface tension	0%–10%	5%–20%	10%–20%	10%–20%
Dispersants	Prevent fine agglomeration and deposit formation	§	‡	‡	‡
Passivator	Prevents staining	§	‡	‡	‡
Anti-foaming agents	Prevent foaming	0–500 ppm	0–500 ppm	0–500 ppm	0–500 ppm

See footnotes at end of table.

(Continued)

Table 2–1 (Continued). Components of the four MWF classes (undiluted)*

Component	Function	Amount			
		Straight oils	Soluble oils	Semi-synthetics	Synthetics
Alkaline reserve	Acts as buffer control	‡	2%–5%	2%–5%	2%–5%
Dyes	Identify, leak detection	‡	0–500 ppm	0–500 ppm	0–500 ppm
Odorant	Masks odor	§	§	§	§
Corrosion inhibitors, anti-rust	Prevent rust film barrier	0%–10%	3%–10%	10%–20%	10%–20%
Biocides, bioresistant components	Control bacterial and fungal contaminants	‡	0%–2%	0%–2%	0%–2%
Extreme pressure additives	Act as reaction lubricant films	0%–40%	0%–20%	0%–10%	0%–10%

*Adapted from Key et al. [1983], ILMA [1990, 1994a], and Howell [1996].
†CRC [1985]. Dissolved water concentrations in mineral oils range from 10 to 100 mol per million carbon atoms, depending on ambient humidity and temperature.
‡Not present in this MWF class.
§Usually present in this MWF class.

2.2.3 Semisynthetic MWFs

Semisynthetic MWFs contain small amounts of oil (5% to 30% in the concentrate) and may be formulated with fatty acids, sulfur, chlorine, and phosphorus derivatives to provide lubrication for higher speeds and feed rates [CRC 1985].

2.2.4 Synthetic MWFs

Synthetic MWFs contain no petroleum oil. The simplest synthetics are made with organic and inorganic salts dissolved in water. They offer good rust protection and heat removal but usually have poor lubricating ability. Others may be formulated with synthesized hydrocarbons, organic esters, polyglycols, phosphate esters, and other synthetic lubricating fluids [CRC 1985]. Synthetics are stable, can be made bioresistant [Passman 1992], and provide effective cooling capacity at high speeds and feeds. They eliminate smoking, reduce misting, and provide detergent action and oxidative stability [Vahle 1982].

2.2.5 MWF Ingredients and Additives

Refined petroleum oils may be used as base oils in all MWFs except the synthetics. The chemical constituents in these refined oils depend on the original crude and the refining processes. Refined petroleum oils are complex mixtures of hydrocarbons (aromatics, naphthenes, paraffins, and cycloparaffins), metal compounds, and organic compounds containing sulfur, oxygen, and nitrogen. Less variability exists among the finished oils as the refining processes increase in severity. Solvent extraction or severe hydrotreating can reduce the total aromatic hydrocarbon content. Severe treatment with fuming sulfuric acid can almost completely remove aromatics, including polyaromatic hydrocarbons (PAHs) [IARC 1984].

2.3 MWF Application

MWFs can be manually applied to the cutting zone of the tool and the work or delivered as a mist in a high-velocity air stream. A continuous stream of MWF delivered by a low-pressure pump (a minimum pressure may be necessary for adequate operation) can be directed through a nozzle at the cutting edge of the machine tool or through the tool and over the work to carry away the metal chips or swarf. A variety of fluid nozzle designs are available, depending on the application needed [Smits 1994]. A distribution system may be used to control MWF flow volume and flow pressure. The MWF recirculating system and sump can be complex and may contain large amounts of MWFs. The MWFs are routinely collected through gravity flow, velocity flow, or conveyorized trenches. They are then recirculated to the cutting zone of the machine tool through filtration systems, chip-handling conveyors, belt skimmers or decantation tanks (to remove contaminating substances such as tramp oils), and chillers or plate-and-frame heat exchangers. Table 2–2 lists general applications of MWFs, and Table 2–3 lists general types of process and ancillary chemicals.

2.4 Deterioration of In-Service MWFs

Physical, chemical, and microbial effects can cause in-service MWFs to deteriorate. Contaminants such as wear debris, rust, weld spatter, lint, metal chips and abrasives, as well as contaminants entering through broken seals, dirty oil filter pipes, chemical residue on components, or the addition of incorrect additives can accelerate MWF breakdown. Depending on the alloy being machined and the machining process, metal particulate or dissolved metal may contaminate the MWFs. Machining or parts manufacture includes a variety of process operations from parts machining to assembly of the finished product. During many of these operations, process chemicals and ancillary lubricants may contaminate the MWFs. Industrial lubricants and in-process cleaners may leak into or be carried by parts being machined and contaminate the fluids.

Table 2–2. General applications of MWFs*

General categories	General application	Formulation technology
Removal fluids	Machining and grinding, honing	Straight or neat oil, soluble or emulsifiable oil, synthetic, semi-synthetic
Forming fluids	Stamping, drawing, coining, cold heading, wire/bar/rod drawing, piercing, forging, rolling, other	Straight or neat oil, soluble or emulsifiable oil, synthetic, semi-synthetic
Protecting fluids†	Fingerprint displacing, indoor or outdoor storage, other	Straight or neat oil, soluble or emulsifiable oil
Treating fluids	Quenching, other	Straight oil, soluble or emulsifiable oil, synthetic

*Reprinted with permission of the Independent Lubricant Manufacturers Association from *Lubes and Greases*, July 1995, Vol. 1, No. 4, based on information provided by the Independent Lubricant Manufacturers Association.

†Protecting fluids are often brought in on sheet steel products during stamping operations and offer shorter-term protection compared with the protection provided by coatings or phosphatized surfaces.

Table 2–4 lists industrial lubricants that are used around machine tools and that may leak into and contaminate the MWFs as "tramp oils." Table 2–5 describes the general use of in-process cleaners in surface preparation during routine machining processes. Many intermediate cleaning steps can be included throughout a component manufacturing process, and in-process cleaners may repeatedly contaminate MWFs. In addition, oil may degrade from excessive temperatures.

The oxidation of MWF oils and constituents can lead to the formation of acids, resins, varnishes, sludges, and carbonaceous deposits. Alkanolamine concentration may increase over time. Addition of makeup water may increase metal salts, which tend to destabilize semisynthetic and soluble MWFs [ILMA 1996]. MWFs may increase in viscosity, and oil-insoluble solids may plug orifices, pipes, and filters, restricting flow or causing sticking of machining components. Water can cause corrosion problems and affect the MWF viscosity and oxidation rate. Other additives such as biocides and anti-corrosives may be depleted with use, requiring routine product addition or supplemental additions to maintain MWF performance.

Additional contaminants from the working environment such as food scraps, floor sweepings, cigarette butts, etc. can cause changes in MWFs. Bacterial and fungal contamination and growth can cause the chemical breakdown of MWFs; in addition, they may release endotoxin and other substances into the MWFs. Microorganism growth and contamination and release of toxins are discussed in Section 4.2.2.

Table 2–3. MWF operations including process chemicals and ancillary lubricants*

Process	Operation	Process chemicals	Ancillary lubricants
Forming	Casting, forging, rolling, stamping, piercing, coining, drawing, and press forming	Die cast lubes, forging compounds, rolling oils, drawing lubricants	Hydraulic fluids, greases, and bearing lubes
Machining	Deburring, boring, milling, honing, drilling, grooving, turning, tapping, chamfering, broaching, and grinding	All classes of MWFs	Spindle oils, gear lubes, way lubes, hydraulic fluids, greases, chain lubes, and bearing lubes
Heat treating	Quenching, martempering, and carburization	All types of quenching fluids, martempering oil, and carburizer	Hydraulic fluids, greases, and bearing lubes
Finishing	Reaming, honing, lapping, grinding, and straightening	Honing oil, tapping compounds, and MWFs	Spindle oils, gear lubes, way lubes, hydraulic fluids, greases, chain lubes, and bearing lubes
Cleaning and surface preparation	Cleaning, drying, degreasing, phosphatizing, and painting	Cleaning compounds, degreasers, paint, and phosphatizing agents	Greases and bearing lubes
Assembly	Assembling	Degreasers and cleaning compounds	Hydraulic fluids and greases

*Reprinted with permission of the Independent Lubricant Manufacturers Association from *Lubes and Greases*, July 1995, Vol. 1, No. 4, based on information provided by the Independent Lubricant Manufacturers Association.

Table 2–4. Industrial lubricants: formulation and application*

Industrial lubricants	Formulation	Application
Hydraulic oils	Rust and oxidation inhibited oils and antiwear hydraulic oils, water glycol fluids, phosphate and polyol esters, water/oil emulsions	Machine tool/transfer line hydraulic systems
Spindle oils	Neat oils	Machine oils
Slidway lubricants	Neat oils	Machine tools, transfer lines
Gear lubricants	High- and extreme-pressure gear oils, open gear lubricants	Machine tools, transfer lines, gear boxes, open gears
Greases	Lithium, aluminum complex, polyurea, barium complex, calcium complex, clay	Bearings
Wire rope lubricants	Pigmented/nonpigmented neat oils, greases	Wire rope

*Submitted by ILMA [1996].

Table 2-5. In-process cleaners*

In-process cleaners	Formulation	Application
Alkaline	High-pH inorganic binders, chelators, surfactants, cosolvents; high-pH organic amines, surfactants, and cosolvents	Component cleaning, rust removal, corrosion prevention
Acid	Low-pH inhibited phosphoric, sulfuric, muriatic	Metal preparation and rust removal
Emulsion	Oil/solvent emulsion surfactants	Component cleaning
Solvent	Hydrocarbon terpene	Component cleaning

*Submitted by ILMA [1996].

CHAPTER 3

Potential for Occupational Exposures to MWFs

Workers can be exposed to MWFs through skin contact by (1) exposure to splashes and aerosols during immersion or flooding of the machine tool or work, and (2) handling parts, tools, and equipment covered with MWFs. Workers may also be exposed to MWFs by inhalation of aerosols [Bennett and Bennett 1987]. During machining of parts, workers are exposed by MWF flow through fluid circulation systems, air cleaners in a recirculating local exhaust ventilation system, adjacent operations, and persistence of fugitive emissions in workroom air.

3.1 The National Occupational Exposure Survey

The National Occupational Exposure Survey (NOES) [NIOSH 1983] was conducted by NIOSH during 1981–82 to estimate the number of workers potentially exposed to chemical, physical, and biological agents. The NOES database consists of a stratified probability sample of 4,490 businesses in 98 U.S. geographic locations representative of the nonagricultural, nonmining, and nongovernment businesses covered under the Occupational Safety and Health Act of 1970 (Public Law 91–596).

The NOES lists an estimated 1.2 million workers who are potentially exposed to agents collectively called *metalworking fluids* in 39 industry codes (2-digit Standard Industrial Classification [SIC] Codes). Approximately 59% of all workers potentially exposed to MWFs were employed in three industrial categories (Table 3–1), and 35% of the total were employed in the category *Machinery, except electrical* (SIC 35).

The largest number (67%) of all workers potentially exposed to MWFs belonged to three occupational groups identified in Table 3–2.

3.2 Occupational Exposures to Mineral Oil Mists

The Integrated Management Information System (IMIS) developed by OSHA tracks a substantial cross-section of industrial occupational exposures and compiles this information under SIC Codes. An examination of airborne mineral oil mist exposures in industries identified by SIC Codes found little evidence of substantial inter-industry differences in mean exposure concentrations. From 1979 to 1995, the occupational exposure data compiled in IMIS demonstrate a steady decline in airborne exposure

Table 3–1. Industries with the largest number of workers potentially exposed to MWFs*

		Workers exposed full time†		Workers exposed part time	
SIC Code	Description	Number	%	Number	%
35	Machinery, except electrical	151,300	37	286,000	34
34	Fabricated metal products	70,900	18	117,300	14
37	Transportation equipment	58,900	15	66,800	8
All	All industries	403,800	100	832,800	100

*Source: NIOSH [1983].
†Note: Workers exposed to one MWF full time may be exposed to a second MWF part time.

Table 3–2. Occupations with the largest number of workers potentially exposed to MWFs*

Bureau of the Census occupational code	Description	Number of workers exposed full time†	Number of workers exposed part time
637	Machinists	171,200	291,600
779	Machine operators (not specified)	56,100	130,300
777	Miscellaneous	60,800	111,900
All	All occupations	403,800	832,800

*Source: NIOSH [1983].
†Note: Workers exposed to one MWF full time may be exposed to a second MWF part time.

concentrations (Table 3–3). The arithmetic mean concentration for all samples collected during this period was 0.92 mg/m^3 (total particulate mass). The percentage of total aerosol exposures of less than 0.5 mg/m^3 increased from 36.7% before 1980 to 73% after 1990. The arithmetic mean concentration for the period 1989–94 was 0.49 mg/m^3.

3.3 NIOSH Health Hazard Evaluations

Since 1967, NIOSH has conducted more than 70 health hazard evaluations (HHEs) of industries with occupational exposures to MWFs or mineral oil aerosols. Skin disorders (skin irritation, eczema, rashes, oil acne) were the most frequently reported health problems, followed by complaints of eye, nose, and throat irritation (mucous membrane irritation) and respiratory symptoms or disorders (breathing problems, cough, chest tightness, asthma).

Exposure data from 38 HHEs indicate that airborne MWF exposures have generally decreased over time. The arithmetic mean personal exposure concentrations (total particulate mass) were 1.23 mg/m^3 (n=21 plants) in the 1970s, 0.57 mg/m^3 in the 1980s (n=15 plants), and 1.0 mg/m^3 in the 1990s (n=2 plants): the latter increase is based on only two plants. The overall mean concentration for the 38 plant-based HHEs was 0.96 mg/m^3. The exposure data collected at these 38 plants show airborne concentrations similar to those in the OSHA IMIS data set. These two data sets indicate an overall reduction in airborne MWF exposures since 1980.

3.4 Reported Exposures in the Automotive Industry

Kriebel et al. [1994], Greaves et al. [1995a,b; 1997], and Robins et al. [1994] examined the respiratory effects and associated MWF airborne exposures for automobile component manufacturing workers. All three investigators reported an arithmetic mean MWF airborne exposure concentration of <1.0 mg/m^3. Kriebel et al. [1994] reported mean exposure concentrations of 0.24 mg/m^3 (total aerosol mass, 7-hole sampler) for straight oil MWF aerosols and 0.22 mg/m^3 for soluble oil MWFs. Greaves et al. [1995a,b; 1997] reported similar concentrations with mean concentrations (thoracic fraction) for several plant surveys; the mean concentration ranged from 0.2 to 0.68 mg/m^3 for straight oil MWFs and from 0.35 to 0.65 mg/m^3 for soluble oil MWFs; it was 0.41 mg/m^3 for synthetic fluids. Likewise, Robins et al. [1994] reported soluble MWF exposures for automotive parts manufacturing workers of 0.1 to 0.6 mg/m^3 (thoracic fraction). Airborne MWF concentrations significantly declined during the period 1958–87, with an arithmetic mean concentration of 5.42 mg/m^3 (total aerosol mass) observed before 1970 and 1.82 mg/m^3 after 1980 [Hallock et al. 1994]. The three data sources (OSHA IMIS, NIOSH HHEs, and the epidemiologic studies mentioned earlier [Kriebel et al. 1994; Greaves et al. 1995a, 1997; Robins et al. 1994, 1997; Sprince et al. 1997]) suggest that the average airborne aerosol exposures in the 1990s are lower (<1.0 mg/m^3) than the 1.8 mg/m^3 aerosol exposures recorded for the 1980s by Hallock et al. [1994].

Table 3–3. Mineral oil mist air-sampling data collected by OSHA inspectors, February 1979–February 1995*

Range of mineral oil mist in samples† (mg/m^3)	Samples collected									
	Before 1980		1980–84		1985–90		After 1990		Total	
	Number	% total	Number	% total	Number	% total	Number	% total	Number	% total
0.00‡	22	20.18	62	12.25	221	25.40	182	34.60	487	24.21
>0.0–≤0.1	1	0.90	15	2.96	58	6.66	37	7.03	111	5.51
>0.1–≤0.3	5	4.58	72	14.22	166	19.08	114	21.67	357	17.75
>0.3–≤0.5	12	11.00	66	13.04	108	12.41	51	9.69	237	11.78
>0.5–≤1	20	18.34	32	6.32	23	2.64	26	4.94	101	5.02
>1	49	44.95	259	51.18	294	33.79	116	22.05	718	35.70
Total	109	100.00§	506	100.00§	870	100.00§	526	100.00§	2,011	100.00§

*Source: IMIS [1995].
†Table includes personal and area samples.
‡Nondetectable.
§Column does not add to 100 because of rounding.

CHAPTER 4

Selected Potentially Hazardous Chemical Ingredients, Additives, and Contaminants

Limited information exists about the chemical components of specific MWFs because of the highly competitive and proprietary nature of the metalworking industry. A wide variety of chemicals may be used in each of the MWF classes, and the risk these chemicals pose to workers may vary because of different manufacturing processes, various degrees of refining, recycling, improperly reclaimed chemicals, different degrees of chemical purity, and potential chemical reactions between components. The intent of this criteria document is not to identify and characterize all chemicals in MWFs that may pose health risks to workers. However, several selected chemicals are briefly discussed here.

4.1 Chemical Ingredients and Additives

4.1.1 Triethanolamine

Savonius et al. [1994] stated that triethanolamine (TEA) may be an animal carcinogen and may cause occupational asthma.

Alkanolamines or ethanolamines—TEA, diethanolamine (DEA), and monoethanolamine (MEA)—may be used in MWFs to stabilize pH or inhibit corrosion. Typically, MWFs contain 2% to 3% MEA or DEA and up to 25% TEA. ILMA has recommended using MWFs with 5% MEA or DEA and up to 25% TEA to calculate exposure risk [CMA 1996]. A typical 10:1 dilution of bulk MWF with water gives a final concentration of 0.5% MEA or DEA and 2.5% TEA. Because of the continual addition of make-up water, ethanolamines tend not to concentrate in MWFs [CMA 1996]. On the basis of a 16% absorption factor and a hand/forearm skin-exposure surface area of 2,300 cm^2, a 78.1-kg worker would have an MEA or DEA exposure potential of 0.24 mg/kg and a TEA exposure potential of 1.2 mg/kg over the course of a typical workday [CMA 1996]. In vitro studies by Sun et al. [1996] indicate that the absorption rate may be even less for MEA and DEA. The Chemical Manufacturers Association (CMA) also estimates potential aerosol inhalation of 0.0032 mg/kg for MEA and DEA and 0.016 mg/kg for TEA. These estimates are based on the average daily human air intake of 10 m^3 for a 78.1-kg worker exposed to MWF containing 0.005% MEA and DEA and 0.025% TEA at the

current OSHA permissible exposure limit (PEL) of 5 mg/m^3 for mineral oil mist [CMA 1996].

Kenyon et al. [1993] reported TEA, DEA, and MEA exposures in the same automotive parts manufacturing plants studied by Eisen et al. [1992] and Woskie et al. [1994]. The results are provided from one plant that used insoluble, soluble, synthetic, and semisynthetic fluids. Personal samples were collected from all operations using synthetic, semisynthetic, and some soluble oil MWFs. TEA in particulate mass samples and TEA, MEA, and DEA in bulk fluid samples were collected and analyzed by gas chromatography. TEA did not account for more than 1% of the particulate mass except when the MWF contained more than 10% TEA in the bulk formulation. All three ethanolamines were found in bulk samples of synthetic and semisynthetic fluids. TEA and MEA were found in soluble fluids. No detectable concentrations of ethanolamines were found in mineral oil, and only low concentrations of ethanolamines were found in soluble fluids. Higher airborne TEA concentrations were found with transfer operations (large complex machines that perform several operations) than with other machining operations. The authors concluded that although airborne TEA concentrations generally increase with increasing percentage of TEA in the bulk fluids, the concentration is also operation-specific.

In 1994, the National Toxicology Program (NTP) released a Board Draft regarding two chronic experimental studies in which Fischer 344/N rats and $B_6C_3F_1$ mice were dermally exposed to concentrations of TEA in acetone for 103 weeks [NTP 1994a]. A final report has not been released as of October 1997.

The NTP stated that "equivocal evidence" showed carcinogenic activity in the TEA-treated male rats. The NTP doubted that this result could be attributed to TEA administration, because of the lack of both a clear dose-response relationship and an increase in the total number of proliferative renal lesions in dosed male rats. Since no significant terminal increase in tumors was found in female rats in the treatment or control groups, the NTP concluded that "no evidence" existed of carcinogenic activity induced in these TEA-treated females [NTP 1994a].

The NTP [1994a] also reported a significant increase (P=0.03) in hepatocellular adenomas in high dose male mice compared with the concurrent controls. No differences were observed in incidence of hepatocellular adenomas for the two lower-dose male groups. When the terminal incidences for hepatoblastomas and hepatocellular adenomas and carcinomas were combined for the high-dose males, they also became statistically significant (P=0.018). However, these male mice were infected with *Helicobacter hepaticus*, which has been associated with increased incidences of hepatocellular neoplasms in male mice. This occurrence may be a confounding factor in the interpretation of carcinogenicity studies [Ward et al. 1994a]. This infection in male mice was a significant factor in the NTP's final determination of "equivocal evidence" of carcinogenic activity

in treated male mice based on the possibility that the increased numbers of hepatocellular adenomas were induced by the *Helicobacter* infection.

Elevated hepatoblastoma rates did not occur in the treated female groups. However, the number of hepatocellular carcinomas increased significantly in the 300-mg/kg treated female group (P=0.02), and the number of hepatocellular adenomas increased significantly in the 1,000-mg/kg treated female group (P<0.001). When these hepatocellular adenomas and carcinomas were combined within each female treatment group, they were only statistically significant for the 1,000-mg/kg dose (P<0.001). Because the carcinoma rate among the 300 mg/kg treated female mice was well below the NTP historical control, and there was no consistent dose-related increase in hepatocellular carcinomas for the other treatment groups. Therefore, the NTP decided that the elevated carcinoma rate observed in this experiment was not related to TEA exposures. Ward et al. [1994b] suggested that female mice have a low susceptibility to *Heliobacter* infection compared with males. This difference suggests that the increased incidence of hepatocellular adenomas was related to the TEA treatment. The NTP concluded that "some evidence" existed of an elevated adenoma rate in the treated female mice.

Hoshino and Tanooka [1978] reported a significantly increased lymphoma incidence (P<0.05) for combined groups of ICR-JCL female mice. However, the combined groups had a low lymphoma incidence rate compared with historical controls, and the increased lymphoma rates in treated mice reported by Hoshino and Tanooka may not have been induced by chronic ingestion of TEA. Konishi et al. [1992] reported no dose-related increased incidence of any tumor in $B_6C_3F_1$ mice treated with TEA in their drinking water for 82 weeks. MaeKawa et al. [1986] reported no significant increases of tumors in F344 rats administered TEA ad libitum in drinking water compared with controls.

In summary, the NTP Board Draft reported that the elevated carcinoma rate observed in female mice was not related to chronic TEA exposures. However, the elevated adenoma rate for the 1,000-mg/kg female mice was higher than the maximum historical control rate for a single study and provided some evidence of an elevated rate. Until the NTP releases its final report, the final interpretation of these results remains unresolved.

The NTP has released a Preliminary Pathology Working Group Chairperson's Report on selected slides from a 2-year chronic dermal study of DEA in $B_6C_3F_1$ mice [NTP 1994b]. Incidences of multiple hepatocellular adenoma, multiple hepatocellular carcinoma, and hepatoblastoma were greater in treated males than in controls. Incidences of multiple hepatocellular adenoma, hepatocellular carcinoma, and multiple hepatocellular carcinoma were greater in treated females than in controls. In addition, the NTP Working Group confirmed that, with very few exceptions, the lesions diagnosed as hepatocellular neoplasms were clearly neoplasms, and the lesions of *Helicobacter* infections were absent.

Regardless of controversies concerning carcinogenicity, occupational asthma has been associated with TEA in MWFs [Savonius et al. 1994], as well as with other aliphatic amines [Chan-Yeung and Malo 1993b; Ng et al. 1995] that are used as components of MWF.

4.1.2 Mineral Oil

Mineral oils (lubricant base oils) refined from petroleum crude oils are complex mixtures of straight- and branched-chain paraffinic, naphthenic (cycloparaffin) and aromatic hydrocarbons [IARC 1984]. Skin cancer of the hands, forearms, and scrotum was reported to be due to long-term exposure of workers to the poorly or nonrefined mineral oils used before the 1950s [Järvholm et al. 1985, Järvholm and Easton 1990; Cruickshank and Gourevitch 1952; Waldron 1983]. Water-based MWFs have not been associated with scrotal cancer because no cases were observed among the grinders who often use soluble oils [Järvholm and Lavenius 1987]. Experimental animal bioassays demonstrated that the skin tumorigenicity of different refinement classes of mineral oils is related to their polycyclic aromatic content [IARC 1984]. More severe refinery methods used since the 1950s have reduced the PAHs in straight oils [Järvholm and Easton 1990; McKee et al. 1990].

The International Agency for Research on Cancer (IARC) has classified untreated and mildly treated oils as Group 1 human carcinogens; the evidence for carcinogenicity to humans is sufficient for untreated and mildly treated oils and inadequate for highly refined oils. Untreated and mildly treated oils have also been classified as Group 2 animal carcinogens; the evidence for carcinogenicity to animals is sufficient for untreated and mildly treated oils and inadequate for highly refined oils [IARC 1987a]. The OSHA hazard communication standard [29 CFR 1910.1200] requires that employers report on the MSDSs that a substance is a carcinogen or potential carcinogen when (1) OSHA has regulated the substance as a carcinogen, (2) the NTP lists the substance on its annual list of carcinogens, or (3) IARC has evaluated the substance and found sufficient or limited evidence of carcinogenicity. According to the IARC process parameters of mild hydrotreatment, an oil processed at a hydrogen pressure of 800 pounds per square inch (psi) or less at temperatures up to 800°F is subject to the OSHA hazard communication standard. ILMA reports that mineral-oil suppliers provide short-term test results to confirm the low PAH content of dermal carcinogenicity for severely hydrotreated or severely solvent refined oils [ILMA 1996]. If untreated or mildly treated oils are used, worker exposure should be reduced to the extent technologically feasible.

4.1.3 Antimicrobial Agents

Antimicrobial agents are incorporated as components in formulated MWFs or added to MWFs before and during use to prevent microbial growth. These agents can be classified by their general function or by their chemical name [Passman 1995]. Table 4–1 lists antimicrobial agents commonly used in MWFs.

Table 4–1. Antimicrobial agents commonly used in MWFs

Chemical name	Trade name
Tris(hydroxymethyl)nitromethane	Tris Nitro
Hexahydro-1,3,5-tris(2-hydroxyethyl)-S-triazine	Grotan® Onyxide® 200 Busan® 1060 Bioban® GK Triadine® 3
Hexahydro-1,3,5-triethyl-S-triazine	Vancide TH
1-(3-Chloroallyl)-3,5,7-triaza-1-azonia adamantane chloride	Dowicil 75
4-(2-Nitrobutyl)morpholine and 4,4'-(2-ethyl-2-nitrotrimethylene)	Bioban® P-1487
O-Phenyl phenol	Dowicide®-1
Sodium 2-pyridinethiol-1-oxide	Sodium Omadine®, 40% aqueous solution
1,2-BIT; 1,2-benzisothiazolin-3-one	Proxel® MW 300 or MW 200
5-Chloro-2-methyl-4-isothiazolin-3-one-2-methyl-4-isothiazolin-3-one	Kathon® 886
2,2-Dibromo-3-nitrilopropionamide	Dow XD–8254 DBNPA
p-Chloro-m-xylenol	PCMX

Some microbiocidal or microbiostatic activities of antimicrobial agents occur through the release of formaldehyde. Formaldehyde releasers are usually soluble in water rather than oil and are more effective against bacteria than fungi. Tris(hydroxymethyl) nitromethane and hexahydro-1,3,5, tris(2-hydroxyethyl)-s-triazine are examples of formaldehyde-releasing antimicrobial agents. Formaldehyde is an airways irritant and recognized cause of occupational asthma [Chan-Yeung and Malo 1993b]. Studies suggest that exposure to certain antimicrobial agents can cause allergic or irritant contact dermatitis [Zugerman 1986]. Concerns have been raised about the potential carcinogenicity of some of these agents because of their formaldehyde-releasing action, although the actual concentrations of formaldehyde released in MWFs have not been thoroughly studied. Formaldehyde is an OSHA-regulated carcinogen [29 CFR 1910.1048]. NIOSH recognizes formaldehyde as a potential occupational carcinogen (Ca); the

REL is 0.016 ppm (TWA) with a 15-min ceiling of 0.1 ppm [54 Fed. Reg. 2651 (1989); NIOSH 1988b].

Cohen [1995] studied the use of the antimicrobial agent triazine hexahydro-1,3,5,tris(2-hydroxyethyl)-s-triazine. His study examined approximately 550 air samples, 300 of which were obtained from workers. All of the personal air samples were below the OSHA action level of 0.5 ppm for formaldehyde [29 CFR 1910.1048], including workers exposed to triazine-containing MWFs [Cohen 1995]. Thorne et al. [1995] reported that airborne concentrations of formaldehyde (formaldehyde-yielding antimicrobial agents as the primary source) ranged from below the detection limit to 0.62 mg/m^3 at an automotive engine plant.

Non-formaldehyde-releasing antimicrobial agents are generally more effective against fungi than formaldehyde releasers but are also effective against bacteria. The phenolic compounds are oil soluble, and the antimicrobial agent derivatives of morpholine and the dioxanes are partially soluble in oil and water [Zugerman 1986; Pryce et al. 1989b]. Sodium 2-pyridinethiol-1-oxide and o-phenyl phenol are examples of non-formaldehyde-releasing biocides.

Nitrated biocides such as Bronopol® (2-bromo-2-nitro1,3-propanediol), 2-methyl-2-nitro-1,3-propanediol, and 5-methyl-5-nitro-1,3-dioxane, which have been shown to release nitrite, can act as nitrosating agents in MWFs. Bioban® P–1487, which is composed of 70% 4-(2-nitrobutyl) morpholine and 30% 4,4'-(2-ethyl-2-nitrotrimethylene) dimorpholine, can dissociate to form nitrite ions. Bioban® P–1487 added to MWF concentrate can directly form N-nitrosomorpholine (NMOR) (an animal carcinogen [IARC 1978b]), which can increase in concentration over time [Mackerer 1989]. Whether this action could result in any measurable worker exposure is unclear.

Antimicrobial agents chosen for the application should be compatible with the MWFs. The chemical reactivity of MWFs may destroy antimicrobial activity; pH, extreme temperatures, and contact with some metals may inactivate or destabilize antimicrobial agents in MWFs. These agents can be combined in a mixture to produce a synergistic effect that is broad spectrum enough to kill or control both bacteria and fungi. In addition, the use of lower concentrations of synergistic antimicrobial agents would reduce worker exposure to these toxic agents; furthermore, microorganisms are not likely to develop resistant mutants to two biocides simultaneously [Rossmoore and Rossmoore 1994].

The U.S. Environmental Protection Agency (EPA) lists more than 70 chemicals as preservatives (antimicrobial agents) and more than 200 active products used as material preservatives in MWFs. EPA is developing exposure assessment methods to evaluate

both dermal and inhalation exposures to 10 commonly used antimicrobial agents. Dang [1997] estimated acute dose rates and lifetime average daily doses for acute (short-term risks) and chronic (long-term cancer risks) exposures.

4.1.4 Chlorinated Paraffins

Chlorinated paraffins are a group of chemicals with carbon chain lengths of 10 to 30 atoms and 40% to 70% (by weight) chlorination. Chlorinated paraffins are used as extreme-pressure additives that are activated by the heat generated during metalworking to form a film between the tool and work to prevent destructive welding, excessive metal transfer, and surface breakdown [Nachtman and Kalpakjian 1985]. Fifty percent of the chlorinated paraffins produced are used as extreme-pressure additives. In 1988, 79.1 million lb of chlorinated paraffins (C_{10-30}, 35% to 64% chlorine) was produced in the United States [USITC 1989].

Nilsen et al. [1981] reported that short-chain chlorinated paraffins (C_{10-13}, 49% to 71% chlorination) administered intraperitoneally to male Sprague-Dawley rats increased liver weight compared with controls. Chlorinated paraffins containing more than 17 carbon atoms did not increase the liver weights. However, the increased liver concentration of microsomal cytochrome P–450 was related to the degree of chlorination rather than the carbon chain length.

The National Cancer Institute (NCI) selected long-chain chlorinated paraffins (C_{23}, 43% chlorine; a mixture of C_{22-26} chlorinated paraffins, with an average chain length of C_{23}) and short-chain chlorinated paraffins (C_{12}, 60% chlorine; a mixture of C_{10-12} chlorinated paraffins with an average chain length of C_{12}) for toxicity and carcinogenicity evaluation. The NTP reported that under the conditions of 2-year gavage studies, clear evidence existed of the carcinogenicity of the long-chain, chlorinated paraffins (C_{23}, 43% chlorine) in male $B_6C_3F_1$ mice, as shown by a dose-related induction of malignant lymphomas [NTP 1986a]. Re-evaluation of this study by the Experimental Pathology Laboratories, Inc. (November 3, 1983) and the Pathology Working Group (February 21, 1984) resulted in the conclusion by the EPA that there is insufficient evidence to conclude that the malignant lymphomas observed in male mice were treatment related and that long-chain chlorinated paraffins should not be classified as potential carcinogens [59 Fed. Reg. 61462]. The Agency further concluded that there was insufficient evidence to list long-chain chlorinated paraffins on the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 list [59 Fed. Reg. 61462].

The NTP also reported clear evidence of the carcinogenicity of the short-chain chlorinated paraffins (C_{12}, 60% chlorine) in F344/N rats [NTP 1986b]. This evaluation was based on increased incidences of hepatocellular neoplasms in males and females, combined adenomas and adenocarcinomas of the kidney tubular cells in males, and combined follicular cell adenomas and carcinomas of the thyroid gland in females. The NTP

study reported evidence of the carcinogenicity of the short-chain chlorinated paraffins for $B_6C_3F_1$ mice, as shown by increased incidences of hepatocellular adenomas in males and females, and combined hepatocellular adenomas or carcinomas in males and females. Female mice also developed increased incidences of follicular cell adenomas and of combined follicular cell adenomas or carcinomas of the thyroid gland [NTP 1986b].

Ashby et al. [1990] tested the same grade of C_{12} chlorinated paraffin used in the NTP study [1986b] and determined that it did not induce unscheduled DNA synthesis activity in rat liver at doses up to 2 g/kg of body weight.

Two short-chain chlorinated paraffins (C_{10-13}, 60% chlorine) and one medium-chain (C_{14-17}, 40% chlorine) chlorinated paraffin were shown to be peroxisome proliferators in Fischer rat and $B_6C_3F_1$ mouse liver. The long-chain (C_{20-30}, 43% chlorine) chlorinated paraffin did not elicit peroxisome proliferation. These studies suggest that short- and medium-chain chlorinated paraffins are associated with nongenotoxic induced peroxisome proliferation and hepatocarcinogenesis [Ashby et al. 1990; Ashby et al. 1994].

EPA agreed in its EPCRA Section 313 list and Section 6607 of the Pollution Prevention Act that for short-chain chlorinated paraffins, the kidney tumors observed in rats were not likely to be relevant to tumor formation in humans. However, EPA did not question the use of $B_6C_3F_1$ mice or the results of the cancer bioassays. EPA did not believe that nongenotoxicity is a sufficient reason to dismiss the relevance to humans of tumor formation by the short-chain chlorinated paraffins. EPA also did not agree that the lack of liver growth, peroxisome proliferation in hepatocytes, and stimulation of replicative DNA in guinea pigs are proof that these effects are specific to rats and mice and have no bearing on tumor formation in humans. Therefore, EPA found sufficient evidence for listing short-chain chlorinated paraffins [EPCRA Section 313 list pursuant to EPCRA section 313(d)(2)(B)] based on the available carcinogenicity data for those chemicals. Thus EPA added the short-chain (C_{10-13}) polychlorinated alkanes (chlorinated paraffins/α-olefins) to EPCRA Section 313. EPA believes that no significant structural differences exist between chlorinated paraffins and chlorinated α-olefins. Both are primarily linear hydrochlorocarbons, and the degree of chlorination of both groups of substances can be controlled. The main difference between chlorinated paraffins and chlorinated α-olefins is that chlorinated paraffins typically manufactured from paraffin mixtures are also mixtures, whereas individual chlorinated α-olefins can be manufactured in moderate-to-high purity. Since EPA has determined that only the short-chain species meet the listing requirements of EPCRA Section 313, the polychlorinated alkanes category will be defined by the following formula and description:

$$C_xH_{2x-y}Cl_y$$

where x=10–13, y=3–12, the average chlorine content ranges from 40% to 70%, and the limiting formula structure is set at $C_{10}H_{19}Cl_3$ and $C_{13}H_{16}Cl_{12}$ [59 Fed. Reg. 61462].

Many MWF manufacturers have reported the removal of short-chain chlorinated paraffins from MWF formulations by substituting chemicals made from other feedstocks such as α-olefins or fats or other chlorinated materials not subject to EPCRA Section 313.

4.1.5 Potential Sensory or Pulmonary Irritants

MWFs may contain ingredients or additives that can be irritating through respiratory or dermal contact. Because of limited research in this area, potentially irritating ingredients and additives have not been completely identified.

In a study by Schaper and Detwiler [1991], aerosols generated from seven unused and undiluted MWFs and three used MWFs (soluble, straight [insoluble], synthetic, and semisynthetic) produced sensory and pulmonary irritation in male Swiss-Webster mice exposed to aerosolized mist at 20 to 2,000 mg/m^3 in a single 180-min inhalation period with a 20-min pre-exposure control time and a 20-min recovery period. Sensory irritants (which stimulate trigeminal nerve endings in the nasal mucosa) produce a lengthening of the expiratory phase of each breath in mice. Pulmonary irritants, which stimulate the vagal nerve endings, produce a pause between breaths in mice [Alarie 1981a; Schaper 1993]. Alarie [1981b] reported that both sensory and pulmonary irritants decrease respiratory frequency proportionally to exposure concentration.

Schaper and Detwiler [1991] observed pulmonary irritation after 2 hr with all MWF aerosol exposures. The mean respiratory frequency rapidly decreased with exposures to all MWF aerosolized mists, plateauing at 2 hr. In low-exposure animals, recovery of respiratory frequency to control levels was prompt following discontinuation of exposure. However, slower recovery occurred in animals exposed at higher concentrations. At high exposure concentrations, mean tidal volume decreased by 30% to 50% and respiratory frequency decreased 70% to 80%. Little change occurred in lung weight or lung volume displacement in mice exposed to concentrations capable of inducing a 50% reduction in respiratory frequency. The most significant histopathologic changes were found 24 hr after exposure. Mild interstitial pneumonitis occurred in animals exposed to unused and used soluble oil fluids, unused and used semisynthetic fluids, and unused and used straight oil fluids. Moderate interstitial pneumonitis and bronchopneumonia occurred in animals exposed to a second unused soluble oil MWF sample. No histopathologic changes were seen in mice exposed to a third unused soluble oil MWF sample or in mice exposed to an unused synthetic fluid sample. On the basis of the 50% reduction in respiratory frequency, the three semisynthetic/synthetic MWFs were more irritating than the five soluble oil fluids. All eight were more potent than the two straight oil fluids. There was no significant difference in potency between the three neat fluids and

their corresponding in-service fluids. Schaper and Detwiler [1991] concluded that these results do not imply that other sets of straight oil and in-service fluids are equally potent or that the relative order of potency will always be the following: synthetic/semisynthetic>soluble>straight.

In a recent study by Schaper and Detwiler-Okabayashi [1995a], the authors examined the sensory and pulmonary irritant properties of the three major components (tall oil fatty acids, sulfonic acid, and paraffinic oil) of one of the three unused soluble oil MWFs described earlier. As in the previous study, male Swiss-Webster mice were administered generated aerosol mists (particulate mass median aerodynamic diameter of 1 to 2 μm, standard deviation [SD] 2.0) for 180 min with 20-min pre-exposure and 20-min postexposure recovery times. Sensory and pulmonary irritation were evaluated through the recordings of tidal volume and respiratory frequency. In this study, tall oil fatty acid acted mainly as a sensory irritant, and sulfonic acid acted as a pulmonary irritant. Animals exposed to either agent did not fully recover normal breathing patterns, and the mean respiratory frequency remained below control levels. Paraffinic oil produced sensory irritation at the beginning of exposures, with pulmonary irritation effects occurring between the second and third hour. Recovery was incomplete, although respiratory frequency returned toward control levels.

Schaper and Detwiler-Okabayashi [1995a] also assessed the sensory and pulmonary effects of two component mixtures (sulfonic acid/tall oil fatty acids, sulfonic acid/paraffinic oil, and tall oil fatty acid/paraffinic oil). Mixtures containing sulfonic acid provoked pulmonary irritation earlier in the exposures than did the tall oil fatty acid/paraffinic oil. Likewise, recovery was poor for all the mixtures but the latter, for which some recovery was observed. The sensory and pulmonary effects of the unused soluble oil MWF closely matched those of paraffinic oil and tall oil fatty acid/paraffinic oil.

The decreases in respiratory frequency for each of the components and mixture are proportional to the logarithms of exposure concentrations. This result suggests (at least with these components) that the sensory and pulmonary irritation effects of all three components are additive and not synergistic. These studies provide evidence that some components of arbitrarily selected MWFs are pulmonary irritants in experimental animals. These findings are consistent with the adverse health effects observed in the studies of respiratory symptoms and pulmonary function in exposed workers. Schaper and Detwiler-Okabayashi [1995b] has suggested an approach to using the results of these studies to derive an occupational exposure limit. However, NIOSH has relied primarily on the epidemiologic data to establish an REL for MWFs.

4.2 Hazardous Contaminants

Exposure to hazardous contaminants in MWFs may present health risks to workers. Contamination may occur from (1) process chemicals and ancillary lubricants

inadvertently introduced, (2) contaminants, metals, and alloys from parts being machined, (3) water and cleaning agents used for routine housekeeping, and (4) contaminants from other environmental sources at the worksite. Bacterial and fungal contaminants may metabolize and degrade the MWFs to hazardous end products as well as elaborate endotoxins, exotoxins, and tissue-damaging enzymes. A few selected chemical and biological contaminants of MWFs are discussed in the following subsections.

4.2.1 Nitrosamines

Potentially carcinogenic nitrosamines have been identified in MWFs studied in the 1970s and early 1980s. The formation and concentration of nitrosamines in MWFs depend on: (1) the concentrations of amine and nitrosating agent, (2) the type of amine (primary, secondary, or tertiary), (3) the presence of catalysts or inhibitors, (4) the pH of the MWF, (5) the temperature of the fluid, and (6) the time of contact between amine(s) and nitrosating agent(s) [Loeppky et al. 1983]. Some nitrosamines may form under work conditions such as the extreme heat and pressure generated by machinery [Fan et al. 1977; Kipling and Waldron 1976; NIOSH 1976]. Lijinsky et al. [1972] demonstrated that TEA could be nitrosated to form N-nitrosodiethanolamine (NDELA), a nitrosamine that IARC has classified as a Group 2B carcinogen (possibly carcinogenic to humans) [IARC 1978a; Lijinsky et al. 1980, 1984; Lijinsky and Kovatch 1985; Preussman et al. 1982; Lijinsky and Reuber 1984]. Lucke and Ernst [1992] reported that the concentrations of NDELA found in MWFs are related to the amount of DEA in the fluids. Certain biocides can dissociate to form nitrite ions, which may react with alkanolamines to form nitrosamines [Mackerer 1989].

NDELA has reportedly occurred in MWFs containing sodium nitrite and DEA or TEA [Järvholm et al. 1986; Spiegelhalder 1980]. Fan et al. [1977] reported 0.02% to 3% concentrations of NDELA contamination in several unused synthetic MWFs containing the alkanolamines TEA or DEA and nitrites. The presence of nitrosamines in these samples was reported before the EPA prohibited the addition of nitrosating agents to MWFs containing the triethanolamine salt of tricarboxylic acid, mixed monoamides and diamides of an organic acid, or a TEA salt of a substituted organic acid [40 CFR 747.115 (1990)]. These prohibitions were intended to eliminate or reduce the concentration of contaminating nitrosamines by controlling the precursors. Analysis of some MWFs following the EPA prohibition showed reduced concentrations of nitrosamines. Garry et al. [1986] reported 1 to 5 ppm of N-nitrosodimethylamine (NDMA), N-nitrosodibutylamine (NDBA), and NMOR.

However, some studies show that nitrosamines may form in MWFs that contain TEA or DEA even though nitrites have not been added. Challis et al. [1978] demonstrated the rapid nitrosation of primary and secondary amines by nitrogen oxides; oxygen accelerates nitrosation by converting NO through NO_2 to either of two nitrosating agents, N_2O_3

or N_2O_4. In addition, nitrosamine formation from NO and amines is accelerated under specific conditions by formaldehyde, paraformaldehyde, thiocyanate, nitrophenols, and certain metal salts (e.g., ZnI_2, CuCl, $AgNO_3$, $SnCl_2$, $CoSO_4$, and $HgCl_2$) [Challis et al. 1978; Keefer and Roller 1973; Boyland et al. 1971; Davies and McWeeny 1977; Loeppky et al. 1983; Okun and Archer 1977].

Keefer et al. [1990] reported NDELA contamination (0.05 to 58.8 ppm) of synthetic, semisynthetic, straight oil, and soluble concentrates (Table 4–2).

Table 4–2. NDELA and nitrite/nitrate concentrations in unused MWF concentrates*

MWF	NDELA (ppm)	NO_2/NO_3 (ppm)
Synthetic	0.05–58.80	9–111
Semisynthetic	0.43–4.55	15–17
Petroleum-based	0.11–0.16	10–72

*Adapted from Keefer et al. [1990].

In May 1993, EPA issued the Significant New Use Rule for alkali metal nitrites intended for use in MWFs. Manufacturers or companies that plan to manufacture, import, or process alkali metal nitrites (i.e., nitrites of lithium, sodium, potassium, rubidium, cesium, and francium) for use in MWFs must comply with the reporting requirements under Section 5(a)(2) of the U.S. EPA Toxic Substances Control Act.

4.2.1.1 NIOSH Reports of Nitrosamine Contamination

On the basis of a report on NDELA contamination in new and used MWFs [Keefer et al. 1990], NIOSH researchers began a preliminary nitrosamine contamination survey of MWFs [NIOSH 1992]. They collected bulk fluid and personal air samples during HHEs [NIOSH 1992] of the metalworking industry. During 1992–93, 47 samples of straight, soluble, semisynthetic, and synthetic MWFs (both new and used) were collected at 4 sites, and 29 air samples were collected at 2 sites.

The air samples were analyzed for seven nitrosamines, including NMOR, which may be formed from NDELA by dehydration and cyclization. The results were negative (limit of detection ranged from 0.01 to 0.04 μg per sample) except for one sample in which NMOR was detected at 0.12 μg per sample (air concentration about 0.1 $\mu g/m^3$). That sample was from a site using a straight oil MWF [NIOSH 1992].

All MWF bulk samples were analyzed for NDELA. In addition, the samples from one site (designated Site A) were reanalyzed for NDELA and for seven other nitrosamines; only NMOR was found. The results (Table 4–3) ranged from undetected to 4.7 ppm for NDELA and 0.04 to 17 ppm for NMOR. NMOR was found in all six samples analyzed, and NDELA and NMOR were found in all three samples of straight oils. NDELA was detected in only one of eight MWF concentrates, but it was found in half (22 of 44) of the used fluids produced from those concentrates. These results suggest that NDELA may form during use. Also, the results for Fluid G at site C suggest that some process factors influence nitrosamine formation.

The degradation of nitrosamines in MWFs is less well understood, but (like the formation) it may also depend on the pH of the fluids, the type of machining operation, types of microbial species and numbers, metal and alloys being machined, and length of fluid use.

4.2.1.2 Carcinogenicity of Nitrosamines

IARC has classified N-nitrosodiethylamine (NDEA) and NDMA. Group 2A agents—*probably carcinogenic to humans*. This group classification includes agents for which limited evidence exists of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals [IARC 1987b]. IARC has classified NDBA, NDELA, and NMOR as Group 2B carcinogens—*possibly carcinogenic to humans*. This category includes agents for which inadequate evidence exists of carcinogenicity in humans, but sufficient evidence exists of carcinogenicity in experimental animals [IARC 1987b].

The NTP has determined that sufficient evidence exists for the carcinogenicity of NDBA, NDELA, NDMA, and NMOR in experimental animals based on animal studies cited by IARC [NTP 1991].

OSHA has classified NDMA as a *cancer suspect agent* (29 CFR 1910.1003 and 1910.1016). Without establishing a PEL, OSHA promulgated standards in 1974 to regulate the industrial use of NDMA, identified as an occupational carcinogen. The changes in MWF composition since the EPA prohibitions in 1984 and 1990 have reduced the concentration of nitrosamine, as demonstrated by Garry et al. [1986], Keefer et al. [1990], and NIOSH [1994a]. However, as these studies show, low concentrations of nitrosamines are still found in some MWFs.

4.2.2 Microbial Contamination

4.2.2.1 Ecology

Historically, microbial contamination of MWF has been a problem in the metalworking industries, primarily because of microbial growth effects on fluid quality and performance. Fluid degradation from microorganisms may result in changes in fluid viscosity,

Table 4–3. Concentrations of NDELA and NMOR found in MWF field samples from four sites

MWF type and identification	Sample site	Sample condition	Nitrosamine concentration (ppm)	
			NDELA	NMOR
Straight oil:				
Fluid A	A*	Unused	0.14, 0.35	0.04
Fluid B	A	Unused	0.44, 4.7	17.0
Unknown	A	Used	3.00, 0.18	0.16
Soluble oil:				
Fluid C	B	Concentrate	ND†	NA‡
		Used	ND	NA
		Used	ND	NA
		Used	ND	NA
		Used	ND	NA
	C	Concentrate	ND	NA
		Used	ND	NA
		Used	ND	NA
		Used	ND	NA
		Used	ND	NA
Fluid D	D	Concentrate	1.90	NA
		Used	0.05	NA
		Used	0.66	NA
Semisynthetic oil:				
Fluid E	D	Concentrate	ND	NA
		Used	ND	NA
		Used	0.48	NA
		Used	0.29	NA
		Used	0.61	NA

See footnotes at end of table.

(Continued)

Table 4–3 (Continued). Concentrations of NDELA and NMOR found in MWF field samples from four sites

MWF type and identification	Sample site	Sample condition	Nitrosamine concentration (ppm)	
			NDELA	NMOR
Synthetic oil:				
Fluid F	A	Concentrate	ND, ND	0.09
		Used[§]	ND, ND	0.23
		Used[§]	0.34, ND	0.10
Fluid G	B	Concentrate	ND	NA
		Used	0.48	NA
		Used	0.05	NA
		Used	0.40	NA
		Used	0.43	NA
		Used	ND	NA
		Used	0.49	NA
		Used	0.39	NA
		Used	0.56	NA
	C	Concentrate	ND	NA
		Used (steel)	ND	NA
		Used (steel)	ND	NA
		Used (steel)	ND	NA
		Used (steel)	ND	NA
		Used (stainless steel)	0.07	NA
		Used (stainless steel)	0.48	NA
		Used (stainless steel)	0.31	NA
		Used (stainless steel)	0.30	NA

See footnotes at end of table.

(Continued)

Table 4–3 (Continued). Concentrations of NDELA and NMOR found in MWF field samples from four sites

MWF type and identification	Sample site	Sample condition	Nitrosamine concentration (ppm) NDELA	NMOR
Synthetic oil (continued):				
Fluid H	D	Concentrate	ND	NA
		Used	0.67	NA
		Used	0.59	NA
		Used	0.34	NA
		Used	0.61	NA

*Only Site A samples were subsequently analyzed for NMOR and reanalyzed for NDELA (second values).
†ND=not detected; estimated limit of detection=0.05 ppm.
‡NA=not analyzed.
§Water-based fluids presumed to have been prepared from Fluid F concentrate.

and the acid products of fermentation may lower the pH of the fluids, causing corrosion and leaks in the MWF system. Anaerobic bacteria, specifically the sulfate reducers, may produce hydrogen sulfide and other disagreeable and toxic gases. Excessive microbial growth may result in clogged filters and ports and may interfere with the metalworking operation.

Water-based MWFs are excellent nutritional sources for many kinds of bacteria and fungi. The predominant microbial species routinely recovered from MWFs are virtually identical to those routinely recovered from natural water systems. As a group, they exhibit great nutritional diversity. Moreover, many species that grow well on MWF components secrete waste products that serve as nutrients for microorganisms with more restricted nutritional capabilities. Environmental conditions such as alkaline pH, elevated temperature, and the presence of metals favor the development of a population able to survive and grow in conditions generally considered hostile for microorganisms. Attempts to manage microbial growth by the incorporation or addition of biocides may result in the emergence of biocide-resistant strains. Complex interactions may occur among different member species or groups within the population. The growth of one species may result in conditions that are more (or less) favorable to the subsequent establishment of other species. The elimination of one group of organisms may permit the overgrowth of another. All these factors contribute to the establishment of a unique microbial community and to the continuation of change in the population.

4.2.2.2 Hazards

Microbial contamination of MWFs may pose occupational hazards for exposed workers. Tant and Bennett [1956] isolated 29 different bacterial species from emulsion oils, including many that are pathogenic or potentially pathogenic for humans. The most commonly cultured species belonged to the genus *Pseudomonas (P. aeruginosa* and *P. oleovorans)*. Others identified included *Klebsiella pneumoniae, Micrococcus pyogenes* (now *Staphylococcus aureus*), *Escherichia coli, Proteus vulgaris, Aerobacter* (now *Enterobacter*) *aerogenes*, and members of the *Citrobacter* and *Achromobacter* genera. In a later study, Bennett [1972] again identified *Pseudomonas* and *Desulfavibrio* as the two most common genera isolated. Wort et al. [1976] examined samples of soluble oil emulsions and also reported that *Pseudomonas* was the predominantly cultured genus. *Cephalosporium* (*Acremonium*) was the most common fungus isolated [Bennett 1972]. Rossmoore [1986] found *Pseudomonas, Enterobacter, Moraxella, Aeromonas, Acinetobacter, Flavobacterium*, and *Alcaligenes* and the fungi *Cephalosporium, Fusarium, Penicillium, Aspergillus, Cladosporium, Trichoderma, Candida, Botrytis, Saccharomyces, Trichosporon*, and *Cryptococcus* in MWFs from an automotive engine plant.

Although frankly pathogenic organisms such as *Salmonella, Staphylococcus*, and *Legionella* have been isolated from MWFs [Hill and Al-Zubaidy 1979; Herwaldt et al. 1984], most of the organisms associated with MWFs are characterized either as nonpathogens or as "opportunistic" pathogens (those that primarily infect persons with a major abnormality in their natural defenses). Conditions and situations that may result in compromised host defenses include predisposing disease such as diabetes, cancer (especially leukemia), or cystic fibrosis; alcoholism; inherited or acquired immune deficiency; burns, skin cuts and abrasions, or other trauma; invasive medical procedures; and certain medications (e.g., some antibiotics and immunosuppressive drugs).

The bacterial genus most commonly isolated from MWFs is *Pseudomonas*. Despite the frequency and severity of *Pseudomonas* infections in susceptible persons, healthy adults with intact immunity are rarely affected. One study of a worksite with a demonstrated viable count of 1×10^8 colony-forming units per ml of MWF showed no evidence of *Pseudomonas* colonization of the workers' respiratory tracts, even though the organisms were cultured from the MWF [Hill and Al-Zubaidy 1979]. The reason is probably that organisms are rapidly cleared from the lungs of healthy persons. No reports have been published of work-related *Pseudomonas* infections in MWF workers.

Infections are not the only health risks associated with occupational exposure to microorganisms. All microorganisms produce antigens—molecules, often proteins or polysaccharides, that stimulate the immune system. A single exposure to an antigen may result in sensitization. If the sensitized person is exposed again to the same antigen, a hypersensitive or allergic response may occur to an antigenic dose that would elicit little or no reaction from nonsensitized persons. Allergic reactions to inhaled antigens may be

limited to the upper respiratory tract (e.g., allergic rhinitis), or they may affect the airways (e.g., allergic asthma) or the distal portions of the lung (e.g., HP, also known as extrinsic allergic alveolitis). Interest has focused on the possible involvement of microbial antigens in recent clusters of HP among workers exposed to MWF aerosols in operations using synthetic and soluble oil MWFs [Kreiss and Cox-Ganser 1997]. However, the cause of HP in MWF-exposed workers may not be limited to bacterial antigens (see Section 5.3).

Endotoxins (the principle surface antigens in gram-negative bacteria) are heat-stable lipopolysaccharide-protein complexes contained in the cell envelopes of all gram-negative species. Exotoxins are secreted by viable cells as a physiological function. In contrast, endotoxins are released from cells generally as a result of the death of the cell, or the lysis or disruption of the integrity of the outer membrane/cell wall structure [Galanos et al. 1979]. MWFs that have high levels of gram-negative bacteria also have high levels of endotoxins [Mattsby-Baltzer et al. 1989a; Milton et al. 1990].

Endotoxins exhibit similar biological activities (pyrogenicity and increased capillary permeability) regardless of the species of bacteria from which they are derived [Budavari et al. 1989]. Endotoxins were first implicated in occupational disease in 1942 [Neal et al. 1942]. Subsequently, various animal, human, and epidemiologic studies have established a link between exposure to airborne endotoxins and respiratory problems in various workplace environments [Pernis et al. 1961; Cavagna et al. 1969; DeMaria and Burrell 1980; Snella 1981; Burrell and Rylander 1982; Brigham and Meyrick 1986; Castellan et al. 1987; Rylander and Beijer 1987; Jacobs 1989; Burrell and Ye 1990; Gordon et al. 1991; Fogelmark et al. 1992; Rylander and Fogelmark 1994; Rylander and Jacobs 1997]. Also, animal exposure studies conducted by Gordon [1992] demonstrated that the endotoxin content of MWFs predicted respiratory toxicity in a guinea pig model of acute airways obstruction. Therefore, aerosolized endotoxins are suspect causative agents of occupationally related adverse respiratory effects (e.g., chronic bronchitis, abnormal cross-shift declines in pulmonary function, asthma, and other long-term effects) among workers exposed to MWF aerosols [Hill and Al-Zubaidy 1979; Hill 1983; Kennedy et al. 1989; Mattsby-Baltzer et al. 1989b; Gordon 1992; Gordon et al. 1992; Sprince et al. 1994; Robins et al. 1997].

For some time, the Food and Drug Administration has regulated the measurement of endotoxin (pyrogen) in parenteral solutions and on various medical devices manufactured by the pharmaceutical industry [USP 1985; FDA 1988]. However, no standard method exists for measuring airborne endotoxin in environmental samples. Therefore, reported measurements of airborne endotoxin concentrations often exhibit high variability because of differences in collection media, sampling methods, and assay procedures [Milton et al. 1990; Gordon et al. 1992].

Bacteria also secrete other toxins and extracellular enzymes that may present health hazards, although to date no evidence exists that exotoxins or other microbial enzymes have produced adverse health effects in MWF-exposed workers. Theoretically, toxic metabolites and tissue-damaging enzymes may accumulate to concentrations that constitute a threat to exposed workers. In addition to tissue-damaging enzymes, bacterial enzymes are also potentially associated with ill effects. They are highly antigenic and have caused asthma in some work settings [Chan-Yeung and Malo 1993b]. The growth of certain bacteria may result in the production of gases such as ammonia and hydrogen sulfide, which can have toxic or irritant effects.

Fungi (yeasts and molds) also contaminate all water-based or water-contaminated MWFs. Generally, the fungi isolated from MWFs are common saprophytic species that live on decaying organic matter in the environment and are not usually the major microbial contaminant in MWFs. Although no reports have been published about fungal diseases from contaminated MWF exposures, some known health hazards are associated with fungi exposure. Given the opportunity, fungi may infect susceptible hosts (such as the immunocompromised persons discussed earlier) or may cause allergic disease in persons previously sensitized. *Cephalosporium*, a genus commonly isolated from MWFs, has reportedly caused HP in exposed persons [Patterson et al. 1981]. *Penicillium* and *Aspergillus* species, have likewise been implicated in HP and both are common MWF contaminants. In addition, several fungal species isolated from MWFs are known to cause allergic reactions including asthma, but the relationship between fungal contamination and occupational asthma associated with MWF exposures is uncertain.

Fungi also produce toxic metabolites called mycotoxins. *Fusarium* (one of the fungal genera isolated from contaminated MWFs) produces toxins that cause dermal toxicity [Bhavanishankar et al. 1988]. Other genera, including *Cephalosporium,* may also produce these toxins.

4.3 Metals and Metal Alloy Contaminants

Depending on the type of MWF, the grinding or machining process and tools, and the metals or alloys being machined, metals may dissolve into the MWF. In general, straight oils absorb fewer metals than water emulsions, whereas semisynthetics may be less reactive than synthetic fluids. The amount of metal absorbed is directly related to the total metal surface area exposed to the MWF. Higher MWF operating temperatures can result in greater metal solubility. Smaller sumps become more quickly saturated with soluble metals, and concentrations of metals (and other chemicals) increase the longer the fluids are in use. Soluble metals that may contaminate MWFs include lead from leaded steels, leaded aluminum and leaded brass; nickel and chrome from stainless steel; zinc from galvanized steel; and mercury, lead, zinc, and copper from cast and ductile irons [Burke 1994]. Cobalt may also contaminate MWF [Kennedy et al. 1995a].

CHAPTER 5

Occupational Health Risks for Workers Exposed to MWFs

5.1 Nonmalignant Respiratory Effects

Occupational exposure to MWF aerosols is associated with a variety of nonmalignant respiratory conditions, including lipid pneumonia, HP, asthma, acute airways irritation, chronic bronchitis, and impaired pulmonary function. This chapter reviews relevant clinical case reports, surveillance data, and epidemiologic studies of nonmalignant respiratory conditions and their association with exposure to MWF aerosols.

5.1.1 Diseases of the Lung Parenchyma

5.1.1.1 Lipid Pneumonia

Lipid ("lipoid") pneumonia (characterized by lipid deposits within pulmonary macrophages) involves an inflammatory and sometimes fibrotic response of lung tissue to exogenous lipid. In equivalent doses, mineral oils deposited in the lungs are more likely than vegetable oils to be associated with lipid pneumonia; pure synthetic MWF cannot cause lipid pneumonia because it contains no oil. Case reports of lipid pneumonia resulting specifically from occupational exposure to aerosolized oil in metalworking environments have appeared rarely in the published literature. In recent decades, Penes et al. [1990] reported lipid pneumonia in a person who worked for 16 years as a machinist, and Cullen et al. [1981] reported lipid pneumonia in a steel rolling mill worker exposed for 3 years to both straight and soluble oil MWFs. Systematic epidemiologic studies have not assessed the incidence or prevalence of lipid pneumonia among workers exposed to MWFs. However, the apparent rarity of lipid pneumonia associated with occupational exposure to oil mists in metalworking operations suggests that current exposure concentrations are generally insufficient to cause clinical cases of the disease. Clinically diagnosed lipid pneumonia is more frequently associated with nonoccupational aspiration of oily products into the lungs than with inhalation of oil aerosols in occupational settings [Proudfit et al. 1950; Foe and Bigham 1954; Sprince et al. 1994].

5.1.1.2 Hard Metal Disease

Hard metal disease of the lung (caused by inhaled tungsten carbide/cobalt) is characterized by pneumonitis and interstitial pulmonary fibrosis. Metalworkers exposed to MWF

aerosols contaminated with cobalt from tungsten carbide/cobalt tool pieces (primarily in operations involving the grinding of hard metal parts such as cutting tools) are at risk for this disease. Cobalt concentrations averaged 664 mg/L in bulk samples of MWF taken from sumps in some grinding operations [Kennedy et al. 1995a]. Hard metal disease may develop within 2 years of initial exposure and may have a rapid progression; or it may become clinically apparent only after 30 years of occupational exposure [Sprince 1992]. Cobalt toxicity may be enhanced when it is in the ionized form in MWFs used for grinding operations [Sprince 1992].

5.1.1.3 Legionellosis

A large outbreak of Pontiac fever (a self-limited, nonpneumonic form of legionellosis with influenza-like symptoms) was shown to be caused by exposure to contaminated MWF aerosol in an engine manufacturing plant [Herwaldt et al. 1984]. The outbreak occurred on startup following an 8-day shutdown that had allowed bacterial growth in the MWF reservoir. A newly identified species of *Legionella* was isolated from this soluble MWF. Compared with controls, workers with symptoms meeting the case definition criteria had significantly elevated antibody titer to this organism ($P<0.0001$). To date, no cases of legionnaires' disease (the sometimes fatal pneumonic form of legionellosis) have been documented to be associated with exposure to contaminated MWF, and no other outbreaks of MWF-associated nonpneumonic legionellosis have been reported in the scientific literature.

5.1.1.4 HP

HP, also known as allergic alveolitis, involves an immunologic reaction to inhaled antigen and is believed to require prior sensitization to the antigen. This disease is characterized in its acute phase by alveolar inflammation and influenza-like symptoms; in its chronic phase (following repeated exposures), it is characterized by pulmonary fibrosis associated with respiratory impairment. Common antigens associated with HP in nonmetalworking occupational settings include airborne microbes (especially bacterial spores of *Saccharopolyspora* spp., spores of *Thermoactinomyces spp.*, fungal spores of *Alternaria* and *Aspergillus spp.*, and various large-molecular-weight compounds, including proteins). Two cases of HP associated with MWFs were reported during a 3-year period to an occupational respiratory disease surveillance program operating in the United Kingdom [Merideth and McDonald 1994]. Many more cases at a number of facilities in North America have been recently recognized [Rosenman et al. 1994; Bernstein et al. 1995; Rose et al. 1996; Kreiss and Cox-Ganser 1997].

Bernstein et al. [1995] published the first detailed case reports of HP associated with occupational exposure to MWF. A small metalworking shop introduced a synthetic MWF in 1991; 6 to 11 months later, 6 workers developed HP symptoms. Symptoms and other clinical abnormalities resolved in all six workers after they were removed from the

workplace (and after additional corticosteroid treatment in two of the workers). MWF sump samples were found to be contaminated with bacteria, and all six affected workers had precipitating antibodies to one of the bacterial contaminants, *Pseudomonas fluorescens*. Serum-precipitating antibodies to other organisms isolated from the MWF were also present in some of the affected workers. The available data do not permit a definitive conclusion regarding *Pseudomonas* as a cause of the outbreak, particularly since precipitating antibodies to *Pseudomonas* have been found in apparently healthy workers exposed to contaminated MWF [Mattsby-Baltzer et al. 1989a, 1990]. Nevertheless, on the basis of this investigation and by analogy to other occupational settings in which HP is known to occur, microbes that contaminate MWF would be likely etiologic suspects.

Rose et al. [1996] recently reported an additional six cases of biopsy-confirmed cases of HP among MWF-exposed automobile production workers in three different plants. In all cases, episodic respiratory and systemic symptoms were temporally related to the presence of affected workers in work areas where soluble MWFs were in use. One affected worker (a 57-year-old who had not smoked for the preceding 28 years) had been a toolmaker at the same plant for 28 years. Progressive illness resulted in hospitalization for respiratory failure. Physical examination revealed inspiratory crackles; a chest radiograph revealed diffuse interstitial infiltrates; arterial oxygenation was markedly reduced; and pulmonary function tests showed restriction and reduced diffusing capacity. Treatment included corticosteroids and removal from work. Repeat pulmonary function tests 1 year later revealed substantial improvement. At the time of the report, exposures had not been well characterized and no specific agent(s) had been identified as the likely cause.

These and several other recent outbreaks of MWF-associated HP led to a topical workshop sponsored by the International Union, United Automobile, Aerospace and Agricultural Implement Workers of America (UAW)-Chrysler National Joint Committee on Health and Safety [Kreiss and Cox-Ganser 1997]. Participants discussed eight different outbreaks at eight plants involving a total of 98 physician-diagnosed cases of HP. Major conclusions of that workshop included the following:

- A risk of HP is associated with use of microbially contaminated, water-based MWFs characterized by a predominance of "unusual" flora (e.g., *Mycobacteria chelonae* was found in MWF in 4 of the 6 outbreaks in which investigators attempted to isolate *Mycobacteria*).
- Most reported cases occurred despite apparent MWF aerosol exposure concentrations below 0.5 mg/m^3 (TWA).

In the absence of more definitive information on which to base primary prevention, workshop participants identified research needs and outlined secondary prevention strategies aimed at early case identification and removal [Kreiss and Cox-Ganser 1997].

5.1.1.5 Summary

Until recently, all four of these diseases of the lung parenchyma (lipid pneumonia, hard metal disease, legionellosis, and HP) appeared to have been relatively unusual in workers exposed to MWF aerosols. However, these diseases have generally not been systematically studied among workers exposed to MWF aerosol, and the recent emergence of HP-like disease associated with MWF aerosol and the large numbers of workers exposed justify considerable concern [Blanc 1995; Kreiss and Cox-Ganser 1997]. It is possible that HP has been occurring in MWF-exposed workers for many years but has not been detected because HP is sometimes difficult to diagnosis and has only recently been targeted for study among workers exposed to MWF; however, it is also possible that recent changes in the work environment, fluid composition, or biocide use have increased the risk of HP among these workers [Kreiss and Cox-Ganser 1997].

Prevention depends on reducing and eliminating worker exposures to the causative agents. In the case of lipid pneumonia, no reliable quantitative exposure-response data are available, but the apparent rarity of the disorder among MWF-exposed workers suggests that current exposure concentrations are not generally associated with the disease. Prevention of hard metal disease depends largely on keeping exposures associated with operations involving tungsten carbide tools below the current NIOSH REL of 50 $\mu g/m^3$ for cobalt [NIOSH 1988a] (and perhaps limiting them to a concentration considerably lower than that REL) [Kennedy et al. 1995a]. The prevention of contamination of MWFs by *Legionella* spp. would eliminate legionellosis associated with occupational exposure to MWF aerosol. The specific etiologic agent(s) for HP among workers exposed to MWF aerosol remain(s) unknown. However, possible preventive approaches are the control of microbial growth, reformulation of MWFs to eliminate specific components (if any are identified as causative agents), and perhaps the general reduction of MWF aerosol exposures. Caution is warranted with regard to the use of biocide additives to control microbial growth in MWFs: Not only might the biocides be associated with toxic effects on workers who inhale MWF aerosol, but they might suppress the microorganisms that are more susceptible to biocide thereby allowing the overgrowth of less susceptible organisms that may cause HP [Kreiss and Cox-Ganser 1997].

5.1.2 Asthma and Other Disorders of the Pulmonary Airways

5.1.2.1 Background

Recent concerns about the respiratory hazards of occupational exposure to MWF aerosols have focused on airways disorders even more than on HP. A variety of components, additives, and contaminants of MWFs are sensitizers or irritants known to induce new-onset asthma, aggravate pre-existing asthma, and irritate the airways of nonasthmatic workers. These sensitizers, irritants, or toxicants include ethanolamine and other amines, colophony, pine oil, tall oil, metals and metallic salts (e.g., chromium, nickel, cobalt, and tungsten carbide), castor oil, formaldehyde, chlorine, various acids, and

fungal and other microbial contaminants (including gram-negative bacterial endotoxin) [Chan-Yeung and Malo 1993b; Hendy et al. 1985; Kennedy 1992; Michel et al. 1992]. However, only a few of these agents have been documented as causes of MWF-associated asthma.

Symptoms of airways irritation (e.g., cough) occur with sufficient exposure to airborne irritants. In addition to symptoms, the acute airways response to an inhaled irritant often involves short-term, apparently reversible decrements in measured pulmonary function. Repeated exposure to an irritant can evolve into chronic bronchitis, a condition characterized by chronic production of phlegm. Inflammation associated with chronic airways irritation may also cause accelerated decline in lung function, which can ultimately result in symptomatic functional impairment and pulmonary disability.

Asthma is an airways disease with a marked variability in airflow limitation. It can be induced by exposure to an immune sensitizer (classic immunologic asthma) or an irritant agent (irritant-induced asthma). Whether initially induced by a sensitizer or an irritant, symptomatic episodes of immunologic or irritant asthma can be triggered by subsequent exposure to the specific causative agent or any irritant, even at concentrations substantially lower than those tolerated by nonasthmatic persons. Clinical asthma spans a broad range of severity—from occasional mild symptoms to frequent, severe episodes requiring immediate medical attention and sometimes (though rarely) resulting in death. Increasing evidence suggests that worker's occupational asthma is more likely to become chronic (i.e., with irreversible airflow limitation and continuing airways hyperresponsiveness even after removal from exposure) the longer that worker continues to be exposed after onset of the asthma [Chan-Yeung and Malo 1995].

The remainder of this section on asthma and airways disorders reviews evidence relating MWF aerosol exposure to asthma, airways irritation and other respiratory symptoms, chronic obstructive pulmonary disease, and acute reductions in lung function.

5.1.2.2 Asthma

Case reports and observations from surveillance programs

Forbes and Markham [1967] reported two cases of work-related asthmatic illness in workers exposed to MWFs. Both workers (one a machinist using straight oil MWF and the other a hard-metal tool grinder using soluble oil MWF) experienced the onset of asthmatic symptoms while employed, and both experienced increased symptoms on exposure to MWF aerosol. No information was provided on levels of exposure.

Savonius et al. [1994] reported two metalworkers who, after several years of exposure, developed asthma attributed to TEA in the MWF they used. Exposure concentrations were not reported. Neither worker reacted to laboratory inhalation challenge with a MWF containing no TEA. But when challenged with stirred MWF containing TEA,

both workers showed substantial reductions in peak expiratory flow. Two other patients with hyperreactive airways did not respond to a similar inhalation challenge. On the basis of these findings, Savonius et al. [1994] concluded that exposure to TEA vapor may induce asthma. Note that the triggering of asthmatic reactions in these workers did not require exposure to the MWF in aerosol form.

Robertson et al. [1988] reported on 25 workers who were exposed to MWF aerosols and were referred to an occupational health clinic for evaluation of symptoms suggestive of occupational asthma. On the basis of serial peak flow monitoring, 20 of these workers were found to have either definite occupational asthma (i.e., work-related variation in peak flow of at least 20% in more than 75% of monitored workweeks) or equivocal occupational asthma (i.e., work-related variation in peak flow of at least 20% in 25% to 75% of monitored workweeks). The median latent period (i.e., from initial hire to first symptoms) among the 13 definite cases was 12 years (range was <1 to 41 years). One had worked only with straight oil MWF, nine had worked only with soluble oil MWF, two had worked with both straight and soluble oil MWFs, and one had worked with "various" MWFs. MWF aerosol exposure concentrations were not reported. Inhalation challenge testing carried out in 6 of these 13 definite cases resulted in clear-cut asthmatic reactions (maximum immediate or late FEV_1 [forced expiratory volume in 1 sec] reductions ranged from 17% to 42%) in four, and inconclusive reactions in the other two. One of the four with clear-cut reactions reacted to nebulized, used soluble oil MWF (which was microbially contaminated) but not to nebulized, unused (and therefore uncontaminated) soluble oil MWF. The other three reacted to challenge with fresh soluble oil MWF. Interestingly, one of these latter three cases (described in detail by Hendy et al. [1985]), reacted to volatiles from stirred (not nebulized) soluble oil MWFs, to volatiles from the pine oil reodorant contained in the soluble MWF, and to colophony (a related agent known to induce occupational asthma), which was a component of the emulsifier used in the soluble MWF. Further challenges with other constituents of the soluble oil MWF failed to identify any other specific agent(s) responsible for the asthmatic reaction in this individual.

Gannon and Burge [1991] examined data from a physician reporting system for occupational asthma in the West Midlands Region of England. They reported that MWF aerosols and machine tool operators were among the four most frequently implicated agents and occupations, respectively. They also estimated an annual incidence for occupational asthma of 36 per million among metal and electrical manufacturing and repair workers—compared with a rate of less than 12 per million in professional and clerical workers (suggesting a threefold relative risk [RR]). Gannon and Burge [1991] provided no estimates of exposure concentrations for identified cases.

An occupational respiratory disease surveillance program operating in the United Kingdom has provided additional evidence regarding the incidence of work-related asthma associated with MWF aerosols. In 1989, 7 reported cases of occupational asthma were

attributed to MWF exposure, and the estimated annual incidence of reported occupational asthma was approximately 250/million in the *metal making and treating* occupational group—25 times higher than the estimated annual incidence of less than 10/million for the *professional, managerial, clerical, and selling* occupational group [Meredith et al. 1991]. By the end of 1991, a total of 22 cases of MWF-associated occupational asthma were reported in that program [Merideth and McDonald 1994]. A total of 119 cases of occupational asthma—nearly 2% of the estimated cases for the 1989–1996 period in the United Kingdom—were attributed to "cutting oils" [Ross et al. 1997]. No exposure concentrations were provided in any of these surveillance reports.

An occupational asthma surveillance program in Michigan (Sentinel Event Notification System for Occupational Risks [SENSOR]) also provides evidence regarding asthma associated with exposure to MWF aerosol [Rosenman et al. 1995; 1997a,b]. MWFs are reported as the second most common cause of work-related asthma in Michigan, accounting for 13% (137 of 1,047) of the cases of occupational asthma reported during the period 1988–96 [Rosenman et al. 1997a]. Workers identified as cases worked at 54 different facilities, and the majority were employed in metal parts manufacturing. Seventy-five of the cases were employed in the automobile parts manufacturing industry [Rosenman et al. 1995]. Of 773 interviewed coworkers of the reported cases, 21% had developed (since hire) new asthma or new work-related symptoms consistent with occupational asthma (i.e., work-associated daily or weekly shortness of breath, wheezing, or chest tightness) [Rosenman et al. 1997b]. Of 113 coworkers interviewed at 6 facilities with measured MWF aerosol concentrations below 0.5 mg/m^3, 13 (11.5%) reported new onset asthma or symptoms consistent with asthma, compared with 34 of 145 (23.4%) at 7 facilities where measured MWF aerosol ranged from 0.5 to 1.0 mg/m^3, and 30 of 179 (16.8%) at 6 facilities where exposure concentrations were 1.0 mg/m^3 or higher [Rosenman et al. 1997b]. Limitations of these findings include (1) lack of information to enable any assessment of potential for participation bias, and (2) lack of exposure measurements for 13 other facilities where no air sampling was conducted because the industrial hygienist felt that the MWF aerosol concentration was well below the current PEL of 5 mg/m^3 for oil mist (but where 25% of 306 coworkers reported new-onset asthma and/or symptoms suggestive of work-related asthma).

Rosenman et al. [1997b] also found that new-onset asthma or symptoms suggestive of work-related asthma were reported by 10% (18 of 183) of coworkers in 10 facilities using only straight oil MWFs, 23% (27 of 115) of those in 7 facilities using soluble (and no synthetic or semisynthetic) MWFs, 28.6% (4 of 14) of those in 2 facilities using semisynthetic (and no synthetic) MWFs, and 25% (105/420) of those in 12 facilities using synthetic MWFs. Measures of association calculated from these data with this method of categorizing exposure by type of MWF include odds ratios (ORs) of 2.8 (95% confidence interval [CI] =1.4–5.7) for soluble MWFs, 2.9 (95% CI=0.8–14.5) for

semisynthetic MWFs, and 3.1 (95% CI=1.8–5.5) for synthetic MWFs relative to straight MWFs.

An additional eight cases of occupational asthma associated with exposure to MWFs have been reported in New Jersey and Massachusetts, the only other States that have had similar occupational asthma surveillance programs under development over the same period [SENSOR 1996; Reilly et al. 1994]. Also, six newly diagnosed cases of occupational asthma attributed to "cutting oils" were reported by several occupational medicine clinics to the AOEC Occupational and Environmental Disease Surveillance Data-base between 1991 and 1993 [Hunting et al. 1995].

The case reports and surveillance data summarized above provide minimal, if any, information about concentrations of MWF aerosol exposure and therefore cannot be used to define an exposure limit. But they do provide considerable evidence that MWF exposures are associated with the development of work-related asthma. They also provide limited evidence suggesting that risk is higher for soluble oil, semisynthetic, and synthetic MWFs compared with straight oil MWFs.

Research findings

In reevaluating a major cross-sectional respiratory morbidity study, Eisen [1995] described an inverse exposure-response relationship between the synthetic MWF aerosol exposure concentration and the prevalence of self-reported, physician-diagnosed asthma. Excluding those who had developed asthma before employment as a machinist, and using an analysis designed to control for transfer bias, Eisen demonstrated that the incident asthma cases were more than twice as likely as the nonasthmatic machinists to have been exposed to synthetic MWF aerosol in the year of asthma onset. She and her colleagues also observed indications of selective transfer of incident asthma cases away from jobs with exposure to synthetic MWFs ($P<0.10$) [Eisen 1995; Eisen and Greaves 1995]. More definitive analysis of this data by Eisen et al. [1997] is described in more detail below.

Greaves et al. [1995b, 1997] reported a comprehensive analysis of the data previously reported on by Eisen [1995]. Although there was no clear relationship between self-reported, physician-diagnosed asthma and current aerosol exposure concentrations of straight oil, soluble oil, or synthetic MWFs, the results of this analysis did suggest that cumulative exposure to soluble fluids was related to asthma among these workers. Controlling for age, race, smoking, plant, and grinding, past (cumulative) exposure to soluble MWF aerosol (thoracic fraction) was significantly associated with asthma (OR=1.02 per mg/m^3-year; $P<0.05$) despite a low OR for asthma among workers with current exposure to soluble MWFs (OR=0.6). These and related findings again suggest possible selective transfer of affected workers away from jobs with more intense exposure. Note that an OR of 1.02 per mg/m^3-year of exposure suggests a greater than two-fold risk of developing occupational asthma over a 45-year working lifetime of

exposure to MWF aerosol at 1 mg/m^3 (thoracic fraction). This may be an underestimate of effect, as only current workers were included in the study; workers who may have left these three plants as a result of their asthma would not have been included in the study.

Basing an analysis on the same population reported on previously by Greaves et al. [1995b], Eisen et al. [1997] used a cohort approach and proportional hazards model to evaluate the association of post-hire asthma to MWF aerosol exposures. Among 1,788 active workers (including assembly workers) in the analysis, 29 reported asthma initially diagnosed after hire. Based on MWF exposures during the 2-year period preceding diagnosis (to correlate with likely time of asthma onset), incidence rate ratios (RRs) were calculated. With adjustment for age and period of hire (before or after 1970), RRs were as follows: 2.0 (95% CI=0.9–4.6) for straight MWF; 0.5 (95% CI=0.2–1.1) for soluble MWF; and 3.2 (95% CI=1.2–8.3) for synthetic MWF. Aerosol exposures for the six asthmatics who worked with synthetic MWFs during the 2 years before diagnosis averaged 0.6 mg/m^3 (inhalable fraction); the range was 0.36 to 0.91 mg/m^3, and the median was 0.58 mg/m^3.

Kriebel et al. [1994, 1997] studied workers exposed to soluble oil MWFs (142 workers) and straight oil MWFs (74 workers) along with less exposed assembly workers in a major machine shop complex manufacturing automobile transmissions. These investigators found evidence for an association between self-reported physician-diagnosed asthma and work as a machinist. After controlling for age, race, gender, and smoking, machinists exposed to soluble oil MWF reported asthma twice as often as nonmachinists (OR=2.1; 95% CI=0.9–4.6; $P<0.10$); those exposed to straight MWF also reported more asthma (OR=1.4), but this latter finding was more likely than the former to be due to chance ($P>0.10$). In an analysis stratified by whether the asthma diagnosis predated employment as a machinist, Kriebel et al. [1994, 1997] found that the association was stronger for asthma with onset following employment than for asthma predating employment as a machinist. Aerosol exposure measurements were made using samplers with a seven-hole cassette inlet face selected to approximate collection efficiencies of the American Conference of Governmental Industrial Hygienists/International Standards Organization (ACGIH/ISO) size-selective criteria for inhalable mass [Kriebel et al. 1994]. At the time of the questionnaire survey, machinists at this facility who worked with straight oil MWF had a mean aerosol exposure of 0.24 mg/m^3 (inhalable fraction), and those who worked with soluble oil MWF had a mean exposure of 0.22 mg/m^3 (inhalable fraction).

Robins et al. [1997] provided relevant data from a study of machinists exposed to aerosols of soluble MWF and relatively unexposed assembly workers at an automotive transmission manufacturing plant. Among workers who reported not having pre-existing asthma, current asthma was reported and/or a clinically significant cross-shift FEV_1 decrement (of at least 12%) was experienced by 11 of 83 machinists compared with 3 of 44 assembly workers (calculated unadjusted OR=2.1; 95% CI=0.5–12.3).

Personal exposure measurements for the machinists observed to have cross-shift FEV_1 decrements of at least 12% ranged from 0.17 mg/m^3 to 0.82 mg/m^3, with a median just above 0.5 mg/m^3 (thoracic fraction).

Ameille et al. [1995] evaluated self-reported responses to the question "Have you ever had asthma?" from workers employed at a gear-box machining shop with at least 1 year of MWF exposure. Three currently exposed groups and one unexposed group were identified: 40 workers with exposure only to straight oil MWFs; 51 with exposure only to soluble oil MWFs; 139 with mixed exposure to both soluble and straight oil MWFs; and the unexposed group of 78 assembly workers. The four groups were similar with respect to smoking habits. The arithmetic mean exposure (measured as oil mist using a solvent extraction procedure) was 2.6 mg/m^3 (SD=1.8; geometric mean=2.2, geometric SD=1.9) in areas using straight oil MWFs. No sampling was done in areas using soluble MWFs. Currently exposed workers tended to be less likely to report asthma than assembly workers. Based on data provided by Ameille et al. [1995], calculated asthma ORs were 0.9 (0.26–3.34) for current exposure to straight oil MWFs and 0.8 (0.24–3.13) for current exposure to soluble oil MWFs compared with the unexposed assembly workers. Although these findings may indicate that there was no significant effect of exposure to MWF aerosol in this population, the authors presented evidence suggesting that affected workers (particularly from the subgroup currently exposed to soluble MWFs) may have left employment before the study was initiated (see next paragraph). Such selection, if it occurred, would likely have biased the measurement of any association between asthma and MWF aerosol exposure toward the null.

Ameille et al. [1995] found no significant differences in bronchial responsiveness between workers exposed to MWFs and comparison workers, or among subgroups of workers exposed to straight oil and/or soluble oil MWFs. However, the authors noted that prior self-selection away from exposure may have biased their findings: only 2 of 51 workers (4%) exposed to soluble oil MWFs alone over the previous 5 years had been excluded from methacholine testing because of impairment of baseline lung function—compared with 33 of 257 other study participants (13%) (P=0.07). Also, certain aspects of the methods used by Ameille et al. [1995] but not described in their published report may have influenced their findings (see below).

Massin et al. [1996] studied 114 male employees exposed to aerosol from soluble oil MWF in a ball-bearing plant and 55 unexposed workers in other plants in the same region of France. Geometric mean total aerosol concentrations in the machining areas of the ball-bearing plant (measured as dichloromethane-extractable oil) ranged from 65 mg/m^3 in more recent years to 2.20 mg/m^3 before 1990. Five of 113 exposed workers without prior asthma (compared with none of 53 unexposed workers without prior asthma) reported developing physician-diagnosed asthma after being hired at the ball-bearing plant (OR undefined).

Massin et al. [1996] also studied nonspecific airways responsiveness of these exposed and unexposed workers. Although methacholine challenge tests were positive in similar proportions of exposed (10 of 114) and unexposed (4 of 55) workers ($P>0.05$), the mean methacholine dose-response slope was significantly steeper among the exposed workers ($P=0.03$) after adjusting for age and baseline FEV_1. Furthermore, after adjustment for age and baseline FEV_1, slope was significantly related to cumulative exposure to MWF aerosol ($P=0.004$). Citing a personal communication from one of the coauthors of the Ameille et al. [1995] report, Massin et al. [1996] pointed out that similar results were found using the same methods applied to data for workers exposed to aerosol from soluble oil MWF in the study by Ameille et al. [1995]. This has been confirmed by authors of the Ameille et al. [1995] study [Wild and Ameille 1997].

In a prospective study of nonspecific bronchial responsiveness, Kennedy et al. [1995b] followed apprentices in metalworking and other trades over 2 years. Study subjects were nonasthmatic at the beginning of the study, and MWF exposures (total aerosol) in machine shops ranged from nondetectable to 3.65 mg/m^3 (mean 0.46 mg/m^3). Although no clinically obvious cases of asthma occurred in this group over the 2-year period of study, apprentices with at least 1,800 hr of exposure to MWFs were more likely to develop a marked increase in methacholine responsiveness over the period of observation compared with others with less exposure ($P<0.05$). In an analysis of all study subjects, increased bronchial responsiveness was positively associated with exposure to MWF [Kennedy et al. 1995b] and with development of work-related asthma symptoms (wheezing and chest tightness). Increased responsiveness was negatively associated with wearing respiratory protection at least some of the time ($P<0.05$) [Kennedy et al. 1995b]. Further followup of these study subjects is planned.

Summary

Considered in aggregate, the studies summarized above provide evidence indicative of an elevated risk of asthma among workers exposed to MWF aerosol exposure concentrations currently found in large metalworking shops. As suggested by published clinical case reports, asthma induced by MWFs appears to involve known sensitizers in some cases; but various other agents, possibly acting through irritant or inflammatory mechanisms, may be responsible for a high proportion of MWF-associated asthma cases. Table 5–1 presents selected risk estimates for asthma morbidity derived from these studies. Some evidence from cross-sectional studies strongly suggests a tendency for affected workers to transfer away from jobs with exposure to MWF.

With respect to MWF type, exposure to MWF aerosol in operations using synthetic MWFs has been associated with asthma. A State-based surveillance program received 44 reports of occupational asthma attributed to synthetic MWFs during the period 1988–94 [Rosenman et al. 1997b]; however, some of the plants where these cases were identified may also have been using other types of MWF. Also, occupational asthma has

been shown to be related to alkanolamine components commonly found in synthetic MWFs [Savonius et al. 1994]. The overall evidence from the recent research studies suggests an approximate twofold to threefold asthma risk among groups of machinists working with synthetic MWFs exposed to aerosol concentrations averaging from about 0.2 (inhalable fraction) to about 1 mg/m^3 (total oil mist). Elevated risk estimates were found in all three epidemiologic studies relevant to the association of asthma with exposure to synthetic MWF aerosol [Greaves et al. 1995b, 1997; Eisen et al. 1997; Rosenman et al. 1997b] (Table 5–1). One of these three studies had "mixed" results with respect to synthetic MWF aerosol exposure, but the findings were consistent with selection of affected workers away from the most hazardous exposure [Greaves et al. 1995b, 1997]. Findings consistent with a statistically significant, approximately threefold risk resulted from the other two studies—including the study by Eisen et al. [1997], which reanalyzed data from Greaves et al. [1995b] and took transfer bias into account. Estimated MWF aerosol exposures in the 2 years before asthma diagnosis ranged from about 0.4 to 0.9 mg/m^3 (inhalable fraction), with a mean of 0.6 mg/m^3 [Eisen et al. 1997].

Although the evidence suggesting a causal association between asthma and exposure to soluble MWF aerosol is in some ways less consistent than that for synthetic MWF exposures, there have been more studies about the relationship between asthma and exposure to soluble oil MWF aerosol. Case reports have documented asthma caused by exposure to soluble oil MWF [Hendy et al. 1985; Robertson et al. 1988] or to common components of soluble oil MWFs [Savonius 1994]. A surveillance program in Michigan received 13 case reports of occupational asthma attributed to soluble oil MWFs during 1988–94 [Rosenman et al. 1997b], although some of the plants in which these cases worked may have also been using straight oil MWF. Of the seven relevant epidemiologic studies, results consistent with statistically significant elevated risk estimates were presented only by Greaves et al. [1995b, 1997] (for cumulative exposure) and Rosenman et al. [1997b]. Findings of three of the other five studies indicated elevated, though not statistically significant, risk estimates for asthma, with point estimates ranging upward from 2.1 [Kriebel et al. 1994, 1997; Robins et al. 1994, 1997; Massin et al. 1996]. In two studies [Ameille et al. 1995; Eisen et al. 1997], the risk estimates associated with soluble MWF aerosol were less than 1. However, Ameille et al. [1995] found evidence suggesting that affected workers had transferred out of jobs with exposure to soluble MWF aerosol. Such job transfer may have biased findings from that study, and the apparently negative finding of Eisen et al. [1997] must be tempered by a statistically significant positive association between asthma and cumulative exposure to soluble MWF aerosol in the same study group [Greaves et al. 1995b, 1997]. In addition, data from both the Ameille et al. [1995] and the Massin et al. [1996] studies indicated a positive association between increased bronchial responsiveness and cumulative exposure to soluble MWF aerosol [Massin et al. 1996]. Overall, the preponderance of evidence from all these studies indicates that both airways hyperresponsiveness and asthma are associated with exposure to soluble MWF aerosol. The two European

Table 5–1. Estimated risk of asthma associated with MWF aerosol exposure

Study	Population	Fluid class	Aerosol exposure concentration	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value*
Surveillance studies:					
Gannon and Burge 1991	Metal and electrical workers	—	—	—	>3-fold incidence rate (relative to professional/clerical workers [i.e., 36/million versus <10/million])
Meredith et al. 1991	Metal making and treating	—	—	14/56,270	25-fold annual incidence rate (relative to professional/clerical/ selling workers)
Cross-sectional studies:					
Ameille et al. 1995	Automobile parts manufacture	Straight Soluble	Current mean: 2.6 mg/m^3 (SD=1.8) (extractable oil mist)	10/179 (6%) 10/190 (5%) (groups overlap)	OR=0.9 (0.3–3.3) OR=0.8 (0.2–3.1) (relative to assembly) (evidence suggests transfer bias)
Eisen et al. 1997†	Automobile parts manufacture	Straight Soluble Synthetic	See text.	See text.	Incidence RR=2.0 (0.9–4.6) Incidence RR=0.5 (0.2–1.1) Incidence RR=3.2 (1.2–8.3) (relative to assembly or otherwise unexposed for 2-year period before onset, adjusted for period of hire)

See footnotes at end of table.

(Continued)

Table 5–1 (Continued). Estimated risk of asthma associated with MWF aerosol exposure

Study	Population	Fluid class	Aerosol exposure concentration	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value
Cross-sectional studies (continued):					
Greaves et al. 1995b, 1997	Automobile parts manufacture	Straight Soluble Synthetic	Current mean: 0.43 mg/m^3 (SD=0.3) 0.55 mg/m^3 (SD=0.2) 0.41 mg/m^3 (SD=0.1) (thoracic fraction)	 21/364 (6%) 25/452 (6%) 13/226 (6%)	 OR=1.0 (*P*>0.10) OR=0.8 (*P*>0.10) OR=0.8 (*P*>0.10) (evidence of transfer)
			Cumulative: Straight Soluble Synthetic		At 1 mg/m^3 (thoracic fraction) for 45 years: OR=0.6 (*P*>0.10) OR=2.4 (*P*<0.05) OR=2.4 (*P*>0.10)
Kriebel et al. 1994	Automobile parts manufacture	Straight Soluble	Current mean: 0.24 mg/m^3 (SD=0.3) 0.22 mg/m^3 (SD=0.3) (inhalable fraction)	 6/74 (8%) 17/142 (12%)	 OR=1.4 (*P*>0.10) OR=2.1 (0.9–4.6) (relative to assembly)
Massin et al. 1996	Ball-bearing manufacture	Soluble	Current mean (geometric): 1.49 mg/m^3 in cutting area 0.65 mg/m^3 in machining area Past means (geometric): 1.49 mg/m^3 in cutting area 2.20 mg/m^3 in machining area (total extractable-oil aerosol)	 0/53 (0%) (unexposed) 5/113 (4%) (exposed) (post-hire onset among workers without prior asthma)	 OR undefined (exposed relative to unexposed)

See footnotes at end of table.

(Continued)

Table 5–1 (Continued). Estimated risk of asthma associated with MWF aerosol exposure

Study	Population	Fluid class	Aerosol exposure concentration	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value
Cross-sectional studies (continued):					
Robins et al. 1997	Automobile parts manufacture	Soluble	Current mean: 0.44 mg/m^3 (thoracic fraction)	11/83 (13%) (suspect OA)	OR=2.1 (0.5–12.3) (relative to assembly)
Rosenman et al. 1997b	Automobile parts manufacture	Straight	Generally <1.0 mg/m^3	18/183 (10%)	OR=2.8 (1.4–5.7)
		Soluble	Generally <1.0 mg/m^3	27/115 (23%)	OR=2.9 (0.8–14.3)
		Semisynthetic	Generally <1.0 mg/m^3	4/14 (29%)	OR=3.1 (1.8–5.5)
		Synthetic	Generally <1.0 mg/m^3 (oil mist)	105/420 (25%) (suspect OA)	(relative to straight MWF exposure)

*Abbreviations: CI = confidence interval, OA=occupational asthma, OR=odds ratio, RR= rate ratio, SD=standard deviation.

†Analyzed using a cohort approach and proportional hazards model.

studies [Ameille et al. 1995; Massin et al. 1996] reported current mean soluble MWF aerosol exposures ranging from about 0.7 to 2.5 mg/m^3 (total *extractable* oil mist); the U.S. studies reported mean soluble MWF aerosol ranging from about 0.2 (inhalable fraction) [Kriebel et al. 1994, 1997] to about 0.6 mg/m^3 (thoracic fraction) [Greaves et al. 1995b, 1997]. In the other study (for which mean exposures were not reported), most of the air samples taken yielded measurements of less than 1.0 mg/m^3 oil mist [Rosenman et al. 1997b].

The overall evidence also suggests an association between asthma and exposure to straight oil MWF aerosol. A State-based surveillance program received 17 reports of occupational asthma attributed to exposure to straight oil MWFs from the period 1988–94 [Rosenman 1997b]. Furthermore, Rosenman [1997b] found that workers exposed to straight oil MWF aerosol (at plants from which occupational asthma cases had been reported) had a 10% prevalence of new asthma since hire or new work-related symptoms consistent with work-related asthma. For two other studies, the point estimate for risk was elevated (though not statistically significant) [Eisen et al. 1997; Kriebel et al. 1994]. Also, clinical case reports suggest that asthma may be associated with exposure to straight oil MWF aerosol [Forbes and Markham 1967; Robertson et al. 1988] or to compounds commonly found in straight oil MWFs (e.g., TEAs) [Savonius 1994].

Available exposure data have been measured as TWAs over several hours, approximating the duration of a work shift. These measurements do not permit analyses to evaluate the possibility that occasional peak exposures (of relatively high concentration but lasting only a few minutes) may be required to induce MWF-associated airways hyperresponsiveness or clinical asthma. Clinical inhalation challenge studies indicate that in some affected workers, vapor (of MWF components) can trigger asthmatic reactions, even in the absence of aerosol exposure.

5.1.2.3 Symptoms of Airways Disorders

Study findings

Ely et al. [1970] investigated prevalences of cough, phlegm, dyspnea, and wheeze in a cross-sectional study of more than 1,700 plant workers, including 242 "machine hands" primarily exposed to mists from straight oil MWF. Oil mist concentrations were measured with a high-volume air sampler during the period 1955–70. Concentrations ranged from 0.07 to 110.0 mg/m^3 (median=1.0; mean=5.2 mg/m^3). In a multiple regression analysis involving only the exposed group of workers and employing variables such as age and smoking history correlated with job tenure, Ely et al. [1970] found no significant associations between years on the job and symptoms. The investigators did not comment on their finding that none of 49 exposed nonsmokers reported wheezing, versus 6.5% (26/400) of unexposed nonsmokers. One possible explanation for this

observation would be that workers adversely affected by exposure to MWFs may have tended to transfer away from jobs with exposure.

Krzesniak et al. [1981] used a cross-sectional design to compare 531 workers exposed to oil mist in machining operations in a tractor factory with 245 office workers in the same factory. Twenty-four percent of the exposed group and 42% of the comparison group were female, though the two groups did not significantly differ with respect to smoking prevalence. Duration of exposure ranged from 1 to 20 years. The concentration of oil mist exposure ranged between 5 and 99.5 mg/m^3, although MWF classes were not identified, nor were details provided on exposure measurement methods. Compared with unexposed workers, exposed workers reported significantly increased prevalences of cough and phlegm (38.8% versus 17.9%; $P<0.05$) and dyspnea (27.8% versus 9.4%; $P<0.01$). Approximate unadjusted ORs for exposure to oil mist calculated from the data are 2.9 (95% CI=1.98–4.29) for cough and phlegm and 3.7 (2.31–6.25) for dyspnea.

Järvholm et al. [1982] used a cross-sectional design to compare symptoms reported by 164 metal workers exposed for at least 3 years to straight and soluble oil MWFs with those reported by 159 office workers. MWF aerosol exposure concentrations ranged from 0.3 to 18.0 mg/m^3, with median exposures in the five departments studied ranging from 1.1 to 4.5 mg/m^3. The four symptoms that questions assessed were the following: usual cough; usual cough for at least 3 months each year; usual phlegm; and usual phlegm for at least 3 months each year. After controlling for age and smoking, a statistically significant relationship was observed between exposure and reporting of at least one respiratory symptom ($P<0.0001$). Adjusted for age and smoking, the 30-to 65-year-old metalworkers reported more chronic cough (RR=2.8; 95% CI=1.3–6.2) and chronic phlegm (RR= 2.2; 95% CI=1.2–3.9) than the comparison group of office workers. In a related 3-year followup survey of workers who had been asymptomatic at the time of this initial survey, Järvholm [1982] found that exposed workers tended to be more likely than controls to have developed new respiratory symptoms ($P<0.10$). The data provided allow calculation of an unadjusted relative risk of 4.9 (95% CI=0.7–34.2) associated with exposure.

Oxhoj et al. [1982] studied 385 machine shop workers exposed to straight, soluble, semisynthetic, or synthetic MWFs in 27 different facilities. Measured oil aerosol concentrations in these facilities ranged from 0.1 to 2.0 mg/m^3 (median 0.35 mg/m^3). Among smokers, workers with oil aerosol exposures exceeding 0.1 mg/m^3 had significantly higher prevalences of chronic cough (32% versus 18%; $P<0.05$) and chronic phlegm (25% versus 11%; $P<0.05$) than workers with lower exposure to oil aerosol. No symptom differences were reported for various MWF classes. No significant differences in symptom prevalences associated with differences in aerosol concentration were identified among nonsmokers. Likewise, no prevalence differences associated with oil vapor, nitrites, or amines were identified.

Ameille et al. [1995] evaluated chronic respiratory symptoms among workers in a French automobile manufacturing plant. All exposed workers in a gear-box machining shop had at least 1 year of exposure to MWFs. On the basis of exposure during the most recent 5 years, three exposed groups and one unexposed group were defined: 40 workers with exposure to straight oil MWFs only; 51 with exposure to soluble MWFs only; 139 with mixed exposure to soluble and straight oil MWFs; and 78 assembly workers. In areas using straight oil MWFs, the arithmetic mean exposure was 2.6 mg/m^3 (SD=1.8; geometric mean=2.2; geometric SD=1.9). No sampling was done in areas using soluble oil MWFs. The four groups were similar with respect to smoking habits. Symptoms assessed were chronic cough, chronic expectoration, and dyspnea. Those currently exposed to straight oil MWFs had a significantly higher prevalence of chronic cough and/or chronic phlegm (25.7% versus 16.3%; $P<0.05$) as well as a higher prevalence of dyspnea (5.0% versus 2.3%). After controlling for smoking, a statistically significant increased risk of chronic cough was observed with increasing duration of exposure to straight oil MWFs ($P=0.03$). Adjusted for smoking, the OR for chronic cough among those with more than 15 years of exposure to straight oil MWFs was 2.2 (95% CI=1.01–4.85) relative to unexposed assembly workers. Although no statistically significant respiratory symptom findings were reported for workers currently exposed to soluble MWF, point estimates for ORs calculated from data presented in the report were elevated for both dyspnea (OR=1.2; 95% CI=0.2–12.8) and for chronic cough and phlegm (OR=1.2; 95% CI=0.6–2.1). Ameille et al. [1995] provided evidence suggesting that affected workers may have self-selected away from jobs with exposure to soluble oil MWF, which would have the effect of biasing these ORs downward.

Greaves et al. [1993, 1995b, 1997] reported results from a cross-sectional respiratory morbidity study of 1,811 automobile parts (transmission, axle, steering gear) manufacturing workers exposed to three classes of MWF (straight oil, soluble oil, and synthetic) in three plants. Prevalences of respiratory symptoms in 1,042 machining and grinding operators were compared with those among 769 assemblers, only 239 of whom had no history of MWF exposures. Mean current exposures to aerosol (thoracic fraction) from straight oil, soluble oil, and synthetic MWFs were 0.43 (SD=0.26), 0.55 (SD=0.17), and 0.41 (SD=0.08) mg/m^3, respectively. Logistic regression analyses were controlled for smoking, race, age, plant, and whether the worker was employed in grinding operations.

Compared with all assembly workers, Greaves et al. [1995b, 1997] found that machinists more frequently reported all previously described respiratory symptoms, including usual cough (OR=1.4; $P<0.05$), usual phlegm (OR=1.6; $P<0.001$), symptoms of chronic bronchitis (OR=1.5, $P<0.05$), and wheezing on most days (OR=1.3, $P<0.05$).

Individual quantitative concentration of current exposure to MWF aerosol was significantly associated in an exposure-related manner with usual cough (OR=2.0 per mg/m^3; $P<0.05$), usual phlegm (OR=3.1 per mg/m^3; $P<0.05$), symptoms of chronic bronchitis (OR=2.6 per mg/m^3; $P<0.05$), and wheezing most days (OR=2.3 per mg/m^3; $P<0.05$).

Machinists *currently* exposed to aerosol from straight oils were more likely than assembly workers to report usual cough (OR=1.5; $P<0.05$), usual phlegm (OR=1.7; $P<0.05$), wheeze on most days (OR=1.5; $P<0.05$), and symptoms of chronic bronchitis (OR=1.6; $P<0.10$) [Greaves et al. 1995b, 1997]. Based on reported symptoms among three subgroups of these machinists (grouped by exposure concentration) and among assembly workers, trend analyses indicated significant exposure-related increases (per mg/m^3 straight oil MWF aerosol) in usual phlegm (OR=2.2 per mg/m^3; $P<0.05$) and wheeze on most days (OR=2.2 per mg/m^3; $P<0.05$), and exposure-related increase in grade 2 dyspnea (OR=2.3 per mg/m^3; $P=0.06$). Individual quantitative concentration of current exposure to straight oil MWF aerosols was associated with usual phlegm (OR=2.8 per mg/m^3; $P<0.05$) and with wheezing most days (OR=2.1 per mg/m^3; $P<0.10$) [Greaves et al. 1995b].

Machinists currently exposed to soluble oil MWFs at aerosol concentrations exceeding 0.65 mg/m^3 (thoracic fraction) had statistically significant excesses in usual cough (OR=2.0; $P<0.05$) [Greaves et al. 1995b] and chest tightness at least once per week (OR=2.1; $P<0.05$). Exposure-related trend ORs exceeded 1.0 but were not statistically significant, and current exposure to soluble oil MWF aerosols below 0.65 mg/m^3 were not significantly associated with respiratory symptoms. Individual quantitative concentration of current exposure to aerosol of soluble oil MWF was not significantly associated with any of the studied symptoms [Greaves et al. 1995b].

The highest prevalences of respiratory symptoms were observed among machinists currently exposed to synthetic MWFs, who were more likely to report usual cough (OR=1.6, $P<0.01$), usual phlegm (OR=2.1, $P<0.001$), symptoms of chronic bronchitis (OR=1.6; $P<0.10$), wheezing on most days (OR=1.7; $P<0.05$), and chest tightness at least once per week (OR=1.7; $P<0.05$) [Greaves et al. 1995b, 1997]. Based on reported symptoms among three subgroups of these machinists (grouped by aerosol exposure concentration) and among assembly workers, trend analyses indicated significant exposure-related increases (per mg/m^3 synthetic MWF aerosol) in usual cough (OR=4.8 per mg/m^3; $P<0.01$), usual phlegm (OR=7.3 per mg/m^3; $P<0.001$), symptoms of chronic bronchitis (OR=3.5 per mg/m^3; $P<0.05$), wheezing on most days (OR=4.9 per mg/m^3; $P<0.01$), and chest tightness at least once per week (OR=3.9 per mg/m^3; $P<0.01$). Increased usual phlegm (OR=3.1; $P<0.001$) and symptoms of chronic bronchitis (OR=1.8; $P<0.05$) were observed even among the subgroup of workers with lowest current synthetic MWF aerosol exposure (below 0.4 mg/m^3) [Greaves et al. 1995b]. Individual quantitative concentration of current exposure to synthetic MWF aerosol was significantly associated with usual phlegm (OR=10.6 per mg/m^3; $P<0.05$), symptoms of chronic bronchitis (OR=4.4; $P<0.05$), and wheezing most days (OR=4.8; $P<0.05$) [Greaves et al. 1995b, 1997].

Many of the ORs reported above by Greaves et al. [1995b, 1997] may underestimate the true association between MWF aerosol exposure and symptoms because the commonly

used reference group of assembly workers included a majority who had past MWF aerosol exposures. In fact, in further analyses that excluded assembly workers who had past MWF aerosol exposure, Greaves et al. [1995b] found generally higher ORs. Greaves et al. [1995b, 1997] also found that a substantial proportion of the machinists reported improvement in symptoms when away from work, regardless of MWF exposure (though this was more common among machinists exposed to synthetic MWF aerosols).

Greaves et al. [1995b] also analyzed reported symptoms based on *ever* having been exposed to MWFs, both overall and by MWF class. Again, machinists ever exposed to any MWFs more frequently reported usual cough (OR=1.6; $P<0.01$) and usual phlegm (OR=1.9; $P<0.001$) [Greaves et al. 1995b].

Machinists ever exposed to aerosols from straight oil MWFs were more likely than assembly workers to report all respiratory symptoms, including usual cough (OR=1.5; $P<0.10$), usual phlegm (OR=2.2; $P<0.001$), and wheeze most days (OR=1.4; $P<0.10$) [Greaves et al. 1995b]. Based on symptoms among three subgroups of these machinists (grouped by cumulative exposure concentration) and among never-exposed assembly workers, trend analyses indicated statistically significant exposure-related increases in grade 2 dyspnea (OR=1.1 per mg/m^3-year; $P<0.05$) [Greaves et al. 1995b, 1997].

Machinists ever exposed to soluble MWF aerosols more frequently reported all respiratory symptoms, including usual cough (OR=1.5; $P<0.05$), usual phlegm (OR=1.8; $P<0.001$), and grade 2 dyspnea (OR=1.7; $P<0.10$). Even those machinists ever exposed to soluble fluids at cumulative aerosol concentrations below 0.71 mg/m^3-years had statistically significant excesses in usual cough (OR=1.6; $P<0.05$), usual phlegm (OR=1.7; $P<0.05$), and grade 2 dyspnea (OR=1.9; $P<0.05$), but ORs for exposure-related trends were not statistically significant [Greaves et al. 1995b].

Machinists ever exposed to synthetic MWF aerosols were similarly more likely than never-exposed assembly workers to report all respiratory symptoms, including usual phlegm (OR=2.2, $P<0.001$) and grade 2 dyspnea (OR=2.2; $P<0.10$) [Greaves et al. 1995b]. Interestingly, based on reported symptoms among three subgroups of these machinists (grouped by cumulative exposure level) and among assembly workers, trend analyses indicated exposure-related declines in usual phlegm (OR=0.9 per mg/m^3-year; $P<0.05$) and symptoms of chronic bronchitis (OR=0.9 per mg/m^3-year; $P<0.10$), per mg/m^3 synthetic MWF aerosol [Greaves et al. 1995b, 1997]. The investigators suggested that these findings of inverse exposure-response relationship could be explained by selective transfer bias, discussed above with respect to physician-diagnosed asthma in this same population [Eisen 1995; Eisen and Greaves 1995; Eisen et al. 1997].

Based on an analysis of each worker's individual quantitative concentrations of both current and past exposures to each MWF class (straight oil, soluble oil, and synthetic), Greaves et al. [1995b] concluded that past and current exposures to straight oil, soluble

oil, and synthetic MWFs are all related to respiratory symptom prevalence, and that current exposure concentrations appear to be the major determinants of respiratory symptoms. Greaves et al. [1995b, 1997] represents the most comprehensive assessment to date of respiratory symptoms among workers exposed to MWF aerosols. Nevertheless, findings from the study remain somewhat limited by the cross-sectional nature of the study, primarily because it is subject to selection effects.

In another cross-sectional study, Kriebel et al. [1994] studied 216 automotive parts manufacturing workers exposed to straight and soluble oil MWFs in one machine shop compared with 170 assembly workers. The studied shop manufactured specialty transmissions using machine tools, most of which had individual MWF sumps. Average aerosol exposures (inhalable fraction) were 0.24 mg/m^3 (SD=0.27) among workers exposed to straight MWFs, 0.22 mg/m^3 (SD=0.26) among workers exposed to soluble MWFs, 0.08 mg/m^3 (SD=0.05) among assembly workers, and 0.03 mg/m^3 (SD=0.03) among classroom/office workers. After controlling for age, race, gender, and smoking, the investigators found that machinists exposed to straight oil MWFs reported cough almost three times more often (OR=2.9; 95% CI=1.2–6.7) and sinus problems almost twice as often (OR=1.7; 95% CI=0.96–3.0) as the comparison workers. Also, machinists exposed to soluble oil MWFs were more likely than those exposed to straight oil MWFs to report an increase in eye, nose, and throat irritation over the course of the workday (P<0.01). In addition, machinists whose MWF sump had not been refilled during the 3 weeks before the symptom survey were more likely to report cough than those whose sump had been changed within the last 3 days (OR=5.6; 95% CI=4.3–6.9).

Robins et al. [1994, 1997] compared respiratory symptoms among machinists exposed to soluble MWF in an automobile transmission manufacturing plant (mean personal aerosol exposure of 0.44 mg/m^3 [thoracic fraction]) and among assemblers working in an area that was physically isolated from the machining operations. In each of three temporally separated rounds of the study, symptoms were reported by a higher proportion of exposed machinists. The differences were statistically significant for phlegm (OR=3.1; P=0.012) and chronic bronchitis (OR=6.8; P=0.04) in Round 1 [Robins et al. 1997] and for wheezing with dyspnea (OR=4.9; P=0.03) in Round 2 [Robins et al. 1994]. In addition, machinists were about 3 times more likely to develop at least one respiratory symptom (dry cough, cough with phlegm, wheezing, chest tightness or dyspnea) during their Monday shift than were assemblers (P=0.012) [Robins et al. 1994, 1997].

In a study of 114 workers exposed to aerosol from soluble MWF in a ball-bearing plant and 55 unexposed workers from other plants in the same region of France, Massin et al. [1996] found that prevalences of chronic bronchitis, chronic phlegm, chronic cough, and bouts of bronchitis were three to nine times higher in the exposed workers than in unexposed. Adjusting for age and smoking, the higher prevalence of chronic cough or chronic phlegm was statistically significant (adjusted OR=4.90; P=0.002). Likewise,

after adjusting for age and smoking, dyspnea was found to be significantly related to cumulative MWF aerosol exposure (P=0.006). Exposures were measured in terms of total extractable oil mist, and work area geometric mean concentrations ranged from 0.65 to 2.20 mg/m^3.

Sprince et al. [1997] studied symptom prevalence among machine operators (n=183) and unexposed assembly workers (n=66) in an automobile transmission parts manufacturing plant. Machine operators were exposed to one of two types of soluble oil MWF or to a semisynthetic MWF. Geometric mean total aerosol exposures were 0.33 mg/m^3 (range 0.04–1.44 mg/m^3) for machine operators and 0.08 mg/m^3 (range 0.02–0.20 mg/m^3) for assembly workers, as measured by MiniRAMs gravimetrically calibrated to Arizona road dust. (Because these instruments work on the principle of real-time light scattering, they indirectly measure all components of the aerosol, including water and other volatile components. In this regard, these aerosol concentrations are not comparable with those measured with standard filter methods, which do not include volatile components of the aerosol.) Exposure concentrations were very similar for each of the three types of MWFs. Adjusted for smoking, sex, race, and age, machine operators reported significantly more usual cough (OR=3.1; 95% CI=1.4–6.9), usual phlegm (OR=3.1; 95% CI=1.6–6.1), and chest-tightness temporally related to work (OR=5.9; 95% CI=1.4–25.7). Total aerosol exposure-response relationships were positive and statistically significant for both usual cough and usual phlegm. In addition, with respect to symptoms developing during the studied work shift, total MWF aerosol exposure-response relationships were observed for cough and throat irritation. Adjusted ORs for these symptoms were 5.3 (95% CI=1.3–21.8) and 5.1 (1.5–17.5), respectively, for the highest exposure quartile [Sprince et al. 1997].

Rosenman et al. [1997b] reported results of symptom questionnaires administered to coworkers of workers reported as cases of MWF-associated occupational asthma in Michigan. Coworkers reported frequent work-related cough, regardless of the MWF type used: 27 (14.8%) of those exposed to straight oil MWFs; 21 (19.3%) of those exposed to soluble oil MWFs; 4 (28.6%) of those exposed to semisynthetic MWFs; and 90 (21.4%) of those exposed to synthetic MWFs.

Summary

With the exception of one early study [Ely 1970], epidemiological studies of respiratory symptoms present generally consistent and (in the case of the more recent studies) compelling epidemiologic evidence indicating that occupational exposure to MWF aerosols causes symptoms consistent with airways irritation, chronic bronchitis, and asthma. The evidence suggests that each class of MWFs (straight oil, soluble oil, and synthetic) is capable of inducing respiratory symptoms at MWF aerosol exposure concentrations that are currently typical of large metalworking shops. To date, there is no convincing evidence that identifies any particular component or components of MWF aerosol as the

predominant cause of these symptoms, although some irritant components of MWF are clearly suspect [Sprince et al. 1997]. Table 5–2 summarizes selected risk estimates, reflecting roughly a twofold to sevenfold increased risk for various respiratory symptoms associated with mean aerosol exposures ranging from 0.22 mg/m^3 (inhalable fraction) to 0.55 mg/m^3 (thoracic fraction) among groups of workers exposed to MWFs. Also, one of these recent U.S. studies (a very large multiplant study with mean exposures for the major types of MWFs ranging from 0.41 to 0.55 mg/m^3 [thoracic fraction], found statistically significant quantitative exposure-response relationships between cumulative concentration of MWF aerosols and respiratory symptoms [Greaves et al. 1995b, 1997]. Likewise, another U.S. study found significant exposure-response relationships between aerosol exposure concentration and chest symptoms [Sprince et al. 1997]. In addition, the onset or worsening of many symptoms over a work shift [Kriebel et al. 1994; Sprince et al. 1997; Rosenman et al. 1997b], and the reported substantial symptomatic improvement experienced by many affected workers when away from work [Greaves et al. 1995b, 1997] suggests that controlling worker exposures can prevent chronic effects induced by MWF aerosol exposure and for reversing early MWF-induced airways effects, through control of worker exposure to MWF aerosol.

5.1.2.4 Cross-Sectional Studies of Lung Function

Study findings

Ely et al. [1970] published the first report regarding pulmonary function among workers occupationally exposed to MWF aerosol, primarily mineral oil aerosol at the following concentrations: median, 1.0 mg/m^3; mean, 5.2 mg/m^3; range, 0.07–110.0 mg/m^3, as measured by a high-volume sampler. Tenure for the 242 exposed workers ranged from less than 1 to 38 years. After adjustment for cigarette smoking (in terms of both cigarette years and smoking years), salary grade, and other factors, the number of years on the job was not a statistically significant independent predictor for either forced vital capacity (FVC) or FEV_1. Beyond issues of possible exposure misclassification resulting from the use of job tenure as a surrogate for exposure, lack of unexposed controls, small numbers, and limitations of cross-sectional studies in general, the authors pointed out that several factors included in the statistical model were correlated with job tenure. They appropriately cautioned that "when predictors are correlated, one is unable to place any interpretation on the coefficients in the regression equation" [Ely et al. 1970]. The negative pulmonary function findings of this study are therefore not compelling as evidence against an adverse effect of occupational exposure to MWF aerosol.

Järvholm et al. [1982] measured spirometry in a cross-sectional study of 164 metal workers exposed for at least 3 years to straight and soluble oil MWFs and in 159 office workers. MWF aerosol exposure concentrations ranged from 0.3 to 18.0 mg/m^3 (oil mist), with median exposures in the five areas studied ranging from 1.1 to 4.5 mg/m^3. A multivariate analysis stratified by smoking status and controlled for age and height

Table 5–2. Estimated risk of respiratory symptoms associated with MWF exposures

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value*
Cross-sectional studies:						
Ameille et al. 1995	Automobile parts manufacture	Straight	2.6 mg/m^3 (SD=1.8) (oil mist)	Chronic cough/phlegm	46/179 (26%)	OR=1.6 (0.8–3.3)
				Dyspnea	9/179 (5%)	OR=2.0 (0.4–19.5) (relative to assembly)
				Chronic cough		OR=2.2 (1.0–4.9) (>15 years of exposure to straight oil MWF, relative to 0 years, adjusted for smoking)
		Soluble	Not measured	Chronic cough/phlegm	43/190 (23%)	OR=1.2 (0.6–2.1)
				Dyspnea	6/190 (3%)	OR=1.2 (0.2–12.8) (relative to assembly)
Greaves et al. 1995b, 1997	Automobile parts manufacture	All types (aggregated)	Current mean (thoracic fraction)	Usual cough	268/1042 (26%)	OR=1.4 (P<0.05)
				Usual phlegm	269/1042 (26%)	OR=1.6 (P<0.001)
				Wheeze most days	246/1042 (24%)	OR=1.3 (P<0.05)
				Chronic bronchitis	138/1042 (13%)	OR=1.5 (P<0.05) (relative to all assembly workers)
		Straight	0.43 mg/m^3 (SD=0.3)	Usual phlegm	89/364 (24%)	OR=2.2 per mg/m^3 (P<0.05)
				Wheeze most days	89/364 (24%)	OR=2.2 per mg/m^3 (P<0.05)
				Dyspnea	49/364 (13%)	OR=2.3 per mg/m^3 (P=0.06)
		Soluble	0.55 mg/m^3 (SD=0.2)	Usual cough	96/452 (21%)	OR=2.0 (P<0.05)
				Chest tightness	72/452 (16%)	OR=2.1 (P<0.05) (>0.65 mg/m^3 relative to assembly)

See footnotes at end of table.

(Continued)

Table 5–2 (Continued). Estimated risk of respiratory symptoms associated with MWF exposures

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value
Cross-sectional studies (continued):						
Greaves et al. 1995b (continued)		Synthetic	0.41 mg/m^3 (SD=0.1)	Usual cough Usual phlegm Chronic bronchitis Wheeze most days Chest tightness	76/226 (34%) 79/226 (35%) 38/226 (17%) 81/226 (36%) 45/226 (20%)	OR=4.8 per mg/m^3 (P<0.01) OR=7.3 per mg/m^3 (P<0.001) OR=3.5 per mg/m^3 (P<0.05) OR=4.9 per mg/m^3 (P<0.01) OR=3.9 per mg/m^3 (P<0.01) (All above ORs are adjusted for age, race, sex, grinding, and plant. See text for additional risk estimates, including quantitative risk estimates for cumulative exposure to MWF aerosols.)
Järvholm et al. 1982	Bearing ring manufacture	Straight plus soluble	Range: 0.3–18.0 mg/m^3 department-specific Medians: ranged from 1.1 to 4.5 mg/m^3 (oil mist)	Chronic cough Chronic phlegm	13/110 (12%) 22/110 (20%)	RR=2.8 (1.3–6.2) RR=2.2 (1.2–3.9) relative to unexposed)

See footnotes at end of table.

(Continued)

Table 5–2 (Continued). Estimated risk of respiratory symptoms associated with MWF exposures

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value
Kriebel et al. 1994	Automobile parts manufacture		Current mean (inhalable fraction):			
		Straight	0.24 mg/m^3 (SD=0.3)	Cough	(19%)	OR=2.9 (1.2–6.7)
				Sinus problems	(51%)	OR=1.7 (1.0–3.0) (relative to assemblers; controlled for age, race, smoking)
		Soluble	0.22 mg/m^3 (SD=0.3)	Acute eye, nose, and throat irritation	(10%–19%)	(*P*<0.01) (compared to straight)
Krzesniak et al. 1981	Tractor parts manufacture	Not specified	Range: 5–99.5 mg/m^3 (oil mist)	Cough and phlegm	206/531 (38.8%)	OR=2.9 (2.0–4.3)
				Dyspnea	44/245 (17.9%)	OR=3.7 (2.3–6.3) (relative to unexposed)
Massin et al. 1996	Ball-bearing manufacture	Soluble	Current mean (geometric): 1.49 mg/m^3 in cutting area 0.65 mg/m^3 in machining area	Chronic bronchitis	9/114 (8%)	
				Chronic cough or phlegm	36/114 (32%)	OR=4.90 (*P* = 0.002)
				Bouts of bronchitis	19/114 (17%)	
				Dyspnea	30/114 (28%)	OR=2.28 (*P*= 0.10) (above ORs relative to unexposed controls, adjusted for age and smoking)
			Past means (geometric): 1.49 mg/m^3 in cutting area 2.20 mg/m^3 in machining area (total extractable oil aerosol)			OR=1.44 (*P*= 0.006) (above OR expressed per 10 mg-yr/m^3, adjusted for age and smoking)

See footnotes at end of table.

(Continued)

Table 5–2 (Continued). Estimated risk of respiratory symptoms associated with MWF exposures

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Number cases/ number exposed	Risk estimate and 95% CI or *P*-value
Oxhoj et al. 1982	27 machine shops	All classes	Range: 0.1–2.0 mg/m^3 Median: 0.35 mg/m^3 (oil mist)	Chronic cough Chronic phlegm	(32%) (25%)	PR=1.8 (X^2 P<0.05) PR=2.3 (X^2 P<0.05) (relative to <0.1 mg/m^3)
Sprince et al. 1997	Automobile parts manufacture	Soluble plus semi-synthetic	Current geometric mean (total aerosol by MiniRAM): 0.33 mg/m^3 (range 0.04–1.44)	Usual cough Usual phlegm Chest tightness Acute chest tightness Acute throat irritation Acute cough		OR=3.1 (1.4–6.9) OR=3.1 (1.6–6.1) OR=5.9 (1.4–25.7) OR=4.5 (1.3–15.2) OR=5.0 (1.7–14.7) OR=4.0 (1.2–14.1) (relative to assemblers; controlled for smoking, etc.)
Cross-sectional study (panel):						
Robins et al. 1994; 1997	Automobile parts manufacture	Soluble	Current mean (thoracic fraction): 0.44 mg/m^3	Phlegm Chronic bronchitis Wheeze and dyspnea Acute eye, nose, and throat irritation		OR=3.1 (P=0.01) OR=6.8 (P=0.04) OR=4.9 (P=0.03) (relative to assemblers) (P=0.01)
Cross-sectional and longi-tudinal study:						
Järvholm 1982	Bearing-ring manufacture	Straight plus soluble	Range: 0.3–18.0 mg/m^3 department-specific Medians: ranged from 1.1 to 4.5 mg/m^3 (oil mist)	Chronic bronchitis New respiratory symptoms among asymptomatic workers	17/164 (10%) 14/49 (29%)	RR=1.8 (1.1–2.9) RR=4.9 (0.7–34.2) (relative to unexposed over a 3-year period and adjusted for age and smoking)

*Abbreviations: CI=confidence interval, OR=odds ratio, PR=prevalence ratio, RR=risk ratio, SD=standard deviation.

revealed no significant differences in FVC or FEV_1 between the exposed metal workers and the office workers. Exposed and office workers who had respiratory symptoms at the initial survey were followed up 3 years later [Järvholm 1982]. Though the difference did not achieve statistical significance, the 58 men exposed to MWFs experienced mean 3-year reductions in FEV_1 and FVC of 30 and 40 ml, respectively, compared with mean increases of 50 and 20 ml for FEV_1 and FVC, respectively, among the 27 office workers. Small numbers of subjects limited the power of this study.

Krzesniak et al. [1981] studied lung function in metal workers exposed to MWF aerosol in a tractor factory in Poland, comparing a group of 531 metal workers (exposed from 1 to 20 years) with a group of 245 office workers. Women comprised 24% of the exposed and 42% of the comparison group. The MWF class was not specified, but the exposure was described as an oil mist with airborne concentrations ranging between 5 and 100 mg/m^3. Though smoking was slightly more prevalent in the exposed group than in the control group (59.7% versus 53.4%), a univariate analysis was conducted. Reduced FEV_1/FVC ratios were more frequent among the exposed workers than among the controls (35.6% versus 11.4%; $P<0.05$), as were reduced forced expiratory flow $_{25-75\%}$ ($FEF_{25-75\%}$) (33.3% versus 18.4%; $P<0.05$) and reduced $FEF_{200-1200}$ (15.8% versus 2.8%; $P<0.05$). Approximate unadjusted ORs for oil mist exposure calculated from the data provided by Krzesniak et al. [1981] are as follows: 4.3 (95% CI=2.75–6.85) for decreased FEV_1/FVC; 2.2 (95% CI=1.52–3.30) for decreased FEF_{25-75}; and 6.39 (95% CI=2.90–16.61) for decreased $FEF_{200-1200}$.

Oxhoj et al. [1982] communicated the results of a Danish study of 385 machine shop workers exposed to straight oil, soluble oil, semisynthetic, or synthetic MWFs in 27 different facilities. Measured oil aerosol concentrations in these facilities ranged from 0.1 to 2.0 mg/m^3 (median 0.35 mg/m^3). Controlling for age, height, and smoking, an analysis of spirometry data from 295 exposed male workers revealed no significant differences between four worker subgroups based on current exposure to straight oil, soluble oil, semisynthetic, or synthetic MWF. The authors summarized their rather limited spirometry findings by concluding that "if the four kinds of exposure influence ventilatory lung function, they do it to approximately the same degree" [Oxhoj et al. 1982].

In a study based in a French automobile manufacturing plant, Ameille et al. [1995] found no significant differences in baseline percentage of predicted lung function between four exposure groups (straight oil, soluble oil, mixed straight and soluble oil MWF, and unexposed control), which did not differ by smoking habits. Mean spirometry parameters were generally lower for the group of workers exposed to straight oil MWFs (mean total oil mist concentration was 2.6 mg/m^3) compared with the other groups, although the authors concluded that the study size was too small to detect significant differences in mean FEV_1 between exposure groups. After controlling for pack-years, linear regression analysis indicated that current smokers had significantly decreasing trends in FEV_1, $FEF_{25-75\%}$, and maximal flow rates at 50% and 75% of

exhaled with increasing duration of exposure to straight oil MWFs. This finding suggests a synergistic relationship between smoking and straight oil MWF exposure. No similar effects were observed for workers exposed to soluble oil MWF.

Greaves et al. [1993, 1995a] studied pulmonary function of 1,745 automobile parts manufacturing workers employed in machining and grinding operations. Machinists (352 currently exposed to straight MWF, 441 to soluble MWF, and 226 to synthetic MWF) were compared with 726 assembly workers, 239 of whom had never been exposed in metalworking operations. Current exposures to aerosols (thoracic fraction) of straight oil MWFs (mean concentration=0.43 mg/m^3; SD=0.26), soluble MWFs (mean=0.54 mg/m^3; SD=0.17), or synthetic MWFs (mean=0.41 mg/m^3; SD=0.08) were measured. The relationships between pulmonary function and both current and cumulative exposures were evaluated. Previously exposed assemblers were not included in analyses that considered current exposures only. Multivariate analyses controlled for age, height, race, smoking, grinding operation, and plant.

In terms of unadjusted mean lung function, Greaves et al. [1995a] found that approximately 18% of workers ever exposed to any MWFs had abnormal FEV_1 values (i.e., less than 85% of predicted), approximately 25% in excess over the 14% abnormal rate among never-exposed assemblers ($P>0.10$). Mean percentages of predicted and residual (observed minus predicted) FEV_1 values were significantly reduced ($P>0.05$) for the three groups of metalworkers who were ever-exposed to straight oil, soluble oil, or synthetic MWFs, but not for the group of never-exposed assembly workers.

Analyzing the data trichotomized by current aerosol exposure, Greaves et al. [1995a] found trends of declining function with increasing exposure for both straight and soluble oil MWFs. At the highest current exposure categories (>0.54 mg/m^3 for straight oil MWF and >0.65 mg/m^3 for soluble oil MWF), mean percentage of predicted FEV_1 (not adjusted for smoking) was significantly reduced ($P<0.01$). The exposure-related trend was inverted in a similar analysis of current exposure to synthetic MWF, the lowest exposure category (<0.18 mg/m^3) having the lowest mean percentage predicted FEV_1 ($P=0.06$). For both straight oil MWF and soluble oil MWF aerosols, individual quantitative concentration of current aerosol exposures resulted in negative exposure-response coefficients (adjusted for smoking) for percentage of predicted FEV_1 and percentage of predicted FVC ($P<0.05$) and for their residuals (observed value minus predicted value) ($P<0.10$). Adjusted for age, height, race, smoking, plant, and grinding, the coefficients for FEV_1 (-197 ml per mg/m^3) and FVC (-229 ml per mg/m^3) residuals with respect to current straight oil MWF aerosol exposure concentrations were marginally significant ($P=0.06$). Coefficients for soluble and for synthetic MWF aerosol exposures were also negative, although they did not achieve statistical significance.

Analyzing the data trichotomized by cumulative aerosol exposure concentrations, Greaves et al. [1995a] found trends of declining mean percentage of predicted lung

function with increasing exposure to straight and to soluble oil MWFs. At the highest exposure tertile (>1.71 mg/m^3-years for straight oil MWF and >3.41 mg/m^3-years for soluble oil MWF), mean percentage of predicted FEV_1 (unadjusted for smoking) was significantly reduced (P<0.001). Prevalence rates of abnormal FEV_1 among subgroups with highest cumulative aerosol exposures were greater than among never-exposed assembly workers for exposure to straight oil MWF (20.4% versus 14.2%; P=0.06; RR=1.4) and for exposure to soluble MWF (21.9% versus 14.2%; P<0.01; RR=1.5). Also, FEV_1 residuals were negative and statistically significant for the highest exposure categories of both straight MWFs (-117 ml; P<0.001) and soluble MWFs (-139 ml; P<0.001). Similar to the findings in relation to current exposures, there was an inverse trend with increasing exposure category among workers ever exposed to synthetic MWF; prevalences of abnormal FEV_1 were 19.8%, 17.1%, and 13.6% for the lowest to highest cumulative exposure groups, respectively. The lowest exposure group (<0.18 mg/m^3-years) had an abnormality prevalence RR of 1.4 relative to the never-exposed assemblers (P=0.07), representing a 40% excess.

In multiple linear regression analysis considering both current and past exposures simultaneously, Greaves et al. [1995a] found that accelerated decline in FEV_1 was significantly related to past exposures to aerosols from straight oil (FEV_1 residual = -5 ml per mg/m^3-year; P<0.05) and from synthetic MWFs (FEV_1 residual = -7 ml per mg/m^3-year; P<0.10) but not to past exposures to soluble oil MWFs (FEV_1 residual = -1 ml per mg/m^3-year; P>0.10) or to current exposures.

The results of the Greaves et al. [1995a] study show that adverse pulmonary function effects are associated with cumulative exposures to aerosols from straight and synthetic oil MWFs and less consistently with aerosols from soluble oil MWF. In this population, cumulative exposure appeared to be more important than current aerosol exposure concentrations in predicting pulmonary function. Greaves et al. [1995a] suggest that the increased impairment associated with lower current or lower cumulative exposures to synthetic MWF in the categorical exposure analysis may reflect a tendency for selective transfer of affected workers from jobs with higher MWF aerosol exposure to jobs with lower exposures. The investigators expressed caution with respect to the lack of clear evidence of adverse effects of exposure to soluble oil MWFs. Among other reasons for this caution, they pointed out that most of the studied workers exposed to straight oil or synthetic MWFs had at sometime also been exposed to soluble oil MWFs and that very few of the workers exposed to soluble oil MWFs had not also been exposed to straight oil or synthetic MWFs. As a result, inferences about health effects specific to major types of MWFs cannot be made with certainty based on findings of Greaves et al. [1995a].

Kriebel et al. [1994, 1997] studied lung function in transmission manufacturing workers exposed to soluble oil and straight oil MWFs in one machine shop compared with assembly (and office/classroom) workers. Average aerosol exposures (inhalable fraction)

were 0.24 mg/m^3 (SD=0.27) among workers exposed to straight oil MWFs, 0.22 mg/m^3 (SD=0.26) among workers exposed to soluble oil MWFs, 0.08 mg/m^3 (SD=0.05) among assembly workers, and 0.03 mg/m^3 (SD=0.03) among classroom/office workers. After adjustment for age, race, sex, height, and smoking, Kriebel et al. [1994, 1997] observed a statistically significant (P<0.05) deficit in baseline FEV_1 of 115 ml (approximately 3%) associated with exposure to soluble oil MWF. No similar significant difference was associated with exposure to straight oil MWF.

After statistical adjustment for smoking status, Massin et al. [1996] found no significant difference between the mean baseline spirometry of 114 male ball-bearing plant workers exposed to aerosol from soluble oil MWF and that of 55 unexposed male workers from other plants in the same region of France. Also, after adjustment for smoking, baseline FEV_1 was not found to be related to oil mist concentration. This cross-sectional study involved 85% of exposed workers at the studied plant, and these workers had been exposed for a mean duration of 15 years SD=8 years). Exposure concentrations were measured as total extractable oil mist, and work area geometric means ranged from 0.65 mg/m^3 for the machining area in recent years to 2.20 mg/m^3 for that same area before improved exposure controls were installed at the plant in 1990.

Sprince et al. [1997] studied Monday morning spirometry among machine operators (n=183) and unexposed assembly workers (n=66) in an automobile transmission parts manufacturing plant. Machine operators were exposed to one of two types of soluble oil MWF or to a semisynthetic MWF. No information was provided regarding possible previous MWF aerosol exposures among assemblers. After adjusting for smoking, the investigators found no significant differences in percentage of predicted FEV_1 or FVC between machine operators and assembly workers; mean values of FEV_1 unadjusted for smoking were 92% and 93%, respectively. Likewise, no difference was noted in baseline spirometry among machine operators by MWF type, and there was no significant difference associated with current total aerosol exposure concentration. Geometric mean total aerosol exposures, as measured by MiniRAMs gravimetrically calibrated to Arizona road dust, were 0.33 mg/m^3 (range 0.04 to 1.44 mg/m^3) for machine operators and 0.08 mg/m^3 (range 0.02 to 0.20 mg/m^3) for assembly workers. These aerosol concentrations are not comparable with those resulting from standard filter methods. If the exposures in this plant had been measured with a direct gravimetric filter method, the levels would likely have been lower (i.e., equivalent to the nonvolatile proportion of the aerosol entering the sampler). Notably, after adjusting for smoking, Sprince et al. [1997] did find a significant relationship between baseline percentage of predicted FEV_1 and exposure to airborne concentration of viable bacteria (P=0.025).

Summary

Results of these cross-sectional studies of lung function generally parallel those from studies of respiratory symptoms among workers exposed to MWF aerosols. Table 5–3 presents selected risk estimates that generally indicate that occupational exposure to

Table 5–3. Estimated risk of chronic lung function effects associated with MWF aerosol exposure

Study*	Population	Fluid class	Aerosol exposure concentration	Health effect	Risk estimate and 95% CI or *P*-value†
Ameille et al. 1995	Automobile parts manufacture	Straight	Current mean: 2.6 mg/m^3 (oil mist)	FEV_1 in smokers	↓ trend with years of exposure (P=0.004)
				FEF_{25-75} in smokers	↓ trend with years of exposure (P=0.005)
				V_{75} in smokers	↓ trend with years of exposure (P=0.01)
				V_{50} in smokers	↓ trend with years of exposure (P=0.02)
				V_{25} in smokers	↓ trend with years of exposure (P=0.004) (above all adjusted for pack-years of smoking)
Greaves et al. 1995a	Automobile parts manufacture		Current mean (thoracic fraction):		
		Straight	0.43 mg/m^3 (SD 0.3)	FEV_1 (<85% predicted)	PR=1.4 (>0.54 mg/m^3 relative to never exposed)
		Soluble	0.55 mg/m^3 (SD 0.2)	FEV_1 (observed-predicted)	−197 ml per mg/m^3 (P=0.06)‡
		Synthetic	0.41 mg/m^3 (SD 0.1)	FEV_1 (<85% predicted)	PR=1.4 (>0.65 mg/m^3 relative to never exposed)
				FEV_1 (<85% predicted)	PR=1.4 (<0.18 mg/m^3 relative to never exposed) (evidence for transfer)
			Cumulative mean (thoracic fraction):	FEV_1 (<85% predicted)	PR=1.4 (P=0.06) (>1.71 mg/m^3-years relative to never exposed)
		Straight	2.29 mg/m^3-years (SD 7.6)	FEV_1 (observed-predicted)	−5 ml per mg/m^3-year (P<0.05)†
		Soluble	6.40 mg/m^3-years (SD 14.2)	FEV_1 (<85% predicted)	PR=1.5 (P<0.01) (>3.41 mg/m^3-years relative to never exposed)
		Synthetic	0.39 mg/m^3-years (SD 2.9)	FEV_1 (<85% predicted)	PR=1.4 (P=0.07) (<0.18 mg/m^3-years relative to never exposed) (evidence of transfer)
				FEV_1 (observed-predicted)	−7 ml per mg/m^3-year (P<0.10)†

See footnotes at end of table.

(Continued)

Table 5–3 (Continued). Estimated risk of chronic lung function effects associated with MWF aerosol exposure

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Risk estimate and 95% CI or *P*-value
Kriebel et al. 1994; 1997	Automobile parts manufacture	Soluble	Current mean: 0.22 mg/m^3 (SD 0.3) (inhalable fraction)	FEV_1	−115 ml ($P<0.05$) (relative to assemblers)
Krzesniak et al. 1981	Tractor parts manufacture	Not specified	Range 5–99.5 mg/m^3	Decreased FEV_1/FVC Decreased $FEF_{25-75\%}$ Decreased $FEF_{200-1200}$	OR=4.3 (2.8–6.9) OR=2.2 (1.5–3.3) OR=6.4 (2.9–16.6) (above ORs all relative to unexposed)
Massin et al. 1996	Ball-bearing manufacture	Soluble	Current mean (geometric): 1.49 mg/m^3 in cutting area 0.65 mg/m^3 in machining area	FVC FEV_1 FEV_1/FVC	$P = 0.14$ $P = 0.06$ $P = 0.30$
			Past means (geometric): 1.49 mg/m^3 in cutting area 2.20 mg/m^3 in machining area (total extractable oil aerosol)	FEF_{25-75} $Vmax_{50}$ $Vmax_{25}$ (all the above indices were expressed as standardized residuals relative to predicted values)	$P = 0.11$ $P = 0.24$ $P = 0.54$ (above P values refer to differences from means of control subjects after adjustment for smoking)
Sprince et al. 1997	Automobile parts manufacture	Soluble/ semi-synthetic	Current geometric mean: 0.33 mg/m^3 (range 0.04–1.44) (total by MiniRAM)	FEV_1	No significant differences (machine operators relative to assemblers; by type of MWF; or by MWF aerosol exposure concentration)

*All are cross-sectional studies.

†Abbreviations: CI=confidence interval, FEF=forced expiratory flow, FEV=forced expiratory volume, FVC=forced vital capacity OR=odds ratio; PR=prevalence ratio; SD=standard deviation.

‡Adjusted for smoking, grinding, and plant.

MWF aerosols is associated with reduced pulmonary function. Although the observed reductions in pulmonary function may, in part, be acute and reversible, their stronger relationship with past exposures than with current exposures [Greaves et al. 1995a] suggests that they may well be substantially chronic and irreversible. The observed adverse lung function effects are attributable to straight oil, soluble oil, and synthetic MWFs at exposure concentrations recently observed in large metalworking shops. Moreover, evidence from the largest study [Greaves et al. 1995a] involving several different plants using three different major types of MWFs at mean aerosol exposures ranging from 0.41 to 0.55 mg/m^3 (thoracic fraction) suggests that pulmonary function effects associated with cumulative exposure to MWF aerosol occur in a dose-related manner. Some pulmonary function evidence suggests possible interaction between smoking and exposure to MWF aerosol in reducing lung function [Ameille et al. 1995]. Although the actual degree of self-selection away from MWF exposure by affected individuals is not known, such a phenomenon would bias cross-sectional studies toward underestimating the effects of exposure. The lack of association between MWF aerosol exposure and lung function observed in some studies may be attributable to such selection, to statistical power limitations related to study size, to aerosol concentration, to exposure duration, and/or to MWF aerosol composition.

5.1.2.5 Cross-Shift Studies of Acute Effects on Lung Function

Study findings

Kennedy et al. [1989] studied cross-shift changes in lung function in 89 automobile manufacturing workers exposed to MWF aerosols who had worked for at least 5 years, compared with 42 "unexposed" assembly workers. The assembly workers were exposed to aerosol concentrations ranging from 0.07 to 0.44 mg/m^3 (inhalable fraction). The machinists selected for the study had worked with one MWF class (straight oil, soluble oil, or synthetic) for at least the past 6 months at concentrations ranging from 0.16 to 2.03 mg/m^3 (inhalable fraction). Geometric mean exposures for assembly workers and machinists were 0.18 and 0.66 mg/m^3 (inhalable fraction), respectively [Woskie 1996]. These workers were recruited from the same population used in a cross-sectional study reported by Eisen [1995] and Greaves et al. [1995a,b]. The investigators noted that more than 25% of eligible machinists who were invited to participate declined, and that machinists who chose not to participate had significantly lower mean percentage of predicted FEV_1 and FVC at 90% and 92%, respectively (both $P<0.01$). The three other groups (participating machinists, participating assembly workers, and nonparticipating assembly workers) all had comparable lung function, with mean percentage of predicted values ranging from 98% to 100%. This raises the possibility that the study did not include those machinists at greatest risk.

In an analysis stratified by MWF class, Kennedy et al. [1989] found that, regardless of MWF class, more than 20% of exposed machinists experienced a cross-shift FEV_1

decrement of at least 5%, compared with fewer than 10% of assembly workers (RR=2.5; $P<0.05$). In a logistic regression analysis controlling for race, history of childhood asthma, and smoking, acute Monday FEV_1 decrements of at least 5% were associated with straight MWF exposure (OR=5.8; 95% CI=1.1–29.0), soluble MWF exposure (OR=4.4; 95% CI=1.0–20.0), and synthetic MWF exposure (OR=6.9; 95% CI=1.4–35.0). Geometric mean exposures (total inhalable fraction) to MWF aerosol were 0.78 mg/m^3 for those working with straight oil MWF, 0.82 mg/m^3 for those working with soluble oil MWF, and 0.56 mg/m^3 for those working with synthetic oil MWF [Woskie 1996]. A history of childhood asthma was also strongly associated with cross-shift decrement (OR=9.1; 95% CI=1.3–66).

In assessing exposure-response relationships, Kennedy et al. [1989] trichotomized exposure to MWF aerosol (thoracic fraction) and found a significantly increased incidence of cross-shift FEV_1 decrements of at least 5% on each of two separate days of testing for the "high" exposure group (<0.55 mg/m^3) and the "medium" exposure group (0.20–0.55 mg/m^3) compared with the group exposed at lower aerosol concentrations (<0.20 mg/m^3). Even for the "medium" exposure group relative to the lower exposure group, the difference in incidence was statistically significant ($P<0.01$). In a logistic regression analysis controlling for race, smoking, and history of childhood asthma, incremental ORs for increasing exposure category were 1.8 (95% CI=0.9–3.3) for the Monday testing, and 2.0 (95% CI=1.0–3.8) for the Friday testing. Based on their observations, Kennedy et al. [1989] concluded that airways narrowing is a common response to MWF exposure and that the concentration of MWF aerosol at which no such response would be expected would be less than 0.20 mg/m^3 (thoracic fraction). Using a conversion factor of 1.4 derived from Kennedy et al. [1989], Woskie [1996] estimated no effect level is probably less than approximately 0.28 mg/m^3 (inhalable fraction) of MWF aerosol.

Kriebel et al. [1994, 1997] studied cross-shift FEV_1 decrements among 216 machinists exposed to straight and soluble MWF aerosols. The mean aerosol exposure concentration for the exposed machinists was approximately 0.23 mg/m^3 (inhalable fraction), or only about one-fourth the exposure concentrations for the cross-shift study of machinists reported by Kennedy et al. [1989]. The incidence of cross-shift FEV_1 decrements of 5% or greater was substantially lower than that observed by Kennedy et al. [1989], so the investigators initially employed a more sensitive (but less specific) 4% or greater cut-off to categorize FEV_1 decrements. Using inhalable mass exposure cut-points equivalent to the thoracic mass exposure cut-points employed by Kennedy et al. [1989], Kriebel et al. [1994] analyzed data from all study participants and observed a relative risk for 4% or greater FEV_1 decrement of 3.4 (95% CI=1.6–7.2) for the subgroup with "high" exposures (≥0.77 mg/m^3) compared with the group with "low" exposure (≤0.28 mg/m^3). Relative risks for machinists exposed to straight oil MWF aerosols were 2.3 (95% CI=0.6–8.7) for "medium" exposure and 5.3 (95% CI=1.9–14.9) for "high"

exposure compared with "low" exposure; relative risks for machinists exposed to soluble MWF aerosols were 0.6 (95% CI=0.1–2.3) for "medium" exposure and 3.3 (95% CI=0.8–13.9) for "high" exposure.

A further analysis using the more traditional 5% cutoff for FEV_1 response also showed a relationship between categorical MWF aerosol exposure and cross-shift FEV_1 response at lower concentrations [Kriebel et al. 1997]. The adjusted relative risks for cross-shift FEV_1 decrement were 2.3 (95% CI=1.0–5.0) for "medium" exposure (i.e., 0.08 to 0.15 mg/m^3) and 3.2 (95% CI=1.2–8.7) for "high" exposure (i.e., $\geq$0.15 mg/m^3) compared with "low" aerosol exposure (i.e., $\leq$0.08 mg/m^3). This suggests that a no-effect level is probably below 0.15 mg/m^3 (inhalable fraction) for MWF aerosol.

Additional analyses of these same data attempted to identify specific characteristics of MWF aerosol exposures that may cause the observed acute respiratory effects. In an analysis based on a 4% cut-point for cross-shift FEV_1 decrement, and aerosol exposure cut-points equivalent to those of Kennedy et al. [1989], risk of FEV_1 decrement was clearly associated with increasing exposure for those whose sump had not been refilled during the previous 3 days: RR= 1.8 (95% CI=0.6–5.0) for "medium" exposure (0.28–0.77 mg/m^3) and RR=5.9 (95% CI=0.6–5.0) for the "high" exposure ($\geq$0.77 mg/m^3) group, relative to the "low" ($\leq$0.28 mg/m^3) exposure group. Among those with less than 3 days since MWF sump refill, there were no acute FEV_1 decrements in the "medium" and "high" exposure categories, so a similar exposure-response relationship was not observed using the Kennedy cut-points. Using cut-points selected on the basis of the distribution of exposures, an exposure-response relationship was observed among those with more than 3 days since refill but not among those whose sumps had been filled more recently. However, the robustness of these observations relating to time since sump refill is questionable, as Kriebel [1996] reported that results of analogous analyses based on 5% or greater decrements in FEV_1 were inconsistent.

These same investigators [Kriebel et al. 1994; Sama et al. 1997] also evaluated risk associated with specific MWF aerosol components, including endotoxin and sulfur. Endotoxin exposures were low (geometric mean <9 endotoxin units/m^3), and there was no observed statistically significant association of acute ventilatory response with endotoxin exposure. Of four elements (chlorine, chromium, nickel, and sulfur) considered as *a priori* exposure indices, only sulfur was associated with cross-shift FEV_1 decrements. Hydrogen sulfide is a decomposition product of sulfurated hydrocarbons—a known respiratory irritant and a common contaminant of MWFs; petroleum sulfonates, which may decompose to sulfur dioxide, are also known pulmonary irritants commonly used in formulating soluble MWFs [Kriebel et al. 1994; Sama et al. 1997]. Comparing machinists exposed above the median of 3.2 $\mu g/m^3$ sulfur with those exposed to lower concentrations of airborne sulfur, the investigators found an apparent association between exposure to sulfur in MWF aerosols and cross-shift FEV_1 decrement $\geq$5% (OR=3.3;

95% CI=1.0–10.7). In subsequent analyses using exposure cut-points that divided the studied workers into those with exposures in the uppermost quartile, the middle half, and the lowermost quartile, a statistically significant exposure response trend (P=0.02) was observed: RR=1.5 (95% CI=0.3–6.4) for the "medium" exposure group (range, 2.5–4.4 $\mu g/m^3$; median, 3.4 $\mu g/m^3$) and RR=3.7 (95% CI=0.9–16.1) for the "high" exposure group (>4.4 $\mu g/m^3$; median, 5.6 $\mu g/m^3$), relative to the "low" exposure group (<2.5 $\mu g/m^3$; median, 2.1 $\mu g/m^3$) [Sama et al. 1997]. The relationship between sulfur exposure and cross-shift FEV_1 decrement was observed even at sulfur concentrations well below those at which ambient air pollution effects have been observed, leading to speculation that sulfur may not be the causal agent but may serve only as a marker of particularly irritating exposure conditions [Kriebel et al. 1995; Sama et al. 1997].

Robins et al. [1994, 1995a, 1997] studied cross-shift pulmonary function changes experienced by automobile transmission parts manufacturing workers exposed to soluble MWFs in the same concentration ranges as those studied by Kennedy et al. [1989]. By department, average MWF aerosol exposure (thoracic fraction) ranged from approximately 0.1 to 0.6 mg/m^3. For the assembly workers, median aerosol exposure was 0.14 mg/m^3, the 75th percentile was 0.15 mg/m^3, and the maximum exposure was 0.31 mg/m^3. The rate of cross-shift FEV_1 decrement of at least 5% was consistently higher among exposed workers for all three Mondays on which testing was done. Six of 85 exposed workers demonstrated clinically significant (≥19%) cross-shift FEV_1 decrements compared with none of the 46 workers in the assembly group (one tailed P=0.07). Using three exposure categories nearly equivalent to those used by Kennedy et al. [1989], Robins et al. [1994, 1995a, 1997] found evidence of a dose-related risk of cross-shift FEV_1 decrement of 5% or greater on Mondays. Aggregating observations from all three Mondays of the study and assuming independence of observations on the same individual on different Mondays, data from their report [Robins et al. 1994] permit calculations of unadjusted RRs for cross-shift decrements greater than 5% of 1.34 (95% CI=0.76–2.36) for "medium" exposure (0.16–0.47 mg/m^3, thoracic fraction) and 1.98 (95% CI=1.11–3.52) for "high" exposure (>0.47 mg/m^3) relative to "low" exposure (<0.16 mg/m^3). The median personal MWF aerosol exposures of machinists experiencing cross-shift FEV_1 decrements ≥12% ranged from 0.17 to 0.80 mg/m^3 (median, 0.5 mg/m^3) [Robins et al. 1994].

The presence of chronic symptoms and the development of respiratory symptoms on Monday were each associated with larger cross-shift FEV_1 decrements on Monday. Based on multiple regression analyses that excluded all workers who reported that they currently had asthma (and other influential outliers on a model-by-model basis), the magnitude of cross-shift FEV_1 decrement was consistently related to higher airborne bacteria exposure among current smokers with lower baseline FEV_1/FVC ratio. Robins et al. [1995b] reported that 25% of smokers with evidence of pulmonary obstruction at baseline (Monday preshift FEV_1/FVC ratio ≤0.72) experienced a cross-shift decrement

of FEV_1 of at least 10%, compared with only 5% of other study subjects. After controlling for other factors related to pulmonary function decrement, they found an increasing trend in risk of a 10% or greater cross-shift FEV_1 decrement with increasing levels of exposure to both MWF aerosol and airborne bacteria among obstructed smokers, but not among other study subjects. For obstructed smokers, model-derived ORs were 3.1 (95% CI=0.9–10.3), 6.0 (95% CI=2.3–15.8), and 8.8 (95% CI=2.7–28.8) for exposure to MWF aerosol concentrations at 0.14, 0.34, and 0.57 mg/m^3 (thoracic fraction), respectively, compared with other workers exposed at 0.14 mg/m^3 (OR=1, by designation). For other study subjects, corresponding ORs were 1.0 (95% CI=0.6–1.6) and 1.0 (95% CI=0.4–2.2) for exposures of 0.34 and 0.57 mg/m^3, respectively. For obstructed smokers, model-derived ORs were 4.4 (95% CI=1.8–10.7), 6.1 (95% CI=2.4–15.3), and 7.5 (95% CI=2.6–22.1) for exposure to airborne bacteria concentrations at 0.2, 1.0, and 3.0 bacteria/cubic centimeter (cc) (thoracic fraction). For other study subjects, corresponding ORs were 1.0 (by designation), 0.5 (95% CI=0.4–1.1), and 0.5 (95% CI=0.2–1.1). Robins et al. [1997] have also presented model-based comparative ORs for 10% or greater cross-shift FEV_1 decrements for obstructed and nonobstructed workers, regardless of smoking status. The exposure-related trends in ORs closely approximated those summarized in the above paragraph, suggesting an important interaction effect of exposure and baseline airways obstruction (regardless of smoking status) on acute airway response to MWF aerosol.

Robins et al. [1997] also developed predicted fractional cross-shift FEV_1 changes for various levels of baseline obstruction and exposure. These findings indicate a predicted average 10.1% (± 0.03) drop in FEV_1 at a MWF aerosol exposure level of 0.57 mg/m^3 compared with a 3.3 % (± 0.01) drop at 0.14 mg/m^3 for exposed workers with a baseline FEV_1/FVC of 0.6.

Sprince et al. [1997] studied Monday preshift and postshift spirometry among machine operators (n=183) and unexposed assembly workers (n=66) in an automobile transmission parts manufacturing plant. Machine operators were exposed to one of two types of soluble oil MWF or to a semisynthetic MWF. After adjusting for age, race, sex, and smoking, the investigators found no significant differences between machine operators and assemblers in terms of proportions experiencing an FEV_1 decrement ≥5%; unadjusted proportions were 16% for machine operators and 12% for assemblers. Likewise, there was no association between ≥5% FEV_1 decrements and MWF type or exposure concentrations among machine operators. Findings were similar with cross-shift FEV_1 decrement values analyzed as continuous data. Mean FEV_1 decrement was slightly larger among machine operators (−1.5%) compared with assemblers (−0.51%), but this difference was not statistically significant. Nor was magnitude of cross-shift FEV_1 decrement significantly associated with MWF type or exposure concentration among machine operators. Geometric mean total aerosol exposures (as measured by MiniRAMs gravimetrically calibrated to Arizona road dust) were 0.33 mg/m^3 (range

0.04 to 1.44 mg/m^3) for machine operators and 0.08 mg/m^3 (range 0.02–0.20 mg/m^3) for assembly workers. These aerosol concentrations are not comparable with those resulting from standard filter methods. If exposures in this plant had been measured with a direct gravimetric filter method, the concentrations would likely have been lower by a factor equivalent to the nonvolatile proportion of the aerosol entering the sampler.

Summary

Four studies evaluated acute (cross-shift) lung function decrements in workers exposed to MWF aerosols. Table 5–4 presents selected risk estimates from four relevant studies. All but one of these studies found that incidence of cross-shift FEV_1 decrement is associated with occupational exposure to MWF aerosol. The evidence indicates that exposures to aerosols generated during the use of straight oil, soluble oil, or synthetic MWFs all cause acute reductions in ventilatory function at MWF aerosol exposure concentrations currently typical of large metalworking shops. Moreover, in all three studies with affected worker populations, these acute airflow reductions occurred in a dose-related manner and were attributable to MWF aerosol at concentrations in excess of approximately 0.5 mg/m^3 (thoracic fraction). In two of the three studies, they were found to be statistically significant at substantially lower aerosol concentrations. Kennedy et al. [1989] found increasing risk of cross-shift declines occurring at MWF aerosol concentrations above approximately 0.20 mg/m^3 (thoracic fraction), and the results of Kriebel et al. [1997] indicate that a no-effect level for cross-shift FEV_1 decrements may be on the order of 0.10 mg/m^3 (inhalable fraction) or lower.

Previous history of childhood asthma appears to be a predictor of increased risk of acute lung function decrements associated with MWF aerosols [Kennedy et al. 1989], though such decrements occur even in the absence of such history [Robins et al. 1997]. Some evidence suggests that smoking (both active and possibly passive) and/or baseline airways obstruction may increase susceptibility to cross-shift lung function decrement induced by occupational MWF aerosol exposures [Kennedy et al. 1989; Robins et al. 1997]. Consistent with results of toxicological studies that indicate variability in airways effects of various aerosolized MWFs (summarized elsewhere in this document), the specific composition of MWF aerosols is also undoubtedly an important potential predictor of acute airways effect. Specific exposure characteristics evaluated in one or more epidemiological studies include bacterial counts, endotoxin, fungal counts, and various elements including sulfur. Some of these specific characteristics are promising as indicators of MWF aerosol potency in terms of airways effects, but existing data are insufficient to displace the much better documented gravimetric aerosol concentration as the best current indicator of potential potency of MWF aerosol. Given the complexity of MWF aerosol composition, it is questionable whether a single specific exposure index will ever be shown to be better than generic gravimetric measurements of MWF aerosol exposure when used alone to assess potential risk.

Table 5–4. Estimated risk of cross-shift lung function associated with MWF aerosol exposure

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Risk estimate (95% CI* or *P*-value)
Kennedy et al. 1989	Workers in automobile parts manufacturing	All classes	Range 0.16–2.03 mg/m^3 (inhalable fraction)	Cross-shift FEV_1 decline (≥5%)	RR=2.5 (P<0.05) (relative to assemblers)
			Current mean: 0.75 mg/m^3 (inhalable fraction)	Cross-shift FEV_1 decline (≥5%): Monday	OR=1.8 (0.9–3.3)
				Cross-shift FEV_1 decline (≥5%): Friday	OR=2.0 (1.0–3.8) (above 2 ORs are for incremental increase in exposure trichotomized at 0.2 mg/m^3 and 0.55 mg/m^3— thoracic fraction)
		Straight	Current mean: 0.81 mg/m^3 (inhalable fraction)	Cross-shift FEV_1 decline (≥5%)	OR=5.8 (1.1–29) (relative to assemblers)
		Soluble	0.88 mg/m^3 (inhalable fraction)	Cross-shift FEV_1 decline (≥5%)	OR=4.4 (1.0–20) (relative to assemblers)
		Synthetic	0.62 mg/m^3 (inhalable fraction) (above exposure data from Woskie [1996])	Cross-shift FEV_1 decline (≥5%)	OR=6.9 (1.4–35) (relative to assemblers)
Kriebel et al. 1994, 1997	Workers in automobile parts manufacturing	Straight	Current mean: 0.24 mg/m^3 (SD=0.3) (inhalable fraction)	Cross-shift FEV_1 decline (≥4%)	RR=2.3 (0.6–8.7) (0.28–0.77 relative to ≤0.28 mg/m^3)
				Cross-shift FEV_1 decline (≥4%)	RR=5.3 (1.9–14.9) (≥0.77 relative to ≤0.28 mg/m^3)
		Soluble	0.22 mg/m^3 (SD=0.3) (inhalable fraction)	Cross-shift FEV_1 decline (≥4%)	RR=3.3 (0.8–13.9) (≥0.77 relative to ≤0.28 mg/m^3)
		Straight/soluble (aggregated data)		Cross-shift FEV_1 decline (≥5%)	RR=2.3 (1.0–5.0) (0.08–0.15 relative to ≤0.08 mg/m^3)
				Cross-shift FEV_1 decline (≥5%)	RR=3.2 (1.2–8.7) (≥0.15 relative to ≤0.08 mg/m^3)

*Abbreviations: CI=confidence interval, FEV_1=forced expiratory volume in 1 sec, OR=odds ratio, RR=risk ratio, SD=standard deviation.

(Continued)

Table 5–4 (Continued). Estimated risk of cross-shift lung function associated with MWF aerosol exposure

Study	Population	Fluid class	Aerosol exposure concentration	Health effect	Risk estimate (95% CI or *P*-value)
Robins et al. 1994; 1997	Workers in automobile parts manufacturing	Soluble	Current mean: 0.44 mg/m^3 (thoracic fraction)	Cross-shift FEV_1 decline (≥20%)	RR=undefined (*P*=0.07) (relative to assemblers)
				Cross-shift FEV_1 decline (≥5%)	RR=1.34 (0.76–2.36) (0.16–0.47 relative to ≤0.16 mg/m^3)
					RR=1.98 (1.11–3.52) (≥0.47 relative to ≤0.16 mg/m^3)
Sprince et al. 1997	Workers in automobile parts manufacturing	Soluble/ semisynthetic	Current mean: 0.33 mg/m^3 (range 0.04–1.44) (total by MiniRAM)	Cross-shift FEV_1 decline	No significant differences (machine operators relative to assemblers, by type of MWF, or by exposure concentration)

5.1.3 Discussion

With the exception of infrequent case reports of lipid pneumonia or asthma, essentially no scientific literature published before the past two decades attributed nonmalignant respiratory disease to MWF aerosol exposures. This lack of early evidence may be at least partly attributable to limited prior research on this issue. Lipid pneumonia (a health risk associated with exposures to airborne concentrations of oil-containing MWF) currently appears to be a much less important occupational health concern than disorders such as HP, acute airways irritation, asthma, chronic bronchitis, and potentially irreversible chronic obstructive impairment of lung function.

Recent studies are not entirely consistent in documenting exposure-response relationships between MWF aerosol exposures and respiratory symptoms and lung function effects (both acute and chronic), including clinically recognized asthma. Nevertheless, for each MWF class, frequent adverse respiratory effects have been clearly attributable to MWF aerosol concentrations in excess of approximately 0.5 mg/m^3 (thoracic fraction) in most recent epidemiological studies, and to even lower aerosol concentrations in some of these studies. Given the complexity of MWF aerosol composition, gravimetric aerosol measurements cannot be considered entirely specific for the hazard potential of MWF aerosol. Various specific characteristics of MWF aerosol exposures have been evaluated in some recent studies, and some have yielded promising findings. However, available data regarding these specific aerosol characteristics is very limited, and nonspecific gravimetric measurement of aerosol exposure remains a reasonably robust indicator of the risk of adverse airways effects. These gravimetric exposure concentrations are expressed in terms of TWAs. The possibility exists that short-term peak exposures are more important determinants of at least some of the airways disorders induced by MWF aerosols (e.g., asthma), but no epidemiologic studies to date have assessed MWF aerosol exposures with respect to short-term peak exposures.

Despite an impressive amount of research recently carried out on the airways effects of exposure to MWF aerosol, the potential importance of various adverse acute airways effects attributed to MWF aerosol is not entirely clear. Particularly in view of the increasing documentation that asthma can be caused by occupational exposure to MWF aerosols, acute symptoms and acute airflow reduction measured across a shift should be considered an important health outcome. In some exposed workers, these acute reactions may be manifestations of attacks of already diagnosed asthma; in others, acute reactions may be manifestations of newly developed but not yet diagnosed asthma. With regard to this latter possibility, it is notable that symptoms of episodic cough, wheeze, and phlegm have been shown to predate (by more than 2 years on average) diagnosis of asthma in the much better studied occupational asthma associated with western red cedar dust [Chan-Yeung et al. 1982]. Although asthma can be mild in many affected individuals, it can be quite debilitating. Moreover, even after removal of affected workers from exposure, occupational asthma frequently persists as a chronic condition

[Chan-Yeung and Malo 1993a]. It is not unreasonable to suggest that the natural history of MWF-associated asthma, although not yet well described, is similar to asthma associated with other better studied occupational agents.

In many exposed workers, acute respiratory symptoms and/or modest functional decrements may never develop into clinical asthma. Nevertheless, they are often quite bothersome to the affected workers, even causing him or her to seek medical treatment [Rosenman et al. 1997b]. They can also serve as biomarkers of potentially hazardous occupational exposure that should be better controlled. Furthermore, repeated modest acute airways effects, though apparently reversible upon removal from exposure, may ultimately lead to irreversible impairment and chronic pulmonary disability. No studies have yet been carried out among exposed metalworkers to relate acute decrements caused by MWF aerosols with chronic airways obstruction. In fact, with the exception of one very limited study [Järvholm 1982] and another study now in progress [Kennedy et al. 1995b], there has been no prospective study of long-term change in lung function among metalworkers exposed to MWF aerosols. For a variety of other occupational respiratory hazards, however, gradually emerging evidence has indicated a link between acute and chronic lung function effects [Peters 1974; Wegman et al. 1982; Weill 1984; Tabona et al. 1984; Becklake et al. 1988; Hankinson and Hodous 1983; Christiani et al. 1994; Glindmeyer et al. 1994; Becklake 1995; Schwartz et al. 1996]. It seems entirely plausible that an analogous phenomenon occurs with regard to adverse pulmonary function effects of occupational exposure to MWF aerosol.

5.2 Tumorigenic Effects in Animals

Few animal data have been published on the tumorigenicity of MWFs. NIOSH is aware of only six animal studies that have examined the tumorigenicity of MWFs [Gilman and Vesselinovitch 1955; Desoille et al. 1973; Jepsen et al. 1977; Wang and John 1988; Gupta and Mehrotra 1989; McKee et al. 1990]. Three of these studies reported only findings related to the skin [Gilman and Vesselinovitch 1955; Jepsen et al. 1977; Gupta and Mehrotra 1989]. Of these three studies, one examined unrefined cutting oil [Gilman and Vesselinovitch 1955], one examined solvent-extracted cutting oil [Jepsen et al. 1977], and the third study did not specify how the cutting oil was refined (although the cutting oil was probably highly refined, as the PAH content was only 5.22%) [Gupta and Mehrotra 1989]. The study by Gilman and Vesselinovitch [1955] found that among mice receiving a skin application of soluble cutting oils formulated from unrefined distillates three times weekly for 310 days, 61% developed skin tumors (of whom 22% had carcinomas) compared with no tumors present in the unexposed control group. Jepsen et al. [1977] found that among mice receiving skin applications of solvent-extracted cutting oils, 80% and 0% of mice developed papillomas after exposure to undiluted and diluted soluble oil, respectively. Jepsen et al. [1977] also studied paraffin-based and naphthalene-based straight oil MWFs. They found that 45% and 0% of mice developed

papillomas after exposure to unused and used paraffin-based solvent-refined straight oil MWF (level of refining unspecified), respectively; they also found that 40% and 100% of mice developed papillomas after exposure to unused and used naphthalene-based straight MWF (level of refining unspecified), respectively. Another study found that both unused and used cutting oils were potent skin tumor initiators [Gupta and Mehrotra 1989]. These investigators found that among mice given a single application of the cutting oil and three times weekly application of a promoting agent (12-0-tetradecanoylphorbol 13-acetate [TPA]), 90% and 60% of mice developed benign skin tumors after exposure to unused and used cutting oil.

Three other animal studies examined the tumorigenic effects of MWF exposure on the skin and other organs [Desoille et al. 1973; Wang and John 1988; McKee et al. 1990]. One study of 20 mice receiving a skin application of used cutting oils (type of refining was not specified) one to three times weekly for 6 months found that two developed pulmonary cancer, and one of the two mice also developed skin cancer [Desoille et al. 1973]. None of the 20 control mice developed cancer. In another animal study, pancreatic carcinoma was found in 9 of 40 Wistar rats orally given undiluted "rust-proof cutting fluid" consisting of sodium nitrite, TEA, and polyethylene glycol for 2 years, whereas none of the 40 control rats developed pancreatic cancer ($P<0.01$) [Wang and John 1988]. All three of the components reported to be in the "rust-proof cutting fluid" (sodium nitrite, TEA, and polyethylene glycol) are components that can be found in some MWFs used in the United States. Finally, one other study found no evidence of carcinogenicity from solvent-extracted cutting oils [McKee et al. 1990].

The animal data are limited in the types of MWFs tested and the outcomes examined. The variety and complexity of MWFs are immense. Even within general classes of MWFs, one can find a wide variety in terms of composition and component concentration (see Chapter 2). Understandably, it would be difficult to select "representative samples" of MWFs for use in animal studies whose findings could be generalized to a wide variety of MWFs. To add to the complexity, chronic application of unused MWFs in animal studies would not be representative of worker exposure to in-use fluids.

In conclusion, there is inadequate animal evidence for the carcinogenicity of MWFs currently in use. Because the carcinogenic activity of individual MWFs depends on the severity of processing of the base oils, and because of the nature and concentration of additives and contaminants and the conditions of use, the existing animal data provide only limited usefulness when interpreting the human data.

5.3 Carcinogenic Effects

There has been concern since the 1940s that occupational exposures to some MWFs may be associated with skin and scrotal cancer, and since the 1970s the concern has

included cancer at other organ sites. This chapter provides a review of the epidemiologic studies that examined the association between MWF exposure and cancer.

5.3.1 Criteria for Inclusion

To be included in this review, an article had to be published in a peer-reviewed journal. Articles were identified from computerized database searches, recommendations from reviewers of earlier drafts of the review, and from references cited in relevant articles. Studies providing data on the association between MWF exposure and cancer were grouped into three categories based on their study design: (1) retrospective cohort mortality and cancer incidence studies of MWF-exposed cohorts and associated nested case-control studies, (2) proportionate mortality ratio (PMR) studies of occupational groups exposed to MWF and associated case-control studies, and (3) population-based studies (primarily case-control interview studies of specific cancer sites that examined cancer risks associated with MWF exposure, or with occupations likely to have MWF exposure [metal machinists, grinders, toolmakers]). The category *population-based studies* includes hospital-based case-control studies because their usual intent is to estimate risks in the general population. For fuller discussion about these study designs and their interpretations, the reader is referred to a textbook on occupational epidemiology [Monson 1990] as well as standard epidemiologic textbooks [Mausner and Kramer 1985; Kleinbaum et al. 1982]. To present the results of the review systematically, the data have been summarized by cancer site in both tables and text.

Not included in the reviews by cancer site are hypothesis-generating studies that examined broad occupational categories based on census or death certificate data. The results of such studies have been summarized separately for all sites combined. A single epidemiologic study of genetic endpoints will also be briefly reviewed.

5.3.2 Studies of Cancer in Broad Occupational Groups

Studies have been conducted that evaluated the risks for many specific cancers among many different occupations and/or industries, some of which had the potential for MWF exposure [Hrubec et al. 1992; Guralnick 1963; Howe and Lindsay 1983; Tola et al. 1988; Milham 1983; Petersen and Milham 1980; Gallagher and Threlfall 1983; Williams et al. 1977; Decoufle et al. 1977; Dubrow and Wegman 1984; Bulbulyan et al. 1992; Magnani et al. 1987; Hall and Rosenman 1991; Greenland et al. 1994]. For the most part, the intent of these studies was hypothesis generation. These studies have included populations from many different geographic areas (e.g., United States, United Kingdom, Finland, Canada, Australia, the Netherlands, and Sweden).

Inherent weaknesses of this type of study include the use of broad occupational categories to define MWF exposure, use of potentially inaccurate sources (death certificates, census data) to define the occupation, the large number of associations tested (which

means that some associations are expected to be statistically significant by chance alone and the inability to control for important confounders such as smoking and alcohol. With these limitations in mind, the findings from these studies are important for suggesting the presence of associations between MWF exposure and particular cancers. For each of the following cancer sites, two or more of the studies found significantly increased risks among occupations with potential MWF exposure (e.g. machinists, grinders, and toolmakers), or industries with potential MWF exposure (e.g., machine shops, metal fabrication): esophageal cancer [Magnani et al. 1987; Hall and Rosenman 1991], stomach cancer [Howe and Lindsay 1983; Hrubec et al. 1992], colorectal cancer [Guralnick 1963; Dubrow and Wegman 1984], lung cancer [Milham 1983; Petersen and Milham 1980; Hrubec et al. 1992; Gallagher and Threlfall 1983; Howe and Lindsay 1983], bladder cancer [Milham 1983; Petersen and Milham 1980; Hrubec et al. 1992], leukemia [Petersen and Milham 1980; Howe and Lindsay 1983; Decoufle et al. 1977], and all cancers combined [Hrubec et al. 1992; Gallagher and Threlfall 1983].

5.3.3 Investigations of Selected Cancers

Table 5–5 describes the cohort studies and PMR studies designed to assess the mortality and/or morbidity of MWF-exposed workers (the population based studies are not included in this table since most of them are specific for each cancer site). The Eisen et al. [1992] and Tolbert et al. [1992] studies have the most statistical power to assess the association between MWF exposure and the risk for cancer because the number of subjects with malignant neoplasms in these studies is an order of magnitude larger than in any of the other cohort studies. Tolbert et al. reported the findings for workers employed at Plants I and II, whereas Eisen reported the findings for workers at Plants I, II, and III. To avoid reporting the results for workers from Plants I and II twice, the findings from these plants are summarized from the report by Tolbert et al. [1992] only, and only the findings from Plant III are summarized from the Eisen et al. [1992] report. Tolbert's findings for Plants I and II were used because her analyses examined the cancer risks associated with exposure to specific classes of MWF. For the purpose of tabulating the number of cohort studies reporting site-specific data for each cancer, Plants I and II [Tolbert et al. 1992] are counted as a single "study," and Plant III is counted as a second study [Eisen et al. 1992].

In general, an RR estimate >1.00 is considered to be statistically significant if the lower bound of the 95% CI for the RR estimate was ≥1.00 or if the two-sided *P* value was ≤0.05 (conversely, an RR estimate <1.00 is considered statistically significant if the upper bound of the 95% CI is <1.00, or if the *P* value is ≤0.05). In tabulating the number of studies with significantly positive findings for each site, a study was counted as statistically significant if the RR estimate overall, or in a relevant major subgroup, was statistically significant. Although statistical significance is not the sole criteria of importance in interpreting the results of a single study or summarizing data from multiple studies, it

Table 5-5. Description of the MWF-exposed cohort and proportionate mortality studies

Author	Type of study/ analysis	Study population	Employment criteria for inclusion	Total number of subjects	Number of malignant neoplasms	Years of followup
Acquavella et al. 1993	SMR*	White workers at a metal-working facility in Iowa; 59% held factory jobs (mortality data in following tables includes only the factory workers)	Hired between 1950 and 1967 and employed at least 6 months	White men = 2,664 White women = 966	White = 103	1950–87
Decoufle 1978	SMR	Blue collar workers at a metal machining plant in north central U.S. (machined gray iron castings)	At least 5 yr of employment in oil-mist-exposed jobs between 1938 and 1967	White men = 2,485	139	To 1/1/68
Eisen et al. 1992	SMR	Plant III: Saginaw Steering Gear (manufactures steering gears)	Employed at least 3 yr between 1939 and 1/1/85	White men = 8,983	White = 183	1941–1/1/85
Järvholm and Lavenius 1987	SIR	Grinding and turning department workers employed at a bearing-ring manufacturing plant in Sweden	Exposed at least 5 yr and employed at any time between 1950 and 1966	White men = 792	67	1958–83
Järvholm et al. 1985	SIR	Turning department workers employed at bearing-ring manufacturing plant in Sweden	Employed at any time between 1960 and 1980	White men = 682	24	1960–80

See footnotes at end of table.

(Continued)

Table 5-5 (Continued). Description of the MWF-exposed cohort and proportionate mortality studies

Author	Type of study/ analysis	Study population	Employment criteria for inclusion	Total number of subjects	Number of malignant neoplasms	Years of followup
Mallin et al. 1986	PMR	Workers at a diesel engine and construction equipment manufacturer in Illinois (employed 10+ yr; 461 eligible deaths among union workers)	Died between 1/1/70 and 3/31/82 and employed 10 yr or more; plant began operation in 1946	White men = 351 Black men = 110	White = 92 Black = 36	1970–2/31/82
Park and Mirer 1996	PMR/ MOR	Workers employed at Detroit area engine plants (Plant 1 and Plant 2)	Employed at least 2 yr, active any time between 1966 and 1987, and died between 1/1/70 and 12/31/89	White men = 1,170 Black men = 613	White = 306 Black = 146	1970–12/31/89
Park et al. 1988	PMR/ MOR	Hourly workers at a ball-bearing manufacturing plant in Connecticut (soluble MWFs predominantly used in grinding operations)	Died between 1/1/69 and 7/31/82 and employed 10 yr or more	White men= 616	White = 157	1969–82
Park et al. 1994	PMR/ MOR†	Workers employed in a tool and die area of an automotive stamping and assembly plant	2 yr of employment before 1/1/89	NA	NA	1978–88

See footnotes at end of table.

(Continued)

Table 5-5 (Continued). Description of the MWF-exposed cohort and proportionate mortality studies

Author	Type of study/ analysis	Study population	Employment criteria for inclusion	Total number of subjects	Number of malignant neoplasms	Years of followup
Rotimi et al. 1993	SMR	Hourly workers at Ohio engine manufacturing plants	Employed any time between 1973 and 1986; also, retired and alive as of 1970; no minimum employment	White men = 5,331 Black men = 1,180	White = 178 Black = 60	1970–87
Silverstein et al. 1988	PMR/ MOR	Union workers at a ball-bearing manufacturing plant in Connecticut	Died between 1950 and 1982, and employed 5 yr or more	White men = 1,532	White = 342	1950–6/30/82
Tolbert et al. 1992	SMR	Hourly workers. Plant I:Gear and Axle, Hamtramak (produces axles and gears) Plant II: Hydra-Matic, Ypsilanti (produces transmissions)	Employed at least 3 yr before 1/1/85	White men = 17,743 Black men = 5,641	White = 1648 Black = ~224 (Plant I only)	1941–1/1/85
Vena et al. 1985	PMR	Union workers at an engine plant (machine and assembly) in New York (before 1950, soluble and insoluble MWFs used; increased use of synthetic MWFs in the mid-1950s)	Died between 1/1/70 and 12/31/79 and employed 10 yr or more; plant began operation in 1938	White men = 472 Black men = 37	White = 128	1970–12/31/79

*Abbreviations: NA=not available, MOR=mortality odds ratio, PMR=proportionate mortality ratio, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

†Only the MOR findings from the tool and die area are provided, because the PMR findings were for workers employed in an automotive stamping and assembly plant where MWF exposures were minimal.

is used as a summary measure in this review because it is applicable to all studies and its meaning is widely understood. CIs, which are preferable to *P* values in interpreting epidemiologic data, are provided in this review for studies where they were reported by the authors.

Tables 5–6 through 5–17 summarize the data generated to examine the association between MWF exposure and risk of cancer at specific organ sites. In an effort to keep the tables to a reasonable size, not all of the RR estimates reported by these studies are included. The Tolbert study provides the risk among those ever exposed to each of the specific classes of MWFs, and the remaining studies provide the risk for all workers with potential MWF exposure and (when available) the risk among workers with the highest duration of employment.

This section provides detailed information only for cancer sites for which there is substantial evidence for an association with MWF exposure (skin, larynx, rectum, pancreas, bladder), and two other sites for which there is more limited evidence for such an association (stomach and esophageal). For other sites, statistically significant (positive or negative) findings are briefly summarized. To keep the discussion to a reasonable length, details presented in the tables are not necessarily repeated in the text.

5.3.3.1 Skin and Scrotal Cancer

Case reports

Since the 1940s, evidence has accumulated to support an association between skin (including scrotal) cancer and occupational exposures to MWFs. Several case reports have identified skin cancer among MWF-exposed workers [Henry 1947; Mastromatteo 1955; Cruickshank and Gourevitch 1952; Cruickshank and Squire 1950; Waterhouse 1971, 1972; Kipling and Waldron 1976; Thony et al. 1976; Fife 1962].

Cohort studies

A cohort study of turners employed between 1960 and 1980 at a Swedish company producing bearing rings found that the MWF-exposed turners had an increased risk for squamous cell carcinoma of the skin (observed=5 [four scrotal, and one facial], exposed=0.3, $P<0.001$) [Järvholm et al. 1985] (Table 5–6). Three additional scrotal cancer cases were identified in the 1987 update of this cohort [Järvholm and Lavenius 1987]. The authors suggest that use of soluble oil MWFs is not associated with scrotal cancer because no cases were observed among the grinders who often use soluble oils [Järvholm and Lavenius 1987]. Furthermore, it should be noted that changes in refinery methods since the 1950s have reduced the straight oil content of PAHs, which have been suggested as the causative agent for MWF-associated skin cancer [Järvholm and Easton 1990; McKee et al. 1990]. Because of the high survival rate for nonmelanoma skin cancer, mortality studies are an inappropriate design for studying this cancer. As would be

Table 5-6. Skin/scrotal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site
Cohort studies:						
Eisen et al. 1992	Michigan	SMR	10	0.61	0.29, 1.13	White auto workers in Plant I—skin cancer
			11	1.06	0.53, 1.89	White auto workers in Plant II—skin cancer
			7	1.27	0.51, 2.62	White auto workers in Plant III—skin cancer
Järvholm and Lavenius 1987	Sweden	SIR	7	†	†	Turners only—scrotal cancer
Järvholm et al. 1985	Sweden	SIR	5	16.6	$P<0.001$	Turners employed between 1960 and 1980—squamous cell cancer of the skin
Proportionate mortality studies:						
Park et al. 1988	Connecticut	PMR	4	1.88	0.51, 4.80	White—skin cancer
Silverstein et al. 1988	Connecticut	PMR	4	0.92	0.25, 2.34	White—skin cancer
Vena et al. 1985	New York	PMR	1	0.60	NS	Based on U.S. mortality, white—skin cancer

(Continued)

*Abbreviations: CI=confidence interval, NS=not statistically significant, PMR=proportionate mortality ratio, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

†Expected cases of scrotal cancer were too few to make a reliable estimate of risk.

Table 5-6 (Continued). Skin/scrotal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Population-based study:						
Rousch et al. 1982	Connecticut	Case control	26	10.5	4.0, 36.9	Workers ever employed as toolmaker, setter, set-up man, hardener, polisher, automatic screw operator, machinist, or machine operator—squamous cell cancer of the scrotum

Table 5-7. Laryngeal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Eisen et al. 1992	Michigan	SMR	2	0.77	0.09, 2.79	White auto workers in Plant III
Eisen et al. 1994	Michigan	Nested case control	28	2.23	1.25, 3.98	Highest exposure to straight MWFs
Tolbert et al. 1992	Michigan	SMR	23	1.98	1.26, 2.98	Ever exposed to straight oil, white
			30	1.41	0.95, 2.01	Ever exposed to soluble oil, white
			8	1.57	0.68, 3.09	Ever exposed to synthetic oil, white
			1	0.50	0.01, 2.78	Ever exposed to straight oil, black
			6	0.91	0.70, 1.17	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	1.76	NS	White
Park and Mirer 1996	Detroit area	PMR	1	0.69	0.02, 3.83	Engine Plant 1, white
			4	1.67	0.46, 4.28	Engine Plant 2, white
Vena et al. 1985	New York	PMR	3	1.81	NS	Based on U.S. mortality, white

(Continued)

*Abbreviations: CI=confidence interval, NA=not available, NS=not statistically significant, PMR=proportionate mortality ratio, SMR=standardized mortality ratio.

Table 5-7 (Continued). Laryngeal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies:						
Ahrens et al. 1991	Germany	Case control	NA	2.2	0.9, 5.3	Ever exposed to mineral oil
Brown et al. 1988	Texas	Case control	5	0.53	0.18, 1.58	Ever worked as machinists
Haguenoer et al. 1990	France	Case control	7	1.8	NS	Employed in metal work or as mechanic for at least 15 yr
Russi et al. 1997	Connecticut	Case control	81	1.48	1.01, 2.16	High machining fluid exposure versus oral cancer controls
				1.05	0.81, 1.35	High machining fluid exposure versus population controls
Wortley et al. 1992	Washington State	Case control	NA	1.8	0.5, 6.2	Ever employed as grinding, abrading, or buffing operator
			19	1.0	0.5, 1.9	Ever employed in precision metal-working
Zagraniski et al. 1986	Connecticut	Case control	22	2.5	1.2, 5.2	Ever worked as machinist
			17	2.1	1.0, 4.7	Ever worked as metal grinder
Zheng et al. 1992	China	Case control	12	1.2	0.5, 3.1	Usual occupation of blacksmith, machine-tool operator, electrician, or other related worker
			25	0.8	0.4, 1.6	Self-reported exposure to lubricant fumes

Table 5-8. Rectal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Decoufle 1978	Michigan	SMR	8	1.25	NS	White
			4	1.29	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	7	1.70	0.68, 3.50	White autoworkers in Plant III
Tolbert et al. 1992	Michigan	SMR	37	1.47	1.04, 2.03	Ever exposed to straight oil, white
			51	1.09	0.81, 1.43	Ever exposed to soluble oil, white
			9	0.92	0.42, 1.74	Ever exposed to synthetic oil, white
			1	0.45	0.01, 2.53	Ever exposed to straight oil, black
			3	0.68	0.14, 1.99	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	0.80	NS	White
Park et al. 1988	Connecticut	PMR	11	3.07	1.54, 5.50	White
Silverstein et al. 1988	Connecticut	PMR	14	1.36	0.81, 2.29	White
Vena et al. 1985	New York	PMR	4	1.38	NS	Based on U.S. mortality, white
			4	2.76	$P<0.05$	Employed in engine plant >20 yr

(Continued)

*Abbreviations: NS=not statistically significant, PMR=proportionate mortality ratio, SMR=standardized mortality ratio.

Table 5-8 (Continued). Rectal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies:						
Gerhardsson de Verdier et al. 1992	Sweden	Case control	25	2.1	1.1, 4.0	Ever exposed to cutting oils
Siemiatycki et al. 1987	Montreal	Case control	13	0.7	90% CI: 0.4, 1.0	Ever exposed to cutting oils

Table 5-9. Pancreatic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	11	2.0	0.9, 3.8	Total workforce
			5	3.6	1.2, 8.3	Factory workers employed >10 yr, hired between 1950 and 1959
Decoufle 1978	Michigan	SMR	8	1.05	NS	White
			1	0.27	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	8	0.87	0.37, 1.71	White auto workers in Plant III
Rotimi et al. 1993	Ohio	SMR	8	0.91	0.39, 1.79	Engine plant, white
			7	3.03	1.21, 6.24	Engine plant, black
Tolbert et al. 1992	Michigan	SMR	34	0.80	0.55, 1.11	Ever exposed to straight oil, white
			61	0.77	0.59, 1.00	Ever exposed to soluble oil, white
			19	1.03	0.62, 1.61	Ever exposed to synthetic oil, white
			8	1.40	0.60, 2.77	Ever exposed to straight oil, black
			19	1.62	0.98, 2.54	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	5	1.19	NS	White
			5	3.57	$P<0.05$	Black

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, NA=not available, NS=not statistically significant, PMR=proportionate mortality ratio, SMR=standardized mortality ratio.

Table 5-9 (Continued). Pancreatic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Proportionate mortality studies (continued):						
Park and Mirer 1996	Detroit area	PMR	10	1.82	0.87, 3.34	Engine Plant 1, white
			11	1.23	0.62, 2.21	Engine Plant 2, white
		MOR	4	3.61	1.04, 12.6	Machining with straight MWF
Park et al. 1988	Connecticut	PMR	8	1.09	0.55, 2.18	White
Silverstein et al. 1988	Connecticut	PMR	24	1.43	0.96, 2.12	White
		MOR	9	3.10	$P = 0.05$	Employed in grinding 10+ yr
		MOR	5	3.71	$P = 0.05$	Employed in machinery 10+ yr
Vena et al. 1985	New York	PMR	11	1.89	$P<0.05$	Based on U.S. mortality, white
			7	2.32	$P<0.05$	Employed in engine plant >20 yr
Population-based study:						
Mack and Paganini 1981	Los Angeles	Incidence	21	1.30	NA	Machinists, white men

Table 5–10. Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site
Cohort studies:						
Decoufle 1978	Michigan	SMR	6	1.2	NS	White—bladder and lower urinary
			2	0.8	NS	White, 5+ yr of heavy oil mist exposure—bladder and lower urinary tract
Järvholm and Lavenius 1987	Sweden	SIR	7	1.04	0.4, 2.2	Grinders and turners—bladder
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	0.78	NS	White—bladder
Park and Mirer 1996	Detroit area	PMR	6	2.16	0.79, 4.70	Engine Plant 1 workers, white—bladder
			5	1.13	0.37, 2.64	Engine Plant 2 workers, white—bladder
		MOR	7	2.99	1.15, 7.77	Grinding with straight MWF—bladder
		MOR	4	2.86	1.14, 7.18	Machining or heat treat employment—bladder
Park et al. 1988	Connecticut	PMR	1	0.24	0.01, 1.31	White—bladder
Silverstein et al. 1988	Connecticut	PMR	14	1.26	0.75, 2.13	White—bladder

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NA=not available, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–10 (Continued). Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Vena et al. 1985	New York	PMR	7	2.28	$P<0.05$	Based on U.S. mortality, white—bladder
			4	2.76	NS	Employed in engine plant >20 yr—bladder
Population-based studies:						
Claude et al. 1988	Germany	Case control	18	2.25	1.0, 5.6	Ever worked as turner— bladder and lower urinary tract
			43	0.84	0.54, 1.3	Ever employed as metal worker—bladder and lower urinary tract
Coggon et al. 1984	Britain	Case control	52	1.3	0.9, 1.9	Ever had an occupation with potential cutting oil exposure—bladder
			21	1.5	0.8, 2.8	Ever had an occupation with potentially high cutting oil exposure—bladder
Gonzalez et al. 1989	Spain	Case control	31	0.77	0.5, 1.1	Ever worked as toolmaker ≥6 months— bladder
			NA	1.86	1.2, 2.8	Ever worked as machinery adjuster, assembler or mechanic ≥6 months—bladder

(Continued)

Table 5–10 (Continued). Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Howe et al. 1980	Canada	Case control	NA	2.7	1.1, 7.7	Ever worked as metal machinist—bladder
Malker et al. 1987	Sweden	Case control	322	1.19	$P<0.01$	Toolmakers or machinists in 1960—bladder
Schifflers et al. 1987	Belgium	Case control	34	2.45	1.28, 4.69	All metal workers—bladder
			8	2.57	0.92, 7.16	Turners—bladder
Siemiatycki et al. 1987	Montreal	Case control	47	1.2	90%CI: 1.0, 1.6	Ever exposed to cutting oils—bladder
Population-based studies:						
Silverman et al. 1983	Detroit	Case control	137	1.1	0.8, 1.5	All metal machinists—bladder and lower urinary tract
			32	1.5	0.9, 2.7	Tool and die worker—bladder and lower urinary tract
Silverman et al. 1989a	U.S.	Case control	102	1.3	1.0, 1.7	Ever worked as machinist ≥6 months— bladder
			51	1.4	0.9, 2.1	Ever worked as drill press operator ≥6 months— bladder
Silverman et al. 1989b	U.S.	Case control	26	1.1	0.6, 1.9	Metal machinery workers— bladder

(Continued)

Table 5–10 (Continued). Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Steenland 1987	Ohio	Case control	11	2.00	NS	Ever worked as grinding machine operator—bladder and lower urinary tract
			45	0.69	$P<0.05$	Ever worked as machinist—bladder and lower urinary tract
Vineis and Magnani 1985	Italy	Case control	16	1.5	0.7, 3.3	Ever employed in machine tools ≥6 months—bladder

Table 5–11. Stomach cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	5	1.4	0.4, 3.2	Total workforce
			2	2.3	0.3, 8.1	Factory workers employed >10 years, hired between 1950 and 1959
Decoufle 1978	Michigan	SMR	17	1.25	NS	White
			11	1.67	NS	White, 5 yr or more of heavy exposure to oil mist
Eisen et al. 1992	Michigan	SMR	4	0.59	0.16, 1.50	White auto workers in Plant III
Järvholm and Lavenius 1987	Sweden	SIR	9	1.11	0.5, 2.1	Grinders and turners
Rotimi et al. 1993	Ohio	SMR	15	2.54	1.42, 4.20	Engine plant workers, white
			2	0.85	0.1, 3.06	Engine plant workers, black
Tolbert et al. 1992	Michigan	SMR	49	1.12	0.83, 1.48	Ever exposed to straight oil, white
			99	1.19	0.97, 1.45	Ever exposed to soluble oil, white
			21	1.28	0.79, 1.96	Ever exposed to synthetic oil, white
			5	0.76	0.24, 1.77	Ever exposed to straight oil, black
			17	1.01	0.59, 1.62	Ever exposed to soluble oil, black

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–11 (Continued). Stomach cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Proportionate mortality studies:						
Park et al. 1988	Connecticut	PMR	11	1.99	1.12, 3.54	White
		MOR	8	6.2	*P*=0.05	Nested case-control study—those workers ever exposed to soluble oil
Park and Mirer 1996	Detroit area	PMR	8	2.09	0.90, 4.11	Engine Plant 1 workers, white
			8	1.30	0.56, 2.57	Engine Plant 2 workers, white
		MOR	3	5.13	1.56, 16.9	Cam-/crankshaft department (Plant 1)
Silverstein et al. 1988	Connecticut	PMR	35	1.97	1.43, 2.72	White
			13	3.39	*P*<0.001	Employed in grinding 10 yr or more
Vena et al. 1985	New York	PMR	4	0.91	NS	Based on U.S. mortality, white
			3	1.37	NS	Employed in engine plant > 20 yr
Mallin et al. 1986	Illinois	PMR	6	1.85	NS	White
Population-based studies:						
Chow et al. 1994	Sweden	SIR	376	1.11	NS	Toolmakers and machinists

(Continued)

Table 5–11 (Continued). Stomach cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies (continued):						
Kneller et al. 1990	China	SIR	191	1.41	$P<0.01$	Metal grinders, polishers, tool sharpeners, machine-tool operators
			193	1.11	NS	Toolmakers, metal pattern makers, metal workers
Siemiatycki et al. 1987	Montreal	Case control	24	1.1	90%CI: 0.8, 1.4	Ever exposed to cutting oils
Other:						
Park 1994	Ohio	MOR	2	9.55	2.3, 40	Ever employed as tool and die worker

Table 5–12. Esophageal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Decoufle 1978	Michigan	SMR	4	1.14	NS	White
			1	0.59	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	6	1.38	0.50, 3.01	White auto workers in Plant III
Järvholm and Lavenius 1987	Sweden	SIR	2	1.25	0.2, 4.5	Exposed to oil mist at least 5 yr
Tolbert et al. 1992	Michigan	SMR	22	1.18	0.74, 1.79	Ever exposed to straight oil, white
			35	1.03	0.72, 1.43	Ever exposed to soluble oil, white
			8	0.99	0.43, 1.94	Ever exposed to synthetic oil, white
			5	0.76	0.24, 1.77	Ever exposed to straight oil, black
			10	0.72	0.34, 1.32	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	1.01	NS	White
Park et al. 1988	Connecticut	PMR	6	1.85	0.68, 4.02	White
Silverstein et al. 1988	Connecticut	PMR	13	1.83	1.07, 3.12	White
Vena et al. 1985	New York	PMR	3	1.16	NS	Based on U.S. mortality, white
			2	1.43	NS	Employed in engine plant >20 yr

*Abbreviations: CI=confidence interval, PMR=proportionate mortality ratio, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–13. Brain/nervous system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site or cell type
Cohort study:						
Decoufle 1978	Michigan	SMR	5	1.5	NS	White—brain and other parts of nervous system
			0	—	—	White, 5+ yr of heavy oil mist exposure—brain and other parts of nervous system
Eisen et al. 1992	Michigan	SMR	7	0.85	0.34, 1.75	White auto workers in Plant III—brain
Tolbert et al. 1992	Michigan	SMR	22	1.08	0.68, 1.64	Ever exposed to straight oil, white— brain
			46	1.24	0.91, 1.66	Ever exposed to soluble oil, white— brain
			6	0.61	0.22, 1.33	Ever exposed to synthetic oil, white— brain
			—	—	—	Ever exposed to straight oil, black— brain
			2	0.77	0.09, 2.78	Ever exposed to soluble oil, black— brain
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	1	†	—	White—brain, nervous system
Park et al. 1988	Connecticut	PMR	4	1.23	0.34, 3.15	White—brain and other CNS

See footnotes at end of table.

(Continued)

Table 5–13 (Continued). Brain/nervous system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Proportionate mortality studies (continued):						
Silverstein et al. 1988	Connecticut	PMR	6	0.99	0.44, 2.19	White—brain and other CNS
Vena et al. 1985	New York	PMR	2	0.71	NS	Based on U.S. mortality, white—brain and other CNS
Population-based studies:						
Carpenter et al. 1988	U.S.	Case control	28	1.57	NS	Ever exposed to cutting oils while employed at nuclear facilities—CNS cancer
Reif et al. 1989	New Zealand	Case control	NA	0.96	0.13, 7.44	Most recent occupation was as a metal processor (smelting, grinding, casting, molders, platers)—brain or other CNS tumor
Thomas et al. 1986	U.S.	Case control	47	2.1	1.2, 3.6	Usual occupation of precision metal worker—brain or other CNS tumor
			26	1.8	0.9, 3.7	Usual occupation as machinist—brain or other CNS tumor
			7	1.8	0.5, 7.4	Usual occupation as tool and die maker— brain or other CNS tumor

See footnotes at end of table.

(Continued)

Table 5–13 (Continued). Brain/nervous system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Population-based studies (continued):						
Thomas et al. 1987	U.S.	Case control	49	1.6	1.0, 2.6	Ever employed at a job with potential cutting oil exposure—astrocytoma

*Abbreviations: CI=confidence interval, PMR=proportionate mortality ratio, NA=not available, NS=not statistically significant, SMR=standardized mortality ratio.
†Numbers were too small to calculate.

Table 5–14. Prostate cancer results from epidemiologic studies of MWF-exposed populations

Authors	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Decoufle 1978	Michigan	SMR	6	0.57	NS	White
			3	0.58	NS	White, 5+ yr of heavy oil mist exposure
Järvholm and Lavenius 1987	Sweden	SIR	6	0.34	0.1, 0.7	Grinders and turners
			6	0.38	0.1, 0.8	Grinders and turners, at least 20 yr since onset of exposure
Rotimi et al. 1993	Ohio	SMR	8	0.87	0.37, 1.70	Engine plant workers, white
			5	1.29	0.41, 3.00	Engine plant workers, black
Tolbert et al. 1992	Michigan	SMR	72	1.16	0.91, 1.46	Ever exposed to straight oil, white
			125	1.08	0.90, 1.28	Ever exposed to soluble oil, white
			26	1.11	0.73, 1.63	Ever exposed to synthetic oil, white
			12	0.98	0.51, 1.72	Ever exposed to straight oil, black
			23	0.98	0.62, 1.47	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	10	1.53	NS	White

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–14 (Continued). Prostate cancer results from epidemiologic studies of MWF-exposed populations

Authors	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Proportionate mortality studies (continued):						
Park and Mirer 1996	Detroit area	PMR	8	1.08	0.47, 2.13	Engine Plant 1 workers, white
			19	1.61	1.03, 2.50	Engine Plant 2 workers, white
		MOR	4	4.52	1.43, 14.3	Tool grinders
		MOR	3	4.51	1.22, 16.6	Workers machining aluminum pistons
Park et al. 1988	Connecticut	PMR	10	0.92	0.50, 1.69	White
Proportionate mortality studies:						
Silverstein et al. 1988	Connecticut	PMR	29	1.00	0.70, 1.43	White
Vena et al. 1985	New York	PMR	7	1.06	NS	Based on U.S. mortality, white
			2	0.72	NS	Employed in engine plant >20 yr
Population-based studies:						
Aronson et al. 1996	Montreal	Case control	58	1.40	1.00, 1.97	Workers with substantial exposure to lubricating oils and greases
Siemiatycki et al. 1987	Montreal	Case control	47	1.2	90% CI: 1.0, 1.6	Ever exposed to cutting oils

Table 5-15. Lung/respiratory system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site or cell type
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	42	1.3	0.9, 1.8	Total workforce
			18	2.2	1.3, 3.4	Factory workers employed >10 yr and hired between 1950 and 1959
Eisen et al. 1992	Michigan	SMR	60	0.91	0.70, 1.17	White auto workers in Plant III
Järvholm and Lavenius 1987	Sweden	SIR	5	0.40	0.1, 0.9	Grinders and turners
			3	0.30	0.1, 0.9	Grinders and turners, at least 20 yr since onset of exposure
Rotimi et al. 1993	Ohio	SMR	81	1.20	0.95, 1.40	Engine plant workers, white
			23	1.35	0.85, 2.02	Engine plant workers, black
Schroeder et al. 1997	Michigan	Nested case control	40	0.56	0.38, 0.82	Workers with highest exposure to synthetic MWFs
Tolbert et al. 1992	Michigan	SMR	251	1.02	0.90, 1.15	Ever exposed to straight oil, white
			478	1.07	0.97, 1.17	Ever exposed to soluble oil, white
			116	1.01	0.83, 1.21	Ever exposed to synthetic oil, white
			35	1.06	0.74, 1.48	Ever exposed to straight oil, black
			64	0.91	0.70, 1.17	Ever exposed to soluble oil, black

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NA=not available, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5-15 (Continued). Lung/respiratory system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	34	1.27	NS	White
			12	1.29	NS	Black
Park and Mirer 1996	Detroit area	PMR	33	0.83	0.60, 1.15	Engine Plant 1 workers, white
			81	1.23	1.00, 1.52	Engine Plant 2 workers, white
		MOR	Not reported	0.89	0.67, 1.2	Workers grinding with soluble MWF
Park et al. 1988	Connecticut	PMR	59	1.23	0.96, 1.57	White men—both primary and secondary lung cancer
		Case control	5	19.3	*P*=0.008	Women ever employed in grinding
Silverstein et al. 1988	Connecticut	PMR	83	0.92	0.75, 1.13	White—both primary and secondary lung cancer
			13	0.62	NS	Workers employed in grinding 10 yr or more
Vena et al. 1985	New York	PMR	48	1.25	NS	Based on U.S. mortality, white
			29	1.40	NS	Employed in engine plant >20 yr

(Continued)

Table 5-15 (Continued). Lung/respiratory system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Population-based studies:						
Coggon et al. 1984	Britain	Case control	113	1.4	1.1, 1.8	Ever had an occupation with potential MWF exposure
			25	1.0	0.6, 1.6	Ever had an occupation with potentially high MWF exposure
Jöckel et al. 1992	Germany	Case control	NA	2.2	1.05, 4.75	Employed 6 months or more as a turner, grinder, driller, or cutter
Siemiatycki et al. 1987	Montreal	Case control	23	1.5	90% CI: 1.0, 2.1	Ever exposed to cutting oils—oat cell cancer of the lung
Other:						
Park et al. 1994	Ohio	MOR	4	1.64	0.56, 4.8	Ever employed as tool and die worker

Table 5-16. Colon cancer from results epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	1	0.1	0, 0.5	Total workforce
Decoufle 1978	Michigan	SMR	17	1.3	NS	White
			7	1.1	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	22	1.47	0.92, 2.22	White auto workers in Plant III
Tolbert et al. 1992	Michigan	SMR	59	0.79	0.61, 1.03	Ever exposed to straight oil, white
			116	0.85	0.70, 1.02	Ever exposed to soluble oil,white
			26	0.83	0.54, 1.22	Ever exposed to synthetic oil, white
			3	0.42	0.08, 1.23	Ever exposed to straight oil, black
			8	0.55	0.24, 1.09	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	10	1.17	NS	White
			2	1.04	NS	Black
Park et al. 1988	Connecticut	PMR	15	1.18	0.71, 1.94	White
Silverstein et al. 1988	Connecticut	PMR	41	1.39	1.03, 1.88	White
			13	1.89	*P*=0.02	Employed in grinding 10 yr or more
Vena et al. 1985	New York	PMR	14	1.49	NS	Based on U.S. mortality, white
			8	1.70	NS	Employed in engine plant >20 yr

(Continued)

*Abbreviations: CI=confidence interval, PMR=proportionate mortality ratio, NS=not statistically significant, SMR=standardized mortality ratio.

Table 5-16 (Continued). Colon cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies:						
Gerhardsson de Verdier et al. 1992	Sweden	Case control	25	1.5	0.8, 2.8	Ever exposed to cutting fluids
Siemiatycki et al. 1987	Montreal	Case control	32	1.0	90% CI: 0.8, 1.4	Ever exposed to cutting oils

Table 5-17. Hematopoietic and lymphopoietic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site
Cohort studies:						
Decoufle 1978	Michigan	SMR	3	0.56	NS	White—leukemia
			2	0.76	NS	White, 5+ yr of heavy oil mist exposure—leukemia
Eisen et al. 1992	Michigan	SMR	9	1.07	0.49, 2.02	White auto workers in Plant III—leukemia
Tolbert et al. 1992	Michigan	SMR	38	1.25	0.88, 1.71	Ever exposed to straight oil, white— leukemia
			75	1.33	1.05, 1.67	Ever exposed to soluble oil, white— leukemia
			16	1.22	0.70, 1.98	Ever exposed to synthetic oil, white—leukemia
			2	0.55	0.22, 1.13	Ever exposed to straight oil, black—leukemia
			4	0.74	0.20, 1.90	Ever exposed to soluble oil, black— leukemia

See footnotes at end of table.

(Continued)

Table 5-17 (Continued). Hematopoietic and lymphopoietic cancer results from epidemiologic studies of MWF-exposed populations

Autor	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	8	1.19	NS	White—lymphatic and hematopoietic
			3	1.36	NS	White—non-Hodgkin's lymphoma
			1	0.38	NS	White—leukemia
			6	3.54	*P*<0.01	Black—lymphatic and hematopoietic
			3	6.87	*P*<0.05	Black—non-Hodgkin's lymphoma
			1	†		Black—leukemia
Park and Mirer 1996	Detroit area	PMR	4	1.03	0.28, 2.63	Engine Plant 1 workers, white—non-Hodgkin's lymphoma and multiple myeloma
			6	0.95	0.35, 2.08	Engine Plant 2 workers, white—non-Hodgkin's lymphoma and multiple myeloma
		MOR	7	4.12	1.10, 15.4	Workers machining with soluble MWF—non-Hodgkin's lymphoma and multiple myeloma

See footnotes at end of table.

(Continued)

Table 5-17 (Continued). Hematopoietic and lymphopoietic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Proportionate mortality studies (continued):						
Park et al. 1988	Connecticut	PMR	7	0.60	0.29, 1.23	White—all lymphopoietic cancer
			1	0.23	0.01, 1.26	White—leukemia
Silverstein et al. 1988	Connecticut	PMR	27	1.03	0.71, 1.50	White—all lymphopoietic cancer
			12	1.10	0.63, 1.94	White—leukemia
			5	0.84	NS	Employed in grinding 10 yr or more—all lymphopoietic cancer
Vena et al. 1985	New York	PMR	8	0.86	NS	Based on U.S. mortality, white—lymphatic and hematopoietic
			4	0.85	NS	Employed in engine plant >20 yr—lymphatic and hematopoietic
Population-based studies:						
Siemiatycki et al. 1987	Montreal	Case control	22	1.3	90% CI: 0.9, 1.8	Ever exposed to cutting oils—non-Hodgkin's lymphoma
Other:						
Park et al. 1994	Ohio	MOR	3	5.38	1.6, 18	Ever employed as tool and die worker

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NS=not statistically significant, SMR=standardized mortality ratio.
†Numbers were too small to calculate.

expected, a significantly elevated risk was not observed in the one cohort mortality study that reported skin cancer mortality (Table 5–6).

PMR studies

Again, as would be expected, a significantly elevated risk was not observed in any of the three PMR studies that reported skin cancer mortality (Table 5–6).

Population-based studies

In a population-based case-control study in Connecticut involving 45 cases of squamous cell carcinoma of the scrotum, those ever employed in an occupation potentially exposed to MWFs (toolmaker, setter, set-up man, hardener, polisher, automatic screw operator, machinist, and machine operator) had an increased risk for this cancer (OR=10.5, 95% CI=4.0–36.9) [Roush et al. 1982].

Conclusion for skin cancer

In conclusion, the large number of case reports, the cancer incidence study, and the case-control study suggest that primarily straight MWF exposure is associated with an increased risk for skin and scrotal cancer. However, as a result of the changes in MWF composition and reduction of impurities over the last several decades, current exposures to straight MWFs may be associated with a substantially reduced risk for scrotal and skin cancer.

5.3.3.2 Laryngeal Cancer

Cohort studies

Only the three automobile manufacturing plants studies conducted by Eisen et al. [1992] and Tolbert et al. [1992] reported site-specific data for laryngeal cancer (Table 5–7). Tolbert et al. [1992] reported a statistically significant standardized mortality ratio (SMR) of 1.98 for laryngeal cancer among whites ever exposed to straight oil, and a nearly significant SMR of 1.41 for soluble oil exposure in Plants I and II combined. The SMR for laryngeal cancer in Plant 3 was not elevated [Eisen et al. 1992]. In a case-control analysis including all three plants and incident as well as deceased cases, a categorized exposure analysis found an OR of 2.23 (95% CI=1.25–3.98) among individuals with >0.5 mg/m^3-years of straight oil particulate exposure. Eisen et al. [1994] also examined the association between laryngeal cancer and specific components or contaminants of MWFs (biocides, steel, iron, aluminum, sulfur, and chlorine). There was some evidence for confounding by sulfur, but models including both exposure variables still had a significantly elevated OR in the highest straight MWF exposure category (OR=1.91, 95% CI=1.01–3.62). Although unable to adjust for smoking and alcohol (two important risk factors for laryngeal cancer) Austin [1982] did not think that these risk factors confounded the results. The author found that the risk of lung cancer and

cirrhosis did not increase with increasing exposure to straight MWFs, suggesting that an association did not exist between straight oil exposure and cigarette smoking or alcohol use.

PMR studies

Among the three PMR studies reporting site-specific results for larynx cancer, the overall PMRs ranged from 1.7 to 1.8 [Park and Mirer 1996; Vena et al. 1985; Mallin et al. 1986]. In the Vena et al. [1985] study, a significantly elevated PMR was found for workers employed less than 20 years and those who were employed after 1950 (PMR=3.95, $P<0.05$ for both subgroups).

Population-based studies

Of six studies that defined occupational categories in sufficient detail to examine risk associated with exposure to MWF, one found a significant risk for "ever employment as a machinist" (SMR=2.5, 95% CI=1.2–5.2) or metal grinder (SMR=2.1, 95% CI=1.0–4.7) after adjustment for smoking and alcohol [Zagraniski et al. 1986]. A case-control study (hospital-based) of 100 laryngeal cancer cases and 100 controls found a nonsignificantly elevated risk among those who self-reported ever having mineral oil exposure (OR=2.2, 95% CI=0.9–5.3, adjusted for smoking and alcohol) [Ahrens et al. 1991]. One other study found an elevation in laryngeal cancer risk among workers with potential MWF exposure; however, this study did not control for smoking or alcohol consumption [Russi et al. 1997].

Conclusion for laryngeal cancer

In conclusion, several studies suggest that MWF exposure may be associated with laryngeal cancer. In particular, the studies by Eisen et al. [1992, 1994] and Tolbert et al. [1992] suggest that laryngeal cancer is associated with exposure to straight oil MWFs.

5.3.3.3 Rectal Cancer

Cohort studies

Aside from the three automobile manufacturing plant studies conducted by Eisen et al. [1992] and Tolbert et al. [1992], only one cohort study has reported site-specific results for rectal cancer [Decoufle 1978] (Table 5–8). Tolbert et al. [1992] reported an association between straight oil exposure and rectal cancer among white but not black workers. The SMR for ever-exposure to straight MWFs among whites was 1.47 (95% CI=1.04–2.03). Poisson regression analyses revealed a trend of increasing rectal cancer risk in relation to years of exposure to straight MWFs ($P<0.0001$). The RR for the most highly exposed group was 3.2 (95% CI=1.6–6.2). Plant III had a nonsignificant excess (SMR=1.70) [Eisen et al. 1992]. The Decoufle [1978] study found a slight excess of rectal cancer mortality that was not statistically significant.

PMR studies

Among the four PMR studies reporting data for rectal cancer, one found a significant excess in the cohort with potential exposure to straight and soluble oil MWFs (PMR=3.07, 95% CI=1.54–5.50) [Park et al. 1988]. Park et al. [1988] did not report the risk for each specific type of MWF exposure. A second PMR study found a significant excess in a subgroup with employment in an engine plant for >20 years (PMR=2.76, $P<0.05$) (although all three types of MWF were used at this plant, their temporal use was not known to the study investigators) [Vena et al. 1985]. Silverstein et al. [1988] found a slight excess of rectal cancer mortality, which was not statistically significant; the risk for various processes was not reported. Mallin et al. [1986] found a risk of <1; however this finding is based on only two rectal cancer deaths.

Population-based studies

A population-based case-control study of incident cases of rectal cancer in Sweden found that male workers ever exposed to cutting fluids had an elevated risk for rectal cancer (OR=2.1, 95% CI=1.1–4.0) [Gerhardsson de Verdier et al. 1992]. However, several of the cases had other occupational exposures that have been associated with an increased risk for rectal cancer—including exposure to asbestos, soot, and combustion gases from coal/coke/wood. In an analysis adjusting for these other exposures, the risk of rectal cancer among cutting-oil-exposed workers was lower (OR=1.4, 95% CI= 0.6–3.5). In another population-based case-control study that examined the association between several cancer sites and occupational exposure to several petroleum-derived liquids, ever having cutting oil exposure was found not to be associated with an increased risk for rectal cancer (OR=0.7, 90% CI=0.4–1.0) [Siemiatycki et al.1987].

Conclusions for rectal cancer

In conclusion, several studies suggest that MWF exposure is associated with rectal cancer. In particular, the findings from the study with the most statistical power suggest that straight oil exposure may be associated with an increased risk for rectal cancer [Tolbert et al. 1992].

5.3.3.4 Pancreatic Cancer

Cohort studies

Among five cohort studies reporting site-specific data for pancreatic cancer, one found a significant excess for black but not white workers [Rotimi et al. 1993], and one found a significant excess for white workers in a subgroup analysis [Acquavella et al. 1993] (Table 5–9). Rotimi et al. [1993] found that black men employed at two Ohio engine manufacturing plants had an excess pancreatic cancer mortality (SMR=3.03, 95% CI=1.21–6.24, based on 7 deaths). However, it should be noted that the authors found no consistent pattern with respect to time since hire or duration of employment, and no pancreatic cancer excess was observed in white workers. Acquavella et al. [1993] reported

that factory workers employed at an Iowa metalworking facility had an increased risk for pancreatic cancer mortality (SMR=2.0, 95% CI=0.9–3.8). The risk appeared to be greatest among factory workers employed 10 or more years who were hired between 1950 and 1959 (SMR=3.6, 95% CI=1.2–8.3); however, the authors did not report whether a specific occupational group was responsible for the elevation identified in this subcohort. Among those in the overall cohort, assembly workers—who (Acquavella et al. state) are unlikely to have MWF exposure—were the occupational group with the highest risk (SMR=3.0, 95% CI=1.0–7.5). By contrast, in those departments identified by Acquavella et al. as having potential MWF exposure, there were 2 observed pancreatic cancer deaths in the overall cohort whereas 3.3 deaths were expected. Tolbert et al. [1992] found excess pancreatic cancer mortality among black workers exposed to soluble MWFs at Plants I and II in Michigan (SMR=1.62, 95% CI=0.98–2.54). In a Poisson regression analysis that controlled for race, age, and gender, an increased risk for pancreatic cancer mortality was observed in those workers with the highest exposures to synthetic MWFs (RR=2.04, 95% CI=0.88–4.72) [Tolbert et al. 1992]. In a case-control analysis that included Plants I, II, and III, a categorized exposure analysis found an OR of 2.23 (95% CI=1.25–3.98) among workers with >1.4 mg/m^3-years grinding with synthetic MWF [Bardin et al. 1997]. However, neither synthetic MWF nor any other measured exposure was found to explain the previously documented excess pancreatic cancer risk among black workers [Bardin et al. 1997]. Although unable to adjust for smoking, an important risk factor for pancreatic cancer [Silverman et al. 1994], Bardin et al. did not think that this risk factor confounded their results because the risk of lung cancer did not increase with increasing exposure to synthetic MWFs. One other cohort study found a nonsignificant elevation in pancreatic cancer mortality; however, this study had limited statistical power [Decoufle 1978].

PMR studies

Among five studies reporting site-specific data for pancreatic cancer, one found a significantly elevated PMR among white workers [Vena et al. 1985], one found a significantly elevated PMR among black but not white workers [Mallin et al. 1986], and two found significantly elevated PMRs among workers machining with straight oil MWF [Silverstein et al. 1988; Park and Mirer 1996]. White men employed at an engine plant for at least 10 years had an excess of pancreatic cancer mortality (PMR=1.89, $P<0.05$), which was higher for those employed more than 20 years (PMR=2.32, $P<0.05$) [Vena et al. 1985]. Use of county referent rates resulted in higher PMRs (employed >10 years, PMR=2.41, $P<0.05$; employed >20 years, PMR=2.97, $P<0.05$). PMRs for nonwhites employed in the engine plants were not reported because of the small numbers of deaths. All three types of cutting fluids were used in the engine plants. Mallin et al. [1986] found a significant excess of pancreatic cancer among black (PMR=3.57, $P<0.05$) but not white (1.19, n.s.) men employed in the manufacture of diesel engines and construction equipment. The PMR for pancreatic cancer was highest among black men who died after 20 years of service (PMR=4.79, $P<0.01$). Another PMR study found an elevation

in pancreatic cancer mortality among whites at a ball-bearing manufacturing plant (PMR=1.43, 95% CI=0.96–2.12) [Silverstein et al. 1988]. Case-control analyses revealed substantially elevated risks associated with 10 or more years of employment in grinding with various MWFs (OR=3.10, P=0.05) and machining with straight oil MWF (OR=5.31, P=0.05). The risk associated with grinding was present only for those with early hire dates (in the early 1930s and before) when straight oil MWFs were "almost exclusively used in grinding." Too few deaths occurred among non-white men for analysis. A PMR study of workers at two engine plants did not observe significant excesses for pancreatic cancer [Park and Mirer 1996]. However, an MOR analysis of these workers found an increased risk among those ever employed in machining with straight oil MWFs (OR=3.61, 95% CI=1.04–12.6, based on 3 cases); but no trend was observed with increasing cumulative exposure. One other PMR study found a nonsignificant elevation in pancreatic cancer mortality; however, a mortality odds ratio (MOR) analysis was not reported [Park et al. 1988].

Population-based studies

One study of white males in Los Angeles county during the period 1972–77 reported a nonsignificant "proportional index ratio" for employment as a machinist [Mack and Paganini-Hill 1981].

Conclusion for pancreatic cancer

In conclusion, several studies have found significantly increased risks of pancreatic cancer among workers exposed to MWF. The evidence is strongest for grinding with synthetic MWF [Bardin et al. 1997] and for machining with straight oil MWFs [Silverstein et al. 1988; Park and Mirer 1996]. Although a number of the studies did not have internally consistent findings (i.e., excesses in black but not white workers, lack of association with duration of MWF exposure), the number of studies with statistically significant findings suggests that exposure to some MWFs may increase the risk of pancreatic cancer.

5.3.3.5 Bladder cancer

Cohort studies

Only two cohort studies reported site-specific data for bladder cancer and neither found a significant excess [Decoufle 1978; Järvholm and Lavenius 1987] (Table 5–10). However, both of these studies are limited by relatively small sample sizes.

PMR studies

Of the six PMR studies that reported site-specific data for bladder cancer, only one reported a significant excess (PMR=2.28, P<0.05), which was among white workers employed in an engine plant [Vena et al. 1985]. The risk was greatest among those first employed during or before 1950 (PMR=3.37, P<0.05). A study of bearing plant

workers also found a nonsignificantly elevated risk for bladder cancer [Silverstein et al. 1988]. Another PMR study of workers at two Detroit-area engine manufacturing plants found nonsignificantly elevated PMRs for bladder cancer [Park et al. 1996]. However, a mortality OR analysis of these workers found a significant association between risk for bladder cancer and cumulative exposures to grinding with straight oil (MOR for the mean cumulative exposure of exposed cases=2.99, 95% CI=1.15–7.77, based on 7 deaths), and in the machining or heat-treat area (MOR for the mean cumulative exposure of exposed cases=2.86, 95% CI=1.14–7.18 based on 4 deaths). Two studies did not find an increased risk for bladder cancer [Park et al. 1988; Mallin et al. 1986], however these studies are limited by small sample size.

Population-based studies

Several case-control studies have also examined the risk of bladder cancer among those whose occupations may involve MWF exposure. Only those studies that controlled for smoking (a known risk factor for bladder cancer [Matanoski and Elliott 1981]) are discussed in detail. In a large population-based case-control study from the United States, Silverman et al. [1989a] found an elevated risk for bladder cancer among white men ever employed as machinists (OR=1.3, 95% CI=1.0–1.7) or drill press operators (OR=1.4, 95% CI=0.9–2.1). Furthermore, among drill press operators, the risk increased with increasing duration of employment (*P* for trend=0.008). Among drill press operators who worked 5 or more years, the elevated risk was present in both those who began work before 1950 (OR=1.7, confidence limits not provided) and those who began work in 1950 or later (OR=2.9, confidence limits not provided). However, among those who were employed as drill press operators for less than 5 years, the risk for bladder cancer was increased only among those who began employment in 1950 or later (OR=2.8, confidence limits not provided). The same study [Silverman et al. 1989b] examined occupational risk factors for bladder cancer among nonwhite men and reported an RR of 1.1 (95% CI=0.6–1.9) for the summary category *metal machinery worker* which was identical to the summary category *metal machinery worker* for whites (RR=1.1, 95% CI=1.0–1.3). The risks for the subcategories *machinists* and *drill press operators* was not broken out for nonwhites, nor was duration of employment as a metal machinery worker examined. In a population-based case-control study from Canada, Howe et al. [1980] found that those ever employed as metal machinists had an increased risk for bladder cancer (OR=2.7, 95% CI=1.1–7.7). A hospital-based case-control study conducted in Germany found that individuals ever employed as turners had an increased risk for bladder cancer (OR=2.25, 95% CI=1.0–5.6), and the risk was consistently elevated with increasing duration of employment (*P* for trend=0.08) [Claude et al. 1988]. This same study also found no increased risk of bladder cancer for the broad category of metal workers (OR=0.84, 95% CI=0.54–1.3). A population-based case-control study from Belgium found that metalworkers had a significantly increased risk for bladder cancer (RR=2.45, 95% CI=1.28–4.69). Subgroup analyses of these workers found the highest risk among turners (RR=2.57, 95% CI=0.92–7.16) [Schifflers et al. 1987].

Another hospital-based case-control study from Italy found that those employed for 6 months or more in the machine-tool industry had an increased risk for bladder cancer (OR=1.5, 95% CI=0.7–3.3) [Vineis and Magnani 1985]. Within the machine-tool trade, the risk for bladder cancer was elevated among turners, especially among turners hired before 1940 and employed more than 10 years (RR=3.1, 95% CI=0.9–10.5). A population-based case-control study conducted in Hamilton County, Ohio, found that grinding machine operators had an increased risk for bladder cancer (OR=2.00, not significant), whereas machinists were found to have a significantly decreased risk (OR=0.69) [Steenland et al. 1987]. Another case-control study did not observe an increased risk for bladder cancer among toolmakers (RR=0.77, 95% CI=0.5–1.1) but did observe an increased risk among machinery adjusters, assemblers, and mechanics (RR=1.86, 95% CI=1.2–2.8) [Gonzalez et al. 1989]. Four other studies found an elevation in bladder cancer risk among workers with potential MWF exposure; however, none of these four studies controlled for smoking [Malker et al. 1987; Coggon et al. 1984; Tola et al. 1980; Dunham et al. 1968].

Conclusions for bladder cancer

In summary, the association between bladder cancer and MWF exposure is well supported by one large and well designed case-control study [Silverman et al. 1989a, b] as well as several other studies conducted in different geographic locations, all of which controlled for smoking. Although none of the cohort studies found a significantly increased risk for bladder cancer, it has been observed that mortality studies may not be suitable for detecting elevated risks for cancers with high survival rates [Schulte et al. 1985; Steenland et al. 1988].

5.3.3.6 Stomach Cancer

Cohort studies

Only one of six cohort studies found a significantly elevated risk for stomach cancer [Rotimi et al. 1993] (Table 5–11). Rotimi et al. [1993] found that stomach cancer mortality was increased among white hourly workers employed at two Ohio engine manufacturing plants (SMR=2.54, 95% CI=1.42–4.20). Using local mortality rates to account for a high proportion of foreign-born workers, the magnitude of association decreased but the SMR for stomach cancer remained significantly elevated and displayed a dose-response relationship with duration of exposure (SMR not provided). Most of the excess in this cohort occurred among those hired before 1955 with 20 or more years since first hire who were employed for 20 or more years. However, the findings from this study should be interpreted cautiously because of limitations identified by the study authors (i.e., limited work history information and lack of data on possible confounding factors such as country of birth and previous employment history.

The Tolbert [1992] and Eisen studies [1992] (the largest and best designed of the cohort studies) did not observe a significant elevation in stomach cancer mortality. Nonsignificant elevations in stomach cancer mortality for white workers were observed in two of the three study plants (Plant 1: SMR=1.08, 95% CI=0.84–1.36); Plant 2: SMR=1.26, 95% CI=0.87–1.77; Plant 3: SMR=0.59, 95% CI=0.16–1.50) [Eisen et al. 1992]. Black men did not have an elevated SMR for stomach cancer associated with either employment at Plant 1 (SMR=0.96, 95% CI=0.56–1.54) or exposure to straight or soluble oil MWFs. Analysis of risks associated with specific fluid types (Table 5–11) indicated slight excesses of stomach cancer in each of the exposure groups. Poisson modeling did not suggest strong exposure-response trends for any of the 3 exposure types, although there was a slight elevation in the highest exposure group for soluble MWFs relative to other strata [Tolbert et al. 1992]. Tolbert et al. [1992] concluded that "the results of the Poisson analysis were not inconsistent with a dose-response relationship between soluble machining fluid and stomach cancer risk." The three other cohort studies found nonsignificant elevations in stomach cancer mortality [Acquavella et al. 1993; Järvholm and Lavenius 1987; Decoufle 1978], two of which were limited by low statistical power [Acquavella et al. 1993; Järvholm and Lavenius 1987].

PMR studies

Three of five PMR studies found a significantly elevated risk for stomach cancer [Silverstein et al. 1988; Park et al. 1988; Park and Mirer 1996]. Silverstein et al. [1988] found that white men employed 5 or more years in a ball-bearing manufacturing plant had an elevated risk for stomach cancer mortality (PMR=1.97, $P<0.001$). The risk was greatest among white men with 10 or more years employment in grinding operations that used primarily soluble MWFs (PMR=3.39, $P<0.001$); this risk was not found among machinists who used straight MWFs. The association with grinding persisted even after adjusting for Central European origin using logistic regression. Silverstein et al. [1988] concluded that their study provided strong evidence that grinding operations using soluble cutting fluids increase the risk for stomach cancer. White men employed in grinding operations at another ball-bearing manufacturing plant were also found to have excess stomach cancer mortality (PMR=3.8, $P=0.006$) [Park et al. 1988]. Workers classified as having soluble oil MWF exposure in a nested case-control analysis were found to have an OR for stomach cancer of 6.2 ($P=0.05$) [Park et al. 1988]. In interpreting these findings Park et al. did not think that there was confounding by the Central European origin of the workers because they found no association between such origin and soluble oil exposure. Another PMR study of workers at two Detroit-area engine manufacturing plants did not find an elevated PMR for stomach cancer at either plant [Park and Mirer 1996]. However, an MOR analysis of these workers found a significant association between risk for stomach cancer and duration of employment in camshaft/crankshaft production at Plant 1 (MOR for the mean employment duration of exposed cases=5.1, 95% CI=1.6–17, based on three deaths), but not at the larger and older Plant 2 (MOR not provided). Workers involved in camshaft/crankshaft production at

Plant 1 were reported to have exposure to semisynthetic MWFs and nitrosamines. Why a similar excess risk was not found in Plant 2 is not clear. Furthermore, this study found no association between stomach cancer and grinding with either soluble oil MWF (MOR=0.91) or straight oil MWF (MOR=0.61). Two other PMR studies found nonsignificant elevations in stomach cancer mortality [Vena et al. 1985; Mallin et al. 1986]; these two studies were limited by low statistical power.

Population-based studies

One of three population-based studies found a significant association between working in an occupation with potential MWF exposure and risk of stomach cancer [Kneller et al. 1990]. A standardized incidence ratio (SIR) study of incident stomach cancer cases reported to the Shanghai, China, Cancer Registry found that men with a current occupation of metal grinder, polisher, tool sharpener, or machine-tool operator had an elevated risk for stomach cancer (SIR=1.41, $P<0.01$) [Kneller et al. 1990].

Other studies

Park et al. [1994] found a significantly increased MOR (9.65, 95% CI=2.3–40) among tool and die workers exposed to MWFs at a stamping plant within the automobile industry. It should be noted that this finding is based on only two stomach cancer deaths.

Conclusions for stomach cancer

In conclusion, limited evidence supports an association between MWF exposure and stomach cancer. The association between stomach cancer and MWF exposure is supported by one cohort study and three PMR/MOR studies. However, the largest and best designed cohort study provides little support for an association [Tolbert et al. 1992; Eisen et al. 1992]. The findings from Park et al. [1988] and Silverstein et al. [1988] suggest that grinding operations using soluble oil MWF may be associated with an elevated risk for stomach cancer.

5.3.3.7 Esophageal Cancer

Cohort studies

Among four cohort studies that reported site-specific results for this cancer, none found a significant excess in the overall analyses (Table 5–12). With Poisson regression analyses, Tolbert et al. [1992] found elevations in esophageal cancer risk among those with straight MWF exposure and synthetic MWF exposure; however, clear dose-response trends were not present.

PMR studies

One of four PMR studies reported a significant excess [Silverstein et al. 1988]. Silverstein et al. [1988] found a PMR of 1.83 for esophageal cancer among MWF-exposed workers (95% CI=1.07–3.12). No further analysis by exposure or job category was

performed by Silverstein et al. [1988]. The other three PMR studies are limited by small numbers of esophageal cancer deaths.

Conclusions

In conclusion, limited evidence exists for an association between esophageal cancer and MWF exposure.

5.3.3.8 Other Sites

Other sites: Equivocal evidence exists regarding the potential association of MWF exposure with cancer of the brain and nervous system, prostate, lung/respiratory system, colon and hematopoietic and lymphopoietic systems (Tables 5–13 through 5–17) and are only briefly summarized here.

5.3.3.9 Brain/Nervous System Cancer

Among three cohort studies that reported site-specific results for brain/nervous system cancer, none found a significant excess (Table 5–13). Tolbert et al. [1992] reported a nearly significant association with soluble oil exposure among whites (SMR=1.24, 95% CI=0.91–1.66); however, Poisson regression analysis found no dose-response trend with soluble oil exposure. None of five PMR studies that reported results for brain/nervous system cancer found a significant elevation. A case-control study using death certificate data to classify occupation reported a significant association between all brain cancers and *usual occupation of precision metal worker* (OR=2.1, 95% CI=1.2–3.6) [Thomas et al. 1986]. An case-control interview study of astrocytic brain tumors (including cases identified in the Thomas et al. [1986] study) reported an OR of 1.6 (95% CI=1.0–2.6) for *ever employed at a job with potential cutting oil exposure* [Thomas et al. 1987].

5.3.3.10 Prostate Cancer

Among four cohort studies that reported site-specific results for prostate cancer, none showed a significant excess in the overall analyses (Table 5–14). Tolbert et al. [1992] observed slight excesses for each exposure group among the white males and a mild exposure-response trend for exposure to straight machining fluid (P=0.03). The rate ratio for ≥7.5 years of straight oil machining fluid exposure was 1.5 (95% CI=1.01–2.29). One study found a significant deficit of prostate cancer among *grinders and turners* (SMR=0.34, 95% CI=0.1–0.7) and among *grinders and turners* with at least 20 years since onset of exposure (SMR=0.38, CI=0.1–0.8) [Järvholm and Lavenius 1987]. Among 5 PMR studies that reported site-specific results for prostate cancer, one showed a significant excess [Park and Mirer 1996]. Park and Mirer [1996] found that workers at one of two Detroit-area engine manufacturing plants had an elevated PMR for prostate cancer. The MOR analysis of workers at these two plants found that two activities with

potential MWF exposure were associated with an increased risk for prostate cancer: tool grinding and machining of aluminum pistons.

5.3.3.11 Lung Cancer

Of five cohort studies reporting site-specific results for lung cancer, only one reported a statistically significant increased risk, and this was for a subgroup of workers employed >10 years and hired between 1950 and 1959 [Acquavella et al. 1993] (Table 5–15). Some studies, in fact, provide evidence for a negative association between MWF exposure and lung cancer. Although the SMR analyses in the Tolbert et al. [1992] study showed SMRs >1.00 for workers ever exposed to each of three types of machining fluids, the Poisson regression analyses found a negative association between lung cancer risk and both synthetic MWF exposure (P=0.006), and soluble oil MWF exposure (P=0.09). Findings were similar in a case-control analysis that included all three plants [Schroeder et al. 1997]. Schroeder et al. [1997] suggested that the negative findings may be due to contamination of the water-based fluids by endotoxin-producing gram-negative bacteria. The mechanism proposed by these authors was that endotoxins may stimulate immunologic factors that inhibit the growth of malignant cells in the lung. However, these authors could not rule out other noncausal mechanisms (e.g., selective attrition of susceptible workers or inverse correlation between synthetic MWF exposure and exposure to an unmeasured occupational lung carcinogen). Järvholm and Lavenius [1987] also found that workers exposed to oil mist for 5 or more years had a significantly decreased risk for lung cancer (SMR=0.4, 95% CI=0.1–0.9), even among those with at least 20 years since onset of exposure (SIR=0.30, 95% CI=0.1–0.9) (Table 5–15). Four of five PMR studies report PMRs >1.0, one of which was statistically significant [Park and Mirer 1996]. The PMR study of workers at two Detroit-area engine manufacturing plants found an elevated PMR for lung cancer at only one of the plants [Park and Mirer 1996]. The MOR analysis of these workers did not provide clear evidence that the excess lung cancer risk was due to MWF exposure. A case-control study within a PMR study reported a significantly increased risk for female workers employed as grinders, but the absence of any cases in the comparison group made this an unstable estimate [Park et al. 1988]. Three population based case-control studies report statistically significant ORs associated with various definitions of MWF exposure [Siemiatycki et al. 1987; Jöckel et al. 1992; Coggan et al. 1984].

5.3.3.12 Colon Cancer

Among four cohort studies reporting site-specific data, none show significant excesses (Table 5–16). One of 4 PMR studies was significantly positive [Silverstein et al. 1988]. Silverstein et al. [1988] found a significant excess in colon cancer (PMR=1.39, 95% CI=1.03–1.88) that appeared to be concentrated in workers employed in grinding operations (13 observed, 6.9 expected, PMR=1.89, P=0.02). MOR analyses using logistic regression found no exposure associations for colon cancer.

5.3.3.13 Hematopoietic and Lymphopoietic Cancer

One of three cohort studies reporting data on hematopoietic and lymphopoietic cancers found a significantly increased risk (Table 5–17). Tolbert et al. [1992] found that white men ever exposed to soluble oil MWFs had an increased risk for leukemia (SMR=1.33, 95% CI=1.05–1.67), but Poisson regression models found no evidence for an association between leukemia and any class of MWF. Another SMR study found an elevated lymphopoietic cancer risk in a small subgroup (workers employed 1 or more months in the tool and die area of an automotive stamping plant) (MOR=5.38, 95% CI=1.6–18.0, based on three lymphopoietic cancer deaths) [Park et al. 1994]. Among five PMR studies, none found significantly elevated PMRs in the overall analyses. However, Park and Mirer [1996] found that workers who ever worked in grinding with soluble oil MWFs had an increased risk for non-Hodgkin's lymphoma and multiple myeloma (MOR=4.1, 95% CI=1.1–15). Silverstein et al. [1988] found that workers employed as tool grinders for 10 or more years had an increased risk for lymphopoietic cancer (PMR=4.75, P=0.02). Mallin et al. [1986] found an elevated risk for non-Hodgkin's lymphoma among black workers (PMR=6.87, P<0.05). In each of these three studies, the authors speculated that solvent exposure [Park and Mirer 1996; Silverstein et al. 1988; Mallin et al. 1986] or biocides [Park and Mirer 1996], rather than MWF fluid exposure, were likely to be responsible for the elevated risks. A population-based case-control study that examined the association between several cancer sites and occupational exposure to several petroleum-derived liquids found evidence suggesting a dose-response relationship between cutting oil exposure and an increased risk for non-Hodgkin's lymphoma (OR among those defined as substantially exposed=1.9, 90% CI=1.0–3.1) [Siemiatycki et al. 1987].

5.3.4 Genetic Effects

Only one epidemiologic study was identified that examined genotoxicity among workers exposed to MWF [Fuchs et al. 1995]. In a German study of 65 male metal workers exposed to synthetic MWFs in seven small-to medium-sized plants, those who worked in areas having a NDELA concentration greater than 500 ng/m^3 had a significantly elevated mean number of DNA strand breaks in mononuclear blood cells compared with workers employed in areas with less than 50 ng/m^3 NDELA (1.69 ± 0.34 workers in areas with greater than 500 ng/m^3 NDELA versus 0.76 ± 0.05 for workers in areas with less than 50 ng/m^3 NDELA, P<0.01) [Fuchs et al. 1995]. The average concentration of NDELA present in the cutting fluids at these plants was 20.6 ppm (range 2–135 ppm). In addition, nonsmokers who worked more than 4.5 hr/day had a significantly elevated mean number of DNA strand breaks compared with nonsmokers who worked less than 4.5 hr/day (1.34 ± 0.12 for those working more than 4.5 hr/day versus 0.91 ± 0.12 for those working less than 4.5 hr/day, P<0.02). Airborne concentrations of MWFs were not reported. NDELA is a contaminant that may be present in some MWFs and can be formed in MWFs when DEA or TEA reacts with a nitrosating agent (e.g., nitrite). This

5.3.3.13 Hematopoietic and Lymphopoietic Cancer

One of three cohort studies reporting data on hematopoietic and lymphopoietic cancers found a significantly increased risk (Table 5–17). Tolbert et al. [1992] found that white men ever exposed to soluble oil MWFs had an increased risk for leukemia (SMR=1.33, 95% CI=1.05–1.67), but Poisson regression models found no evidence for an association between leukemia and any class of MWF. Another SMR study found an elevated lymphopoietic cancer risk in a small subgroup (workers employed 1 or more months in the tool and die area of an automotive stamping plant) (MOR=5.38, 95% CI=1.6–18.0, based on three lymphopoietic cancer deaths) [Park et al. 1994]. Among five PMR studies, none found significantly elevated PMRs in the overall analyses. However, Park and Mirer [1996] found that workers who ever worked in grinding with soluble oil MWFs had an increased risk for non-Hodgkin's lymphoma and multiple myeloma (MOR=4.1, 95% CI=1.1–15). Silverstein et al. [1988] found that workers employed as tool grinders for 10 or more years had an increased risk for lymphopoietic cancer (PMR=4.75, P=0.02). Mallin et al. [1986] found an elevated risk for non-Hodgkin's lymphoma among black workers (PMR=6.87, P<0.05). In each of these three studies, the authors speculated that solvent exposure [Park and Mirer 1996; Silverstein et al. 1988; Mallin et al. 1986] or biocides [Park and Mirer 1996], rather than MWF fluid exposure, were likely to be responsible for the elevated risks. A population-based case-control study that examined the association between several cancer sites and occupational exposure to several petroleum-derived liquids found evidence suggesting a dose-response relationship between cutting oil exposure and an increased risk for non-Hodgkin's lymphoma (OR among those defined as substantially exposed=1.9, 90% CI=1.0–3.1) [Siemiatycki et al. 1987].

5.3.4 Genetic Effects

Only one epidemiologic study was identified that examined genotoxicity among workers exposed to MWF [Fuchs et al. 1995]. In a German study of 65 male metal workers exposed to synthetic MWFs in seven small-to medium-sized plants, those who worked in areas having a NDELA concentration greater than 500 ng/m^3 had a significantly elevated mean number of DNA strand breaks in mononuclear blood cells compared with workers employed in areas with less than 50 ng/m^3 NDELA (1.69 ± 0.34 workers in areas with greater than 500 ng/m^3 NDELA versus 0.76 ± 0.05 for workers in areas with less than 50 ng/m^3 NDELA, P<0.01) [Fuchs et al. 1995]. The average concentration of NDELA present in the cutting fluids at these plants was 20.6 ppm (range 2–135 ppm). In addition, nonsmokers who worked more than 4.5 hr/day had a significantly elevated mean number of DNA strand breaks compared with nonsmokers who worked less than 4.5 hr/day (1.34 ± 0.12 for those working more than 4.5 hr/day versus 0.91 ± 0.12 for those working less than 4.5 hr/day, P<0.02). Airborne concentrations of MWFs were not reported. NDELA is a contaminant that may be present in some MWFs and can be formed in MWFs when DEA or TEA reacts with a nitrosating agent (e.g., nitrite). This

study provides evidence that nitrosamine exposure may be genotoxic. However, in 1984, EPA prohibited the addition of nitrosating agents to MWF (as previously discussed in Chapter 6).

5.3.5 Information about Exposure Concentrations

Only a few studies described in this chapter provided information about the MWF exposure concentrations during the decades when the MWF-exposed cohorts were employed [Järvholm and Lavenius 1987; Hallock et al. 1994; Silverstein et al. 1988; Park et al. 1988; Park and Mirer 1996]. A summary of the exposure information from these studies is provided below. Additional detail about MWF exposures can be found elsewhere in this document.

In the Järvholm study, the investigators estimated that cutting oil mist concentrations before 1965 were 5 mg/m^3 or greater in the grinding and turning departments. All workers in this study were exposed to these concentrations, since the criteria for inclusion in the study required employment in the turning or grinding department at any time between 1950 and 1966 and a duration of employment of at least 5 years. In the late 1970s, oil mist concentration was reduced to 2 mg/m^3 in the turning departments and to 3 mg/m^3 in the grinding departments.

Estimates of cutting oil exposures were also made for the three plants studied by Eisen et al. [1992] and Hallock et al. [1994]. The estimates were made by fitting industrial hygiene aerosol concentration measurements made between 1958 and 1987 into a linear statistical model. As demonstrated in Table 5–18, MWF exposures from grinding operations were higher than exposures from machining or assembly operations for all three time periods.

Exposure measurements from which these summaries are compiled may not be representative of the plant environment as a whole. Most (57%) of the industrial hygiene reports did not indicate the reason for sampling. The remainder were done at employee or management request, or they were performed by the State health department [Hallock et al. 1994]. It is possible, therefore, that these averages may be higher than the true plant averages because the measurements represent complaint sampling of higher than average exposures [Hallock et al. 1994].

Similar data were reported by Silverstein et al. [1988] and Park et al. [1988]. Silverstein et al. [1988] reported that between 1949 and 1961, industrial hygiene breathing zone samples for total particulate mass in machining areas had a mean level of 15.9 mg/m^3. Breathing zone samples from grinders taken during 1977–79 and in 1980 had mean total particulate masses of 1.7 and 4.3 mg/m^3, respectively. Park et al. [1988] found that breathing zone total particulate mass concentrations near jobs performed with straight MWFs (machining operations) ranged from 0.07 to 2.8 mg/m^3 between 1972 and 1980.

Table 5–18. Estimated mean aerosol concentrations for grinding, machining, and assembly operations, by time period

Operation	1958–69		1970–79		1980–87	
	Number of measurements	Mean concentration (mg/m^3)	Number of measurements	Mean concentration (mg/m^3)	Number of measurements	Mean concentration (mg/m^3)
Grinding	7	17.96	71	3.44	56	2.28
Machining	25	3.35	128	2.13	61	1.66
Assembly	8	0.94	23	0.52	15	0.64

During these same years, concentrations near grinding operations (which were presumed to be using soluble oil MWFs) ranged from 0.6 to 7.2 mg/m^3. Park and Mirer [1996] report that industrial hygiene data from 1954 and later indicate that more than 75% of the MWF mist samples had concentrations below 5.0 mg/m^3, but concentrations ranged up to 15 mg/m^3. Park and Mirer [1996] reported that MWF mist concentrations appeared generally higher before 1975.

This evidence suggests that grinding operations are associated with higher MWF exposures than machining or assembly operations. This evidence also suggests that exposures to MWFs have been dropping since about 1970. Changes made in the 1970s and 1980s that contributed to the declining exposures include installation of air cleaners, enclosures, and local exhaust ventilation, and improvement in recirculated air filtration systems. However, the impact of other relatively recent changes has yet to be determined (e.g., the impact from higher operating temperatures of modern cutting tools on MWF deterioration and other chemical changes, and the impact of higher cutting speeds on aerosol size distributions).

5.3.6 Route of Exposure

Although the route of MWF exposure is generally through dermal contact or through inhalation, the large size of many airborne MWF droplets can lead to gastrointestinal exposure. A significant proportion of airborne MWF particles is in the nonrespirable (extrathoracic) range (i.e., particles with a mass mean diameter >9.8 μm). Eisen et al. [1994] report that in their study approximately, 20% to 33% of the total particulate was in the extrathoracic range. Large particles generally result in gastrointestinal exposures

since they are filtered out in the nasopharyngeal region and do not reach the airways. In addition, some of the small particles in the thoracic size fraction are captured by the mucocilliary escalator. The mucocilliary escalator transports the particles to the pharynx, where they are swallowed, thereby permitting gastrointestinal exposure.

5.3.7 Conclusion

Substantial evidence exists for increased risk of cancer at several sites (larynx, rectum, pancreas, skin, scrotum, and bladder) associated with at least some of the MWFs used before the mid-1970s. The inconsistencies between studies with respect to the organ sites that were affected, and the variation in the strength of association between the surrogates of exposure and specific sites are most likely related to the diverse nature of MWF mixtures studied, the absence of detailed exposure information, and the limitations of the epidemiologic tools with which MWF exposures have been studied. The evidence is equivocal for an association between MWF exposure and cancer at several other sites, including the stomach, esophagus, lung, prostate, brain, colon, and hematopoietic system.

As described in an earlier section of the criteria document, there are four classes of MWFs. The types and amounts of chemical constituents can vary across these classes. Furthermore, within each class are many formulations that vary in composition and may contain many different additives and impurities. Some MWF constituents are considered carcinogenic in animals (including N-nitrosamines [IARC 1978a] and PAHs [IARC 1983]). Efforts to reduce these potential carcinogenic exposures have been ongoing. Removal of PAHs from MWFs began in the 1950s, and EPA regulations in the 1980s were directed at reducing nitrosamine exposures. Because different epidemiologic study populations may have been exposed to different classes and formulations of cutting fluids, some lack of consistency in site-specific results between studies should be expected when evaluating the carcinogenicity of these substances. Similarly, when comparing studies with limited information about the intensity of exposure, we would expect variation in the strength of association between exposure and the risk of cancer. NIOSH believes that the consistency among the studies is sufficient to support our conclusions.

Given the small number of epidemiologic studies that have adequate exposure characterization, the specific MWF constituent(s) or contaminant(s) responsible for the various site-specific cancer risks remain to be determined. The study with the most statistical power and detailed exposure information [Tolbert et al. 1992] suggests that specific classes of MWFs are associated with cancer at certain sites. However, within these MWF classes, the specific formulations responsible for the elevated cancer risks remain to be identified. Within the Tolbert et al. [1992] study, straight oil exposure was modestly associated with an increased risk for laryngeal and rectal cancer, and there was limited evidence that synthetic oil MWF exposure was associated with an increased risk

for pancreatic cancer. Subsequent case-control studies based on the original cohort have confirmed the association of laryngeal cancer with straight oil MWF [Eisen et al. 1994], and the association of pancreatic cancer with synthetic MWF [Bardin et al. 1997]. The Tolbert et al. study found less evidence that soluble oil exposure is associated with cancer at any specific site. NIOSH believes that it is premature to conclude that all members of the soluble oil class of MWFs were free from carcinogenic risks in the past, since soluble MWFs contain many of the ingredients found in straight oil MWFs—but in different concentrations. Also, many of the epidemiologic studies with positive findings involved exposures to more than one class of MWF.

Non-MWF exposures are unlikely to be responsible for the cancer findings described in this chapter. Smoking and alcohol are associated with some of the cancers observed to be associated with MWF exposure. However, most of the case-control studies controlled for these exposures when appropriate or determined that these exposures were unlikely confounders. Although information about these lifestyle factors are not often collected in occupational cohort mortality or PMR studies, it has been demonstrated that smoking is unlikely to account for RRs >1.3 for lung cancer and other smoking-related diseases [Siemiatycki et al. 1988]. Non-MWF occupational exposures are unlikely to explain the majority of findings, as the common exposure across all of the studies was MWF. Although some non-MWF exposures may have interacted synergistically with MWF exposure to produce some of the observed risks, the existence or extent of such synergism remains to be determined.

The studies that provide the bulk of the evidence suggesting an association between MWF exposure and cancer involved workers employed as early as the 1930s and as late as the mid-1980s. Because there is a latency period of 10 to 20 years between initial exposure to a carcinogen and the initial appearance of a solid-organ cancer caused by that carcinogen, the excess cancer mortality observed in these cohort studies most likely reflects the cancer risk associated with exposure conditions in the mid-1970s and earlier. Over the last several decades, substantial changes have been made in the metalworking industry, including changes in MWF composition, reduction of impurities, and reduction of exposure concentrations. These changes have likely reduced the cancer risks. However, since the epidemiologic data do not usually identify the MWF composition and impurities associated with the cancer risks observed in earlier cohorts, there is insufficient data to conclude that these changes will have eliminated all carcinogenic risks. The risk of cancer from MWF exposures in the mid-1970s and later remains to be determined because a definitive study has not yet been conducted on workers entering MWF-exposed jobs during this period. Thus the NIOSH REL is supported by the substantial evidence associating at least some of the MWFs in commercial use before the mid-1970s with cancer at several sites, and by the potential for current MWFs to pose a similar carcinogenic hazard.

5.4 Dermatologic Conditions

Skin diseases and disorders were reported as the leading occupational illness in the United States during the years 1973–87 [DOL 1988, 1989] and continue to be very common occupational illnesses. The Bureau of Labor Statistics of the U.S. Department of Labor published an occupational skin disease incidence rate of 7.7 per 10,000 full-time workers for 1991 [DOL 1993]. In 1991, the list of industries with the highest incidence rates for skin diseases or disorders included fabricated, screw-machine products (33.3 per 10,000 workers) and general industrial machinery (22.0 per 10,000 workers) [DOL 1993]. Both of these industries involve potential exposure to MWFs.

5.4.1 Cutaneous Disorders

Several cutaneous disorders have been associated with the use of MWFs, including irritant contact dermatitis, allergic contact dermatitis, folliculitis, oil acne, oil keratosis, squamous cell carcinoma, pigmentary changes (melanoderma and leukoderma), oil granuloma, and mechanical injuries from metal shavings [Alomar 1994]. Other cutaneous disorders include nail disorders, paronychia, and photosensitivity reactions. As a generalization, straight oil (insoluble) MWFs are reported to produce folliculitis, oil acne, keratoses, and carcinomas; the water-based oil emulsions (soluble oil and semisynthetic) and synthetic MWFs primarily cause irritant contact dermatitis and occasionally allergic contact dermatitis [Fisher 1986]. Skin carcinomas associated with straight oil MWFs may be of historical interest; refinement techniques such as severely solvent-refined and severely hydrotreated mineral oils have limited the PAH content, which is thought to be the principal skin carcinogen in straight oil MWFs [Järvholm et al. 1990; McKee et al. 1990].

Straight oil (insoluble) MWFs cause follicular and acne-like eruptions on the face, forearms, thighs, legs, and other parts of the body contacting oil-soaked clothing [Finnie 1960; Key et al. 1966]. Oil folliculitis is initially marked by perifollicular erythema, which can further develop into erythematous papules and pustules or furuncles. Tsuji et al. [1992] reported multiple keratoses and a squamous cell carcinoma on the forearms and backs of the hands of a worker exposed for 15 years to straight oil MWFs.

Contact dermatitis of the hands and forearms in workers exposed to soluble oil, semisynthetic, and synthetic MWFs is a common and widespread problem. de Boer et al. [1988, 1989a,b] reported on the prevalence of irritant contact dermatitis and allergic contact dermatitis in a cross-sectional epidemiologic study of 286 workers exposed to MWFs in 10 metalworking factories in the Netherlands. Sixty-one workers (21%) complained of skin problems, mostly of an itchy eruption on the hands and forearms. Dermatitis that cleared or improved during time away from work and recurred after returning to work was reported by 39 workers (14%). On dermatological examination, 39 workers had a dermatitis of irritant or allergic origin for a prevalence rate of 14%

[de Boer et al. 1988, 1989a]. By comparison, the prevalence of dermatitis in a general population study was 4.6% [Coenraads et al. 1983]. Another study of machinists heavily exposed to MWFs showed a 30% prevalence rate of dermatitis [Rycroft 1982]. Sprince et al. [1996] reported that in a study of 4,200 automotive transmission parts workers, machine operators had more combined dermatitis (definite plus possible) compared with assemblers (27.2% versus 13.7%). In a NIOSH HHE investigating exposures to MWFs in an aluminum plant, 11 (14%) of 78 workers reported developing work-related skin irritation during the previous year [NIOSH 1994a]. In another NIOSH HHE conducted in the grinding operations of a metal rod and pin manufacturing facility, 31 (63%) of 49 exposed workers reported itching and burning skin of the hands compared with 20% in an unexposed comparison group [NIOSH 1984]. On skin examination, 18 (37%) of the 49 had moderately severe dermatitis at the time of examination compared with 9% in the unexposed group. Other NIOSH investigations revealed that the prevalence of reported MWF dermatitis in a variety of workplaces ranged from 36% to 67% [NIOSH 1985; 1986a,b; 1989].

Many factors play a role in the development of contact dermatitis, the most important of which is the degree of skin contact with the MWF [Rycroft 1990, Sprince et al. 1996]. Other factors include individual susceptibility, use of personal protective equipment, general factory environment, climate, machine types and control methods, and MWF classes and additives used [Rycroft 1990].

5.4.2 Irritants

Because of the complex composition and variety of potential contaminants of MWFs, the exact etiology of MWF dermatitis is difficult to determine. Several authors have noted that the majority of workers exposed to MWFs (50% to 80%) have irritant contact dermatitis, and the rest have allergic contact dermatitis [Alomar 1994]. The alkaline emulsifiers and solvents contained in soluble and semisynthetic oils are directly irritating to the skin and may change the structure and function of the skin by denaturing keratin, defatting and dehydrating the skin, and causing dryness, fissures, and eczematization [Zugerman 1986]. Irritant contact dermatitis can also be caused by microtrauma from MWF contaminants such as metal shavings and from strong detergents used for handwashing after contact with MWFs. Workers with fair, smooth skin and workers with a history of atopic diseases may be at a higher risk for developing irritant contact dermatitis [Alomar 1994].

5.4.3 Allergens

Primary irritants can also be sensitizers and produce allergic contact dermatitis. Irritant contact dermatitis can lead to a breakdown in the barrier properties of intact skin and allow for penetration of potential sensitizers through damaged skin [Alomar 1994]. Many substances can play a role in allergic contact dermatitis caused by MWF. These

include metal contaminants such as chromium, cobalt, or nickel and components or additives such as mercaptobenzothiazole (MBT), triazines (Grotan BK®), N-methylolchloracetamide (Parmetol K50®), Fordice 78®, P-chloro-m-xylenol (PCMX), O-phenylphenol (Dowicide 1®), alkanolamine borate, 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (Kathon®), paraphenylenediamine, benzisothiazolone (Proxel®), polymethacrylate, ethylenediamine, TEA, colophony, dipentene, Bioban P® CS–1246, P–1487, glycidyl ester of hexahydrophthalic acid, and fragrances [Alomar et al. 1985, 1994; de Boer et al. 1989b; Camarasa et al. 1993; Dahlquist et al. 1984; Damstra et al. 1992].

Skin patch testing has confirmed the allergenic properties of these substances. Thirty-three compounds are included in an oil and cooling fluid skin patch test series (distributed by Chemotechnique Diagnostics AB, Sweden) for the diagnosis of allergic contact dermatitis. This series contains deodorizing agents, bactericides/fungicides/algicides, preservatives, surface active agents, antioxidants, anticorrosive agents, pressure stabilizers, and emulsifiers/emollients. All of these classes of chemicals can be found in MWF and all have been documented to cause allergic contact dermatitis. In addition, workers with allergic contact dermatitis may not have an allergic response to constituents of MWFs, but they may instead respond to the reaction products of the constituents of the MWFs [Shrank 1985]. Even when skin patch testing confirms a skin allergy and a possible etiology for allergic contact dermatitis, it is still impossible to determine what role the allergy played in the dermatitis and what role was played by the irritancy of the MWF preceding, accompanying, or following the sensitization [Rycroft 1990].

The most frequent positives on skin patch testing are obtained from exposure to biocides, corrosion inhibitors, coupling agents, and emulsifiers [Alomar 1994]. In a British study of 174 patients with suspected MWF dermatitis, 43% showed relevant allergic reactions. The most common causes of allergic contact dermatitis in this study were the biocides, especially the formaldehyde releasers [Grattan et al. 1989]. In the de Boer study of 286 metalworkers exposed to MWFs, patch tests were performed on 40 workers. Contact sensitization was established in eight workers. Four of these workers were determined to have allergic contact dermatitis caused by ingredients of MWFs. Of these, three workers were allergic to biocides, and a fourth was allergic to a corrosion inhibitor [de Boer et al. 1989a,b].

5.4.4 Prognosis and Preventive Measures

The prognosis for MWF dermatitis may be poor, as shown in a study of 100 machine operators with documented MWF dermatitis. In a 2-year followup, 78% of those who continued working with soluble oils had not healed; 70% of those who stopped working with the oil had not healed after discontinuing contact with the MWFs [Pryce 1989a]. As shown in this study, primary prevention of MWF dermatitis is key. This could be accomplished through worker protection and engineering controls.

Limiting the dermal exposure of workers to MWFs is the crux of preventive measures. With this goal in mind, preventive measures include [Mansdorf and Lubs 1994; Tucker 1988]:

- Substitution of MWFs, additives, or constituents as appropriate (several studies have indicated an increased skin irritancy potential of semisynthetic MWFs compared with soluble oil MWFs) [Sprince at al. 1996; Wigger-Alberti et al. 1997]
- Process modification, isolation, and ventilation to limit the dispersal of MWFs
- Work practice and administrative controls to assure the proper maintenance of MWFs and workplace cleanliness
- The proper use of personal protective equipment such as protective gloves, aprons, and clothing
- Education and training of the workers regarding dermal effects of MWFs and the importance of personal hygiene in the workplace. MWF-saturated clothing should be changed as soon as possible; skin surfaces that have come in contact with MWFs should be washed as soon as possible with nonirritating and nonabrasive soaps [Zugerman 1986].

CHAPTER 6

Current Occupational Recommendations and Standards

In 1976, NIOSH published *Current Intelligence Bulletin 15: Nitrosamines in Cutting Fluids,* which identified the presence of potentially carcinogenic PAHs and nitrosamines in MWFs and recommended industrial hygiene practices to minimize dermal and respiratory exposures [NIOSH 1976]. OSHA has classified NDMA as a *cancer-suspect agent* [29 CFR 1910.1016]; it is regulated as an occupational carcinogen. Worker exposure to NDMA is controlled through the required use of engineering controls and personal protective equipment, including respirators [20 CFR 1910.1003 and 1910.1016]. NIOSH has identified NDMA as a potential occupational carcinogen and recommends that occupational exposure to NDMA be limited to the lowest feasible concentration [NIOSH 1973].

Particularly in the past, petroleum-based mineral oils used in straight oil, soluble oil, and semisynthetic MWFs were derived through limited refining by vacuum distillation or acid treatment, or they were severely or mildly treated by solvent refinement or hydrotreatment [IARC 1987a]. As noted in Section 4.1.2, the OSHA hazard communication standard [29 CFR 1910. 1200] requires that employers report on the MSDS that a substance is a carcinogen or potential carcinogen when (1) IARC has found sufficient or limited evidence of its carcinogenicity, (2) OSHA has regulated the substance as a carcinogen, or (3) the NTP lists the substance on its annual list of carcinogens.

According to the IARC process parameters of mild hydrotreatment, an oil processed at a hydrogen pressure of 800 psi or less at temperatures up to 800°F is subject to the OSHA hazard communication standard [29 CFR 1910.1200].

In testimony for the OSHA rulemaking on air contaminants [54 Fed. Reg. 2445 (1989)], NIOSH recommended an exposure limit for mineral oil mists of 5 mg/m^3 as a 10-hr TWA with a short-term exposure limit (STEL) of 10 mg/m^3. NIOSH submitted comments to the record noting that certain types of oils and their additives may present a carcinogenic hazard [NIOSH 1988a]. The current OSHA PEL for mineral oil mists is 5 mg/m^3 as an 8-hr TWA. ACGIH has published a notice of intended change for the threshold limit value (TLV) for severely refined mineral oil mist: 5 mg/m^3 as an 8-hr TWA [ACGIH 1997b]. The *Notice of Intended Changes* section of *1997 TLVs® and BEIs®* [ACGIH 1997a] also includes proposed TLVs (8-hr TWAs) for *Oil mist, mineral, sum total of 15 polynuclear aromatic hydrocarbons (PAHs) listed as carcinogens*

by the U.S. National Toxicology Program (NTP). This TWA has the A1—*Confirmed Human Carcinogen* designation.

The current standard for *particulates not otherwise regulated* [29 CFR 1910.1000] may not adequately protect workers exposed to the hazardous components or contaminants of MWFs for which PELs and RELs have not been established. In testimony for the 1989 OSHA rulemaking on air contaminants, NIOSH pointed out that *particulates not otherwise regulated* have health effects beyond those attributed to the physical irritant properties of particulates and that a PEL of 10 mg/m^3 would not prevent the toxicologic effects associated with many of these substances [NIOSH 1988b]. The current OSHA PEL for *particulates not otherwise regulated* is 15 mg/m^3 as an 8-hr TWA for total dust and 5 mg/m^3 as an 8-hr TWA for respirable particulates. The ACGIH TLV for *particulates not otherwise classified* is 10 mg/m^3 (TWA) for inhalable particulates and 3 mg/m^3 (TWA) for respirable particulates. The ACGIH TLV for TEA is 5 mg/m^3 as an 8-hr TWA [ACGIH 1993]. NIOSH, OSHA, and the Mine Safety and Health Administration (MSHA) have not established exposure limits for TEA. Additional exposure limits have been established for individual additives, components, and contaminants of MWFs (see Table 6–1).

On the basis of spirometric data from workers exposed to cotton dust, Rylander et al. [1985] calculated an endotoxin threshold of 33 nanograms (ng)/m^3; Castellan et al. [1987] calculated an endotoxin threshold of 9 ng/m^3. Palchak et al. [1988] suggested an endotoxin action level of 30 ng/m^3 for industrial processes involving large-scale cultures of genetically engineered *E. coli.* Milton et al. [1996] studied endotoxin exposure in a fiber glass manufacturing facility and concluded that endotoxin exposures of 4 to 15 ng/m^3 (mean, 8.9 ng/m^3) and higher were strongly associated with acute effects on peak expiratory flow and FEV_1. NIOSH, ACGIH, and OSHA have not established exposure limits for endotoxin. Table 6–1 presents a partial listing of NIOSH RELs, OSHA PELs, and ACGIH TLVs that are relevant to occupational exposure to MWFs.

Table 6-1. Current recommendations and standards

MWF component	NIOSH REL	OSHA PEL	ACGIH TLV
Acetaldehyde	Ca[*]	200 ppm (360 mg/m^3) TWA	25 ppm (45 mg/m^3) ceiling,[†] A3[‡]
Ammonia	25 ppm (18 mg/m^3) TWA, 35 ppm (27 mg/m^3) STEL[§]	50 ppm (35 mg/m^3) STEL	25 ppm (17 mg/m^3) TWA, 35 ppm (24 mg/m^3) STEL
Cadmium	Metal and compounds: Ca	Metal and compounds: 0.005 mg/m^3	Elemental: 0.01 mg/m^3 TWA, (A2)[**] Compounds: 0.002 mg/m^3 TWA, (A2)
Chlorine	0.5 ppm (1.45 mg/m^3) 15-min ceiling	1 ppm (3 mg/m^3) ceiling	0.5 ppm (1.5 mg/m^3) TWA, 1 ppm (2.9 mg/m^3) STEL
Chromium:[††]			
1. Compounds Cr (II and III)	0.5 mg/m^3 TWA	0.5 mg/m^3 TWA	0.5 mg/m^3 TWA as Cr III, A4[‡‡]
2. Metal	0.5 mg/m^3 TWA	1 mg/m^3 TWA	0.05 mg/m^3 TWA as soluble Cr VI, A1[§§]
3. Cr (VI)	0.001 mg/m^3 TWA	0.1 mg/m^3 TWA	0.01 mg/m^3 TWA as insoluble Cr VI, A1
Cobalt metal dust and fume	0.05 mg/m^3 TWA	0.1 mg/m^3 TWA	0.02 mg/m^3 TWA, A3
Diethanolamine (DEA)	3 ppm (15 mg/m^3) TWA	No PEL	0.46 ppm (2 mg/m^3) TWA (skin)
Formaldehyde	Ca; 0.016 ppm TWA, 0.1 ppm 15-min ceiling	0.75 ppm TWA, 2 ppm STEL	0.3 ppm ceiling (0.37 mg/m^3), A2
Hydrogen sulfide	10 ppm (15 mg/m^3) (10-min) ceiling	20 ppm ceiling, 50 ppm (10-min) maximum peak	10 ppm (14 mg/m^3) TWA, 15 ppm (21 mg/m^3) STEL
Monoethanolamine (ethanolamine) (MEA)	3 ppm (8 mg/m^3) TWA, 6 ppm (15 mg/m^3) STEL	3 ppm (6 mg/m^3) TWA	3 ppm (7.5 mg/m^3) TWA, 6 ppm (15 mg/m^3) STEL
Nickel metal and compounds	0.015 mg/m^3 TWA, Ca	1 mg/m^3 TWA	1 mg/m^3 TWA (metal and insoluble compounds); 0.1 mg/m^3 TWA (soluble compounds)

See footnotes at end of table.

(Continued)

Table 6-1 (Continued). Current recommendations and standards

MWF component	NIOSH REL	OSHA PEL	ACGIH TLV
Oil mist (mineral)	0.4 mg/m^3 TWA (thoracic particulate mass) or 0.5 mg/m^3 (total particulate mass) in metalworking operations	5 mg/m^3 TWA	5 mg/m^3 TWA, 10 mg/m^3 STEL TLV-TWA[***]
Oil mist, mineral, sum total of 15 polynuclear aromatic hydrocarbons (PAHs) listed as carcinogens by the U.S. National Toxicology Program (NTP)	No REL	No PEL	0.005 mg/m^3
Sulfur chloride (sulfur monochloride)	1 ppm (6 mg/m^3) ceiling	1 ppm (6 mg/m^3) TWA	1 ppm (5.5 mg/m^3) ceiling
Triethanolamine (TEA)	No REL	No PEL	5 mg/m^3 TWA
Viable microorganisms (total bacteria and fungi, and single genera)	No REL	No PEL	No TLV

[*]The Ca notation indicates that NIOSH lists this component as a potential occupational carcinogen.
[†]Unless otherwise noted, the ceiling value should not be exceeded at any time.
[‡]ACGIH lists A3 as an animal carcinogen.
[§]The STEL is 15 minutes unless otherwise indicated.
[**]ACGIH lists A2 as a suspected human carcinogen.
[††]Chromic acid and chromates (as CrO_3), chromium (II) and chromium (III) compounds (as Cr), and chromium metal (as Cr). The NIOSH REL (10-hr TWA) is 0.001 mg Cr(VI)/m^3 for all hexavalent chromium—Cr(VI)—compounds. NIOSH considers all Cr(VI) compounds (including chromic acid, tert-butyl chromate, zinc chromate, and chromyl chloride) to be potential occupational carcinogens. The NIOSH REL (TWA) is 0.5 mg Cr/m^3 for chromium metal and chromium (II) and chromium (III) compounds. The OSHA PEL is 0.1 mg CrO_3/m^3 (ceiling) for chromic acid and chromates (including tert-butyl chromate with a "skin" designation and zinc chromate); 0.5 mg Cr/m^3 (TWA) for chromium (II) and chromium (III) compounds; and 1 mg Cr/m^3 (TWA) for chromium metal and insoluble salts.
[‡‡]ACGIH lists A4 as not classifiable as a human carcinogen.
[§§]ACGIH lists A1 as a confirmed human carcinogen.
[***]ACGIH Notice of Intended Change is as follows: the TLV (TWA) is 5.0 mg/m^3 for severely refined and 0.2 mg/m^3 for mildly refined; the TLV (TWA) is 5 µg/m^3, A1 (confirmed human carcinogen) for the sum total of 15 PAHs listed as carcinogens by NTP.

CHAPTER 7

Sampling and Analytical Methods

NIOSH recommends thoracic sampling and gravimetric measurement of MWF aerosol using NIOSH Method 0500 [NIOSH 1994c] with a sampling device that collects the thoracic fraction. The limit of quantitation (LOQ) for this method, or the lowest mass that can be measured with acceptable precision, is 0.13 mg/m^3. If a thoracic sampling device is not available, a total dust sampler can be used and the result can be divided by 1.25 to estimate the thoracic fraction. NIOSH Method 0500 can be used to measure the total material collected. However, when there are simultaneous exposures to nontoxic particulate materials, NIOSH Method 5026 [NIOSH 1994c] or a similar method may be useful to estimate the soluble component of the workroom aerosol.

7.1 Background of Current Methods

The sampling and analytical methods used to assess airborne MWF exposures in the most recent respiratory epidemiologic studies by Kennedy et al. [1989], Greaves et al. [1995a,b, 1997], and Robins et al. [1994] were based on a gravimetric measurement of airborne particles, with some differences in selection of particle size distribution. These methods are susceptible to interference from contaminating materials such as environmental or construction dusts and (infrequently) metal particles. The problem can be reduced by extracting the MWF from the non-MWF particles with an appropriate solvent or solvents. Currently, little or no scientific evidence suggests that "extractable" MWF is superior to thoracic or particulate aerosol as a predictor of adverse health effects from MWF aerosols.

NIOSH is evaluating a provisional method developed by the ASTM E34.50 Committee for separation of MWF from co-sampled material. Samples are collected on polytetrafluoroethylene (PTFE) filters and extracted with a ternary solvent blend. The difference in the weight of the filter before and after collection yields the total mass sampled. The difference in the weight of the filter before and after extraction is the weight of the MWF. This method was successfully evaluated by NIOSH for the extraction of four MWFs spiked onto PTFE filters. The technique is undergoing further evaluation in a large-scale field test. Other methods that have been used for MWF aerosols are listed in Table 7–1.

Table 7–1. Comparison of current MWF analytical methods

Method	Type	Flow (L/min)	Maximum volume	Filter	Pad	Sorbent	Extraction solvent	
							Filter	Sorbent
NIOSH Method 0500	G*	1.0–2.0	133	37-mm, 5.0-µm PVC	Yes	NA	NA	NA
NIOSH Method 0600	G	1.7–2.2	400	10-mm cyclone, 5-µm PVC	No	NA	NA	NA
NIOSH Method 5026	IR	1.0–3.0	500	37-mm, 0.5–0.8 µm PVC or MCE	No	NA	Trichloroethane, trifluoroethane	NA
Chrysler	G	1.0–2.0	133	37-mm, 5.0-µm PVC	Yes	NA	Toluene	NA
Ford FIH 005	G	2.0–3.0	1440	37-mm type A or GFF	Yes	NA	Trichloroethylene or perchloroethylene	NA
Ford FIH 005 (mod)	G, GC	1.0	480	37-mm type A or GFF	Yes	600-mg charcoal tube	Trichloroethylene or perchloroethylene	Carbon disulfide

*Abbreviations: G = gravimetric, GC = gas chromatography, GFF = glass fiber filter, IR = infrared, MCE = mixed cellulose ester, NA = not applicable, PAD = backup pad, PVC = polyvinyl chloride.

7.2 Potential Sampling and Analytical Method Bias and Sources of Error in Measuring MWFs

7.2.1 Sampling According to ACGIH Conventions

The ACGIH [1997b] and the ISO [1995] recommend size-selective sampling to target measurements for specific regions of the respiratory system. ACGIH recommends three types of particle size-selective TLVs: (1) inhalable particulate mass for materials that are hazardous when deposited anywhere in the respiratory tract, (2) thoracic particulate mass TLVs for materials that are hazardous when deposited anywhere within the lung airways and gas-exchange region, and (3) respirable particulate mass TLVs for materials that are hazardous when deposited in the gas-exchange region. Because NIOSH has established the REL primarily to prevent adverse respiratory effects, thoracic sampling is the most appropriate approach when thoracic samplers are widely available and adopted.

7.2.2 Thoracic Samplers

Several options exist for thoracic sampling of MWFs. A personal cascade impactor has been used for measuring the size distribution of aerosols. The information from this impactor can be used to calculate the thoracic fraction of the sampled aerosol [Baron and Willeke 1986]. Alternatively, the stage that cuts at 10 μm can be used to simulate a thoracic preclassifier and the remaining aerosol collected on the downstream filter [Kriebel et al. 1994]. A recently developed sampler uses a cyclone operated at 1.6 L/min that matches the cutpoint of the thoracic curve [Kenny and Gussman 1997; Maynard 1997].

Another sampler that can be used as a thoracic sampler is one designed to match the EPA PM-10 curve. The PM-10 curve is sharper than the thoracic curve; but for typical MWF size distributions (σ_g >2.0, median d_{ae} <20 μm), the use of a sharper cut introduces less than 20% bias. For most of this range of size distributions, the bias is less than 10%.

The CIP-10 sampler is also designed to sample the thoracic fraction [Fabriés 1992; Görner et al. 1994]. This device collects the thoracic fraction on an open-pore foam which is weighed. The CIP-10 sampler is expensive because of its air-moving system (which is integral to the sampler) and because of sampler import costs. However, it has the advantage of sampling at 7 L/min, thereby allowing the collection of short-term samples or more accurate full-shift samples. Another thoracic sampler also uses a porous foam as the size-classifying device [Vincent 1989] but is not commercially available. Chen et al. [1996] have developed a better match to the thoracic curve with a foam-based preclassifier by using two different pore-size foam sections in parallel.

An alternative to the use of a thoracic sampler is the use of a total dust sampler with a correction factor applied to convert to the thoracic fraction. This approach is subject to

bias when the MWF size distribution changes. Although the reported size distributions for some MWFs have a median size smaller than 10 μm [Woskie et al. 1994], the size distribution of MWFs should be measured to ensure that the median size is small. Kriebel et al. [1994] compared total aerosol samples (using a closed-face cassette) with "thoracic" samples (using an impactor with a 50% cut point at 10 μm) and obtained a median ratio of total to thoracic of 1:4. Based on some measured size distributions [Woskie et al. 1994], the calculated median of the ratio of total to thoracic is about 1.25.

7.2.3 Sampler Inlet Biases

Inlet sampling efficiency can be a major source of bias in collecting aerosol particles. This bias generally increases with increasing particle size and increasing external air velocities. Bartley et al. [1994] have addressed the bias involved in sampling respirable aerosol. They reported that sampling bias is highly affected by the aerodynamic diameter of the aerosol being monitored, with biases ranging from +10% to -30% for both the 10-mm nylon cyclone and the Higgins-Dewell cyclone for aerosols with aerodynamic particle size less than 25 μm. Biases are also present in total dust sampling. Chen and Baron [1996] demonstrated a significant bias that depends on the orientation of the sampler to the wind. The orientation of the sampler inlet relative to the worker's body may play an important role—that is, a sampler inlet pointing horizontally away from the body may be more accurate than an inlet pointing downward. An extensive study of the sampling efficiencies of most conventional inhalable or "total" aerosol samplers (including the closed-face cassette) indicates that these samples are biased (especially for larger-diameter particles) and depend on wind speed [Kenny et al. 1997]. However, the bias is relatively small for all tested "total" and inhalable samplers when the median aerosol diameter is less than 25 μm. In one study, measured MWF personal exposure size distributions suggest that typical size distributions may have median aerodynamic diameters smaller than 10 μm [Woskie et al. 1994]. This finding indicates that sampling thoracic MWF aerosols may involve more bias than sampling respirable aerosol—but considerably less bias than sampling total aerosol. Further research is required for a more precise estimate of aerosol sampling bias.

7.2.4 Other Sampler Biases

A number of factors regarding aerosol sampler accuracy have been investigated during the past 30 years. A review by Baron [in press] indicates that factors such as sampler leakage, sampler conductivity, internal flow patterns, and collection medium stability are important in the development of an accurate sampler. Several of these factors are often overlooked in the development of samplers and can contribute significantly to errors in field measurements. During area sampling at a lead abatement site, the 37-mm closed-face cassette was compared with a new sampler. The newly developed sampler produced a variability of 10% relative standard deviation (RSD), and the closed-face cassette produced 100% RSD at 2 L/min [Hauck et al. 1997]. Since the closed-face

cassette violates several factors affecting accuracy and precision, as indicated by Baron, and has poor inlet characteristics [Kenny et al. 1997], it is not surprising that its use results in higher variability. However, because of its common use and availability, the closed-face cassette can be used as a surrogate for thoracic sampling (with the above-mentioned correction factor) until better samplers are available. Together with improved samplers, the closed-face cassette can provide data for comparison with earlier measurements.

Many MWFs have a significant vapor pressure at room temperature. When MWFs are generated as an aerosol, the large increase in surface area allows the equilibrium vapor pressure above the particle surface to be reached more quickly. The droplets evaporate more quickly than as a bulk liquid, especially when the aerosol droplets are collected on a filter. The droplets are then suspended in a high-velocity air stream and can lose volatile components during the sampling period. Two collection techniques have been suggested to reduce the evaporative loss: impaction [Wang and John 1988] and electrostatic precipitation [McAneny et al. 1995]. In both cases, the aerosol is deposited as a bulk liquid on a surface that is somewhat removed from the high-velocity air stream—rather than as a high-surface-area particulate intimately exposed to the air stream in a filter.

Leith et al. [1995] compared filter sampling with electrostatic precipitator sampling in both laboratory [McAneny et al. 1995] and field studies. The electrostatic precipitator collected concentrations that were up to five times greater than those collected by the filter method; this difference indicates significant filter losses. The loss depended on the vapor pressure of the oil, the ambient temperature, the size of the droplets, the type of filter, and the concentration of vapor in the sampled atmosphere. The last factor was indicated by evaporative losses being greatest at low oil mist concentrations when vapor concentration was also expected to be low. The proposed sampling and analytical method using filtration does not take into account evaporation of the MWF. Using this method may increase the variability of results and introduce an uncontrolled bias. Further research may result in recommendation of an improved sampling method that significantly reduces evaporative losses during sampling.

7.2.5 Estimating Total Method Bias

No studies have been performed on the accuracy of thoracic samplers. Further research is required to estimate the method bias.

7.2.6 Estimating Total Method Precision

For a gravimetric technique, the estimated LOQ is 130 μg per filter [Glaser and Shulman 1996; Shulman and Glaser 1997]. This estimate is based solely on the mass at which the gravimetric error becomes 10%. If the analytical finish involves further extraction of the sample, the imprecision is likely to increase. In several analytical

scenarios, the sample is extracted, but different extraction efficiencies are obtained. The maximum imprecision associated with sampling and analysis at the LOQ can be estimated if appropriate estimates of all error sources are known. Table 7–2 lists the potential sources of error (RSDs) for various MWF analytical techniques effective at or near the LOQ. Although the magnitudes of these sources of imprecision are generally unknown, assumptions must be made to allow for their estimation. Generally, the pump precision is assumed to be 0.05. Intersampler variability may be quite large, depending on the orientation of the sampler to the airstream, particle size, particulate static charge, and wind velocity [Bartley et al. 1994; Baron et al. 1995; Kenny et al. 1997; Almich and Carson 1974]. For example, Bartley et al. [1994] have demonstrated an intersampler variability of up to 10% for the 10-mm cyclone. In addition, Almich and Carson [1974] reported a 10% intersampler variability due to charge effects in the 10-mm cyclone and filter. Knight and Kirk [1982] discussed other sources of variability. Although the issue of sampling variability remains to be settled, an upper limit of approximately 0.10 appears rea- sonable for this parameter.

For aerosol sampling only, the analytical imprecision at the LOQ is assumed to be due entirely to the gravimetric analysis and is estimated to be 0.10 at the LOQ. Pooling all sources of analytical and sampling variability enables computation of a maximum relative standard deviation for the total procedure [RSD_T]—0.15 for aerosol sampling at the LOQ.

For a solvent extraction technique, it is reasonable to allow for incomplete extraction of the MWF aerosol. Extractables are removed by washing the filter with a solvent. An aliquot of the sample is then evaporated to dryness in a preweighed cup. The mass difference is then determined. This process may introduce imprecision into the analytical method as a result of the extraction step [$RSD_{extract}$] and reweighing steps [$RSD_{reweighing}$]. The extraction is assumed to be precise regardless of the amount extracted (i.e., [$RSD_{extract}$] is not needed to estimate [RSD_T]). Using techniques described elsewhere, Bevington [1969] and Shulman and Glaser [1997] considered the effect on the overall RSD for three situations in which the fraction extracted corresponded to 10%, 50%, and 90% of the total mass sampled. Even for high levels of extraction efficiency (e.g., 90%) the overall precision of analysis is approximately 0.15.

NIOSH sampling and analytical methods require 95% of all samples collected to fall within +/- 25% of the true mean or standard value, accounting for both bias and imprecision within the sampling method [Kennedy ER et al. 1995]. For a method with zero bias, the maximum suggested RSD is 0.128. Information from a round-robin study of MWF sampling and analytical methods [D'Arcy et al. 1995] indicates that some data collected by three particulate sampling and analysis methods at concentrations ranging from 0.55 to 1.77 mg/m^3 may not meet NIOSH sampling and analytical requirements. Although the round-robin study data are still preliminary, the need for improved sampling and analytical methodology is apparent.

Table 7–2. Potential sources of error (RSDs) for various MWF analytical techniques effective at or near the LOQ

Type of sample	RSD for pump	RSD for intersampler	Fraction extracted	RSD for weighing	Estimated RSD for total process*
Aerosol only	0.05	0.10	NA	0.10	0.150
Extractables only	0.05	0.10	0.1	1.00	1.006
			0.5	0.20	0.229
			0.9	0.11	0.158
Extractables relative to total mass			0.1	1.005	1.005
			0.5	0.224	0.224
			0.9	0.149	0.149

*Values for all sample types except total aerosol are minimum values. The true value depends on the unknown correlation between pump error in the extracted and unextracted portions. The same considerations apply to the sampling error. The minimum value assumes that the RSD for the pump is constant for the different fractions and that the absolute standard deviation for weighing the filter and the collection cup are approximately equal.

If no uncorrectable bias is assumed in these methods, the NIOSH precision requirements would be approached for sampling and analysis of thoracic aerosol and high recoveries of total extractables. For all other sampling and analytical method designs, these criteria would not be met.

7.3 Sampling and Analytical Issues Involved in Establishing the REL

7.3.1 LOQ

Several issues remain to be resolved regarding the sampling and analytical method accuracy and precision for aerosols, particularly for all classes of MWF aerosols. Appropriate sampling and analytical methods should be used to address operations that involve exposure to both MWF and non-MWF material. The standard should be established at a mass concentration that exceeds the LOQ of sampling and analytical methods. Current gravimetric LOQ data indicate that a gravimetric standard of 0.4 mg/m^3 (thoracic particulate mass) is feasible with respect to sampling and analytical methods. NIOSH Method 0500, modified to sample with a thoracic preclassifier, is an acceptable method.

7.3.2 STELs and Ceiling Limits

The ILMA has stated that a STEL or ceiling limit of 2.0 mg/m^3 may be more protective of worker safety and health than a TWA exposure limit; they indicate that such a limit should at least be coupled with a TWA exposure limit [Howell 1996].

One difficulty in adopting either a STEL or a ceiling limit lies in measurement. In the publication *Occupational Exposure Sampling Strategy Manual* [NIOSH 1977] NIOSH recommends that samples taken to determine ceiling limits be collected during periods of maximum expected concentrations. A minimum of three 15-min samples should be taken during each work shift, and the highest of the three measurements should be used to estimate the worker's upper exposure for that shift. In many cases, the work process appears to be relatively constant during the work shift, and random techniques are required to estimate the upper bounds of exposure. For example, to identify at least one 15-min period from those representing the top 20% of exposures with a 95% confidence level, eleven 15-min (nonoverlapping) samples are needed. The total aerosol sampling and gravimetric analysis techniques proposed in this criteria document should provide adequate sensitivity to monitor exposures reliably at a concentration of 2.0 mg/m^3 during a 15-min sampling period. Thus the sampling and analytical costs of determining exposure to a STEL or ceiling limit could range from 3 to 11 times that of a TWA limit. In addition to the sampling difficulties, only one of the epidemiologic studies used real-time sampling to measure short-term exposure [Sprince et al. 1997].

Real-time measuring instruments can be used as an alternative to conventional sampling and analysis using pumps and filters with subsequent gravimetric analysis. Aerosol photometers are real-time aerosol instruments that are reliable, easy to use, and relatively inexpensive. They sample the workroom air and instantaneously measure the concentration of airborne dusts and mists by measuring the amount of light scattered by these materials. Although the results of these measurements are typically displayed with the units mg/m^3, these numbers should be considered as estimates of the true concentration, since the amount of light scattered depends on the characteristics of the aerosol in addition to its concentration. Aerosol photometers respond roughly to particle volume; thus the instrument readings measure any water contained in the MWF. Gravimetric techniques measure only the residual, nonvolatile particles retained on a filter. The aerosol photometer response also depends on the physical configuration of the light-scattering element, the wavelength of light used, and the size and optical properties of the aerosol particles. Thus these instruments must be calibrated by comparing them with gravimetric techniques for each combination of aerosol size and fluid type. The initial cost of an aerosol photometer is approximately 10 times the cost of a conventional sampling pump; however, some of this initial cost is offset by subsequent (potential) savings in analytical costs.

In addition to the difficulty and cost of measuring a STEL or ceiling concentration, few epidemiologic data exist from which to develop criteria for short-term exposures. Thus no recommendations are made for a STEL or ceiling limit in this document.

CHAPTER 8

Basis for the Recommended Standard

8.1 Introduction

Under the authority of the Occupational Safety and Health Act of 1970 (Public Law 91–596), NIOSH was established to develop and recommend criteria for identifying and controlling workplace hazards that could result in occupational illness or injury. To formulate these recommendations, NIOSH evaluates all relevant scientific information about a given hazard. This information includes health effects data, routes of exposure, preventive measures (e.g., engineering controls, safe work practices, personal protective equipment), and the feasibility of controlling hazards and thereby reducing or eliminating adverse health effects.

NIOSH has primarily used peer-reviewed, published articles to form conclusions about health hazards associated with MWF exposures. In addition, NIOSH has reviewed several recent, unpublished epidemiologic investigations of worker exposures to MWFs. These investigations were sponsored by the Occupational Health Advisory Board (OHAB) of the International Union, United Automobile, Aerospace and Agricultural Implement Workers of America and the General Motors Company (UAW-GM) as part of their joint safety and health activities. The OHAB, which is made up of six to seven university scientists, solicits research proposals from academic institutions. Following peer reviews of proposed research projects, OHAB funds, monitors, and facilitates the progress of selected proposals. Final research reports are prepared by the investigators after nonbinding peer review by OHAB. NIOSH included three such investigations [Kriebel et al. 1994; Greaves et al. 1995a,b; Robins et al. 1994] in addition to a traditionally peer-reviewed study by Kennedy et al. [1989] when determining the need for an REL for MWF aerosol. Greaves et al. [1995b] and the studies by Kriebel et al. [1994] and Robins et al. [1994] have now been published [Greaves et al. 1997; Kriebel et al. 1997; Robins et al. 1997; Sama et al. 1997].

This chapter briefly summarizes the major findings from Chapters 5 and 6, which contain the health basis for the proposed REL and the information about past and current exposures to MWF aerosol.

Major changes have been introduced into the U.S. machine tool industry over the last several decades. The overall consumption of MWFs (specifically synthetic MWFs)

increased as tool and cut speeds increased. Advances in automation enabled the machines to be partially enclosed, which facilitated the application and use of local exhaust ventilation. During the 1970s and 1980s, many U.S. plants installed recirculating air cleaners, improved the recirculating air filtration systems, and renovated the factories. The improvements were prompted partly by the ACGIH TLV of 5 mg/m³ for mineral oil mist [ACGIH 1997b] established in the 1960s, and its promulgation by OSHA as a PEL in 1970 [29 CFR 1910.1000].

Hallock et al. [1994] described the effect these improvements had on the automotive industry in reducing exposures to airborne MWFs. Concentrations declined significantly over the 30-year period 1958–87, with an arithmetic mean concentration of 5.42 mg/m³ (total particulate mass) observed before 1970 and 1.82 mg/m³ after 1980. The geometric mean for MWF aerosol concentration at the plants studied by Hallock et al. [1994] was 0.56 mg/m³ after 1980.

Since 1987, MWF exposures in the automotive industry have continued to decline. In the most recent studies of automobile manufacturing, worker exposures to aerosols of straight oil, soluble oil, and synthetic MWFs (mean exposure concentrations in nongrinding operations) were reported to be <1.0 mg/m³ (total particulate mass) [Hallock et al. 1994; Kriebel et al. 1997; Greaves et al. 1995a,b, 1997; Robins et al. 1994]. Kriebel et al. [1997] reported mean exposures (7-hole sampler) of 0.24 mg/m³ to aerosols of straight oil MWFs and 0.22 mg/m³ to soluble oil MWFs. MWF aerosol concentrations generally below 1.0 mg/m³ were also reported by Greaves et al. [1995a,b, 1997], with mean concentrations (thoracic fraction) for several plant surveys of 0.2 to 0.68 mg/m³ (straight oil MWFs), 0.35 to 0.65 mg/m³ (soluble oil MWFs), and 0.41 mg/m³ (synthetic MWFs). Likewise, Robins et al. [1994] reported that MWF aerosol exposures for automotive parts manufacturing workers ranged from 0.1 to 0.6 mg/m³ (thoracic fraction) for soluble oil MWFs.

The occupational exposure data compiled by the NIOSH HHE program (1972 to 1993) also show that exposure to airborne MWFs has generally decreased over time. These data indicate that the arithmetic mean personal exposures were 1.23 mg/m³ (n=21 plants) in the 1970s, 0.57 mg/m³ in the 1980s (n=15 plants), and 1.0 mg/m³ in the 1990s. However, these figures are based on data from only two plants. The overall mean concentration was 0.96 mg/m³ for 38 plant-based HHEs.

This decline in airborne exposures has also been reported in the OSHA IMIS, which compiles the air sampling data from OSHA inspectors (Table 3–3). The OSHA exposure data for mineral oil mist represent a substantial cross-section of industry. These exposure data demonstrate a steady decline in exposure concentrations from before 1980 to the present. The arithmetic mean concentration (gravimetric method analysis) for all samples collected during this period was 0.92 mg/m³ (total particulate mass); for the period January 1991 to April 1995, the arithmetic mean was 0.49 mg/m³.

The increasing percentage of samples with airborne concentrations below 0.5 mg/m³ over time suggests that improvements in engineering controls and work practices have occurred. Before 1980, 37% of the air samples contained MWF concentrations below 0.5 mg/m³ (total particulate mass), whereas 73% of the samples from the most recent period (1991–95) contained concentrations below 0.5 mg/m³ (total particulate mass).

Without a detailed description of the worker exposures (e.g., MWFs or processes or operations using MWFs) for data reported in the IMIS or the NIOSH HHEs, it is not possible to evaluate the technologic feasibility of controlling all MWF aerosol exposures to concentrations below the REL. However, the historical trend in declining exposure concentrations suggests that significant accomplishments have been made in the reduction of exposures. Further investigation and research will be needed to determine more precisely the technologic feasibility of reducing all MWF aerosol exposures to concentrations below the REL.

8.2 Effects of MWF Exposure

8.2.1 Nonmalignant Respiratory Effects

Substantial evidence indicates that workers currently exposed to MWF aerosols have an elevated risk of asthma [Forbes and Markham 1967; Robertson et al. 1988; Savonius et al. 1994]. Published clinical case reports indicate that MWF-induced asthma appears to involve known sensitizers in some cases but that various other agents (possibly acting through irritant or inflammatory mechanisms) may be responsible for a high proportion of cases [Forbes and Markham 1967; Robertson et al. 1988; Savonius et al. 1994]. Table 5–1 presents selected risk estimates for asthma morbidity derived from these studies.

8.2.1.1 Asthma and Synthetic MWFs

Convincing evidence indicates that workers exposed to synthetic MWFs have an increased risk of work-related asthma. Some evidence from cross-sectional studies suggests a tendency for affected workers to transfer away from jobs involving exposure to MWF aerosol. In the Eisen et al. [1997] study (which attempted to control for this job-transfer bias), the adjusted risk estimate for exposure to synthetic MWF aerosol was about three times the risk relative to unexposed populations. Estimated MWF aerosol exposures in the 2 years before diagnosis ranged from 0.36 to 0.91 mg/m³ (inhalable mass), with a mean of 0.6 mg/m³. Risk estimates were elevated in all three studies of asthma and exposure to synthetic MWF aerosol [Greaves et al. 1995b, 1997; Eisen et al. 1997; Rosenman et al. 1995], although the finding in the Greaves [1995b] study was not statistically significant (Table 5–1). Additional evidence indicates that exposure to synthetic MWF aerosol increases airways hyperresponsiveness over time [Kennedy et al. 1995b,c].

8.2.1.2 Asthma and Soluble Oil MWFs

The evidence associating asthma and exposure to soluble oil MWF aerosol is somewhat less consistent than that for synthetic MWFs, but more studies have investigated this relationship. Only Greaves et al. [1995b, 1997] and Rosenman et al. [1997b] presented elevated risk estimates that were statistically significant, but five of the seven epidemiologic studies of soluble oil MWF exposures reported elevated risk estimates for asthma, with point estimates ranging upward from 1.7 [Rosenman et al. 1997b; Greaves et al. 1995b, 1997; Kriebel et al. 1994; Robins et al. 1994; Massin et al. 1996]. Four of these five studies estimated mean current exposures to soluble oil MWF aerosol ranging from 0.22 (inhalable fraction) to 1.49 mg/m³ (total extractable oil aerosol) [Kriebel et al. 1994; Robins et al. 1994; Greaves et al. 1995b, 1997; Massin et al. 1996]. In the other study (for which mean exposures were not reported), 90% (44/49) of the air samples yielded oil mist measurements of less than 1.0 mg/m³ [Rosenman et al. 1997b]. In two studies [Ameille et al. 1995; Eisen et al. 1997], the risk estimates were less than 1, even though exposures were not lower than in the more positive studies. However, Ameille et al. [1995] found evidence suggesting that affected workers had transferred from jobs with exposure to soluble oil MWF aerosol, which may have biased findings from that study. Also, the negative finding of Eisen et al. [1997] is difficult to interpret in view of the statistically significant positive association between asthma and cumulative exposure to soluble oil MWF aerosol in the same study group [Greaves et al. 1995b, 1997]. In addition, Massin et al. [1996] and Wild and Ameille [1997] both found a positive association between increased bronchial responsiveness and cumulative exposure to soluble oil MWF aerosol. Overall, the preponderance of evidence from all these studies indicates that airways hyperresponsiveness and asthma are both associated with exposure to soluble oil MWF aerosol.

8.2.1.3 Asthma and Straight Oil MWFs

The epidemiologic evidence for an association between asthma and exposure to straight oil MWF aerosol is less convincing than that for synthetic and soluble oil MWFs. None of the five studies of straight oil MWFs [Rosenman et al. 1997b; Greaves et al. 1995b, 1997; Eisen et al. 1997; Kriebel et al. 1994; Ameille et al. 1995] documented a significantly increased risk (Table 5–6). Rosenman et al. [1997b] found that workers exposed to straight oil MWF aerosol had a 10% prevalence of new asthma since hire or new work-related symptoms consistent with work-related asthma—a lower prevalence than that found among groups of workers exposed to aerosols of the other major types of MWF. Since the Rosenman study did not include a reference group of unexposed workers, and since the participation rate was not reported, it is unclear whether the 10% prevalence is an elevated rate. In two of the other four studies, the point estimate for asthma risk was elevated [Eisen et al. 1997; Kriebel et al. 1994]. Some clinical case reports suggest that asthma is associated with exposure to straight oil MWF aerosol [Forbes and Markham 1967; Robertson et al. 1988] or to compounds commonly found

in straight oil MWFs [Savonius et al. 1994]. Overall, the risk of asthma exists but is likely to be lower with straight oil MWF aerosol than with other types of MWF aerosols.

Risk may be elevated even at MWF aerosol concentrations below the NIOSH REL. However, the risk for asthma is likely to be dose-dependent and would therefore be expected to be even greater at concentrations exceeding the NIOSH REL.

8.2.1.4 Respiratory Effects Other Than Asthma

In addition to associating MWF aerosol exposures with asthma, evidence also links other adverse respiratory health effects with such exposures. Except for one early study [Ely 1970], epidemiologic studies of respiratory symptoms are generally consistent and (in the case of the more recent studies) provide compelling evidence that occupational exposure to MWF aerosols causes symptoms consistent with airways irritation, chronic bronchitis, and asthma.

The evidence suggests that each class of MWFs (straight, soluble, semisynthetic, and synthetic) can induce respiratory symptoms at MWF aerosol exposure concentrations at or above the NIOSH REL. To date, no convincing evidence identifies any component or components of MWF aerosol as the predominant cause of these symptoms. Roughly a twofold to sevenfold increase in risk for various respiratory symptoms has been associated with mean aerosol exposures ranging from 0.22 mg/m³ (inhalable fraction) to 0.55 mg/m³ (thoracic fraction) among groups of workers exposed to MWFs (Table 5–2). In a large study with mean exposures for the major types of MWFs between 0.41 to 0.55 mg/m³ (thoracic fraction), Greaves et al. [1995b, 1997] found strong and statistically significant quantitative exposure-response relationships between cumulative concentrations of MWF aerosols and respiratory symptoms.

The onset or worsening of many symptoms over a workshift as well as the substantial symptomatic improvement reported by many affected workers when away from work, provide additional evidence that MWF aerosol represents a hazardous exposure. In some affected individuals, respiratory symptoms may precede the development of overt asthma—much as the symptoms of episodic coughing, wheezing, and phlegm predate the diagnosis of asthma by an average of more than 2 years in the much better studied occupational asthma associated with western red cedar dust [Chan-Yeung et al. 1982].

Similarly, studies of acute airflow reductions measured across shifts also provide evidence that exposure to MWF aerosols is associated with asthma. Four studies evaluated acute cross-shift lung function decrements in workers exposed to MWF aerosols [Kennedy et al. 1989; Kriebel et al. 1994, 1997; Robins et al. 1994, 1997; Sprince et al. 1997]. All but one of these studies found that the incidence of cross-shift lung function decrement is associated with occupational MWF aerosol exposures (Table 5–4). The one negative study involved average MWF exposures of 0.33 mg/m³

(range 0.04 to 1.44 mg/m³) measured with a light-scattering device calibrated with Arizona road dust [Sprince et al. 1997]. However, this study revealed a strong association between exposure concentration and acute respiratory symptoms. The studies with straight oil MWF exposures [Kennedy et al. 1989; Kriebel et al. 1994, 1997] offered no evidence that these exposures were less likely to cause the acute drops in lung function than the soluble oil MWF exposures. The evidence indicates that exposure to MWF aerosols causes acute reductions in ventilatory function regardless of the MWF type. Moreover, in all three studies with affected worker populations, these acute airflow reductions occurred in a dose-related manner and were attributable to MWF aerosol concentrations exceeding approximately 0.5 mg/m³ (thoracic particulate mass). In two of the three studies [Kennedy et al. 1989; Kriebel et al. 1994, 1997], the acute airflow reductions were statistically significant at substantially lower aerosol concentrations.

Previous history of childhood asthma appears to increase the risk of acute lung function decrements associated with MWF aerosols, though such decrements occur in the absence of such history. Some evidence suggests that smoking (both active and possibly passive) or baseline airways obstruction may increase susceptibility to cross-shift lung function decrement induced by occupational MWF aerosol exposures [Robins et al. 1997]. Exposure characteristics of MWFs evaluated in one or more of the epidemiologic studies include bacterial count, fungal count, endotoxin, and various elements (including sulfur) [Robins et al. 1997; Kriebel et al. 1997; Sama et al. 1997]. Some of these characteristics show some promise as indicators of MWF aerosol potency, but the data are insufficient to displace the much better documented gravimetric aerosol concentration as the preferred indicator of MWF aerosol potency.

8.2.1.5 Rationale for Reducing MWF Exposures

Reducing MWF exposures to concentrations below the NIOSH REL whenever feasible is prudent because such reductions are likely to decrease the number of new cases of MWF-related asthma in exposed working populations. The evidence of increased asthma risk in some studies and the sharply increased risk of respiratory symptoms and acute pulmonary function changes with exposures above the NIOSH REL suggest that reducing exposures to concentrations below the NIOSH REL will decrease the incidence of all these conditions. Reducing the number of workers with acute respiratory symptoms or decrements in lung function may reduce the number of workers who seek medical evaluation and treatment [Rosenman et al. 1997b]. Though some workers with symptoms or acute respiratory decrements may not develop clinical asthma, they may still seek medical evaluation and treatment. The prevention of asthma is an important priority. Although clinical asthma may be mild in many affected workers, it can sometimes be debilitating. Occupational asthma frequently persists as a chronic condition even after affected workers are removed from exposure

[Chan-Yeung and Malo 1993a]. NIOSH is concerned that the same may be true for MWF-related asthma.

MWF exposures should be reduced to decrease the risk of MWF-related asthma and to decrease the risk of chronic airways disease. Repeated, modest acute airways effects from chronic exposure to MWF aerosol—though apparently reversible when workers are removed from exposure—may ultimately lead to irreversible impairment and chronic pulmonary disability. Acute effects and chronic lung impairment are linked for a variety of other occupational respiratory hazards [Peters 1974; Wegman et al. 1982; Weill 1984; Tabona et al. 1984; Becklake et al. 1988; Hankinson and Hodous 1983; Christiani et al. 1994; Glindmeyer et al. 1994; Becklake 1995; Schwartz et al. 1996]. No studies relate acute decrements caused by MWF aerosols with chronic airways obstruction among exposed metalworkers. Except for one small, older study [Järvholm 1982] and another study now in progress [Kennedy et al. 1995b], no prospective study has been conducted to determine long-term changes in lung function of workers exposed to MWF aerosols. However, completed studies demonstrate that occupational exposure to MWF aerosols causes acute respiratory effects. And based on substantial evidence cited earlier in this paragraph, it is prudent to assert that long-term exposure may cause chronic lung impairment in workers who experience acute respiratory effects.

Six cross-sectional studies of pulmonary function provide some evidence that MWF aerosol exposure has a chronic pulmonary effect [Krzeniak et al. 1981; Greaves et al. 1995a, 1997; Ameille et al. 1995; Massin et al. 1996; Kriebel et al. 1994; Sprince et al. 1997]. Findings from most of these studies generally indicate that occupational exposure to MWF aerosols is associated with reduced pulmonary function (Table 5–3). Three of the four studies with average exposures at or above the NIOSH REL have significant positive findings [Krzeniak et al. 1981; Greaves et al. 1995a; Ameille et al. 1995]. One of the two studies with average exposures below the NIOSH REL has a positive finding [Kriebel et al. 1994]. Pulmonary function evidence suggests that smoking may interact with MWF aerosol exposure to reduce lung function [Ameille et al. 1995; Robins et al. 1997]. Evidence from the largest study involving the major types of MWFs (and adjusted for smoking) suggests that cumulative exposures to straight oil MWF aerosol at a mean concentration of 0.43 mg/m^3 (thoracic particulate mass) and to synthetic MWF aerosol at a mean concentration of 0.39 mg/m^3 (thoracic particulate mass) are both associated with chronic pulmonary function effects that occur in a dose-related manner [Greaves et al. 1995a]. The results are less consistent for current exposure to soluble oil MWF aerosol. The investigators expressed caution about the lack of clear evidence for the chronic effects of exposure to soluble oil MWFs. They noted that most of the workers exposed to one MWF had also been exposed to other MWF types at some time. Overall, these six studies provide limited support for associating MWF aerosol exposures above the NIOSH REL with chronic reductions in pulmonary function.

In addition to work-related asthma and chronic airway effects, current MWF exposures are associated with HP [Bernstein et al. 1995; Rose et al. 1996; Kreiss and Cox-Ganser 1997]. Eight clusters of HP in the automotive industry among MWF-exposed workers have been reported [Kreiss and Cox-Ganser 1997]. MWFs associated with HP are synthetic, semisynthetic, and soluble oil MWFs, all of which are water-based or are diluted with large amounts of water. Microbial contaminants in MWFs are postulated to be the cause of HP outbreaks among workers exposed to MWF aerosol. The outbreaks seem to be associated with unusual flora such as acid-fast bacteria in MWF. *Mycobacterium chelonae* is a common factor in several of the outbreaks. Cases have been associated with MWF concentrations both above and below the NIOSH REL. Some workers with HP have been able to return to jobs that involve no MWF exposure or to jobs that involve exposure to a different MWF. It is not clear whether reducing MWF exposure concentrations alone will effectively reduce the risk of HP.

8.2.2 Cancer

Before the mid-1970s, substantial evidence indicated that at least some MWFs are associated with increased cancer risk at several organ sites (larynx, rectum, pancreas, skin, scrotum, and bladder) (see Section 5.3.3). The studies were not highly consistent with respect to the specific organ sites affected and the strength of association between the disease and the surrogates for exposure data. The inconsistencies are most likely related to the diverse nature of the MWF mixtures studied, the absence of detailed exposure information, and the limitations of the epidemiologic tools used to study the exposures. Because different epidemiologic study populations may have been exposed to different classes and formulations of MWFs, some lack of consistency in site-specific results should be expected when evaluating the carcinogenicity of these substances. The evidence is equivocal for an association between MWF exposure and cancer at several other sites, including the stomach, esophagus, lung, prostate, brain, colon, and hematopoietic system.

The study with the most statistical power [Tolbert et al. 1992] suggests that certain classes of MWFs are associated with cancer at certain sites. However, within these MWF classes, the formulations responsible for the elevated cancer risks are not identified. Within the Tolbert study, straight oil MWF exposure was associated with an increased risk for laryngeal and rectal cancer, and synthetic MWF exposure was associated with an increased risk for pancreatic cancer. Currently, no consistent evidence indicates that soluble oil MWF exposure is associated with cancer at any site. To conclude that no members of the soluble oil class of MWFs posed cancer risks in the past is premature, since soluble oil MWFs contain many of the ingredients found in straight oil MWFs—but in different concentrations. Also, many of the other epidemiologic studies with positive findings involved exposures to more than one class of MWF.

Non-MWF exposures in the MW environment are not likely to be responsible for the cancer findings described in Chapter 5. Smoking and alcohol are associated with some of the cancers associated with MWF exposure. However, the case-control studies controlled for these exposures when appropriate or determined that they were unlikely confounders. Although information about these lifestyle factors is not often collected in occupational cohort mortality or PMR studies, smoking is unlikely to account for relative risks greater than 1.3 for lung cancer and other smoking-related diseases [Siemiatycki et al. 1988]. However, some non-MWF exposures may have interacted with MWF exposure to produce or enhance the observed responses.

The studies that provide the bulk of the evidence associating MWF exposure and cancer involved workers employed as early as the 1930s and as late as the mid-1980s. Because the average latency period is 10 to 20 years between initial exposure to a carcinogen and the appearance of a solid organ cancer, the excess cancer mortality observed in these cohort studies most likely reflects the cancer risk associated with exposure conditions in the mid-1970s and earlier. Over the last several decades, substantial changes have been made in the metalworking industry, including changes in MWF composition and reduction in MWF impurities and exposure concentrations. Efforts to reduce potentially carcinogenic exposures have been ongoing. Removal of PAHs from MWFs began in the 1950s, and EPA regulations in the 1980s were directed at reducing nitrosamine exposures. These changes are likely to have reduced the cancer risks. However, since few epidemiologic data support the association of MWF composition and impurities with the cancer risks observed in earlier cohorts, the data are insufficient to conclude that these changes have eliminated all cancer risks. Furthermore, many workers who entered jobs involving MWF exposures in the mid-1970s or later are now completing the minimum latency period of 10 to 20 years since first exposure, and a definitive study of a large cohort of such workers has not been conducted. Thus the risk of cancer from MWF exposures in the mid-1970s and later remains to be determined.

The NIOSH recommendation for reducing MWF aerosol exposures is supported by substantial evidence associating some MWFs used before the mid-1970s with cancer at several organ sites, and by the potential for current MWFs to pose a similar carcinogenic hazard. However, the primary basis of the NIOSH recommendation is the risk that MWFs pose for nonmalignant respiratory disease.

8.2.3 Dermatologic Effects

Surveillance data from the Bureau of Labor Statistics [DOL 1993] lists industries with potential MWF exposures as having some of the highest incidence rates of skin diseases. Several skin diseases can result from skin contact with MWFs and their contaminants. Straight oil MWFs are often reported to produce folliculitis, oil acne, and keratoses; the water-based oil emulsions (soluble oil and semisynthetic) and synthetic

MWFs primarily cause irritant contact dermatitis and occasionally allergic contact dermatitis [Fisher 1986]. Skin carcinomas are historically associated with the PAH content of mildly refined base oils. Severe refining methods can reduce the PAH content to less than 1% [Skisak 1995].

Contact dermatitis (either irritant or allergic) is the most commonly reported skin disease associated with MWFs. Prevalence rates in cross-sectional epidemiologic studies range from 14% to 30% [de Boer et al. 1988, 1989a,b; Rycroft 1982]. Dermatitis prevalence rates of 14% to 67% have been observed in a variety of workplaces where workers were exposed to MWFs [NIOSH 1984, 1985, 1986a,b, 1989, 1994a]. The impact and significance of dermatitis may go unrecognized because workers often continue to work in spite of active skin lesions, burning, and itching. However, the high prevalence rates of dermatitis indicate that many workers are susceptible to the irritating or sensitizing nature of MWFs and contaminants.

Many factors play a role in the development of dermatitis and other skin diseases in workers exposed to MWFs:

- The MWF class and additives used
- The amount of skin contact with MWFs (e.g., through splashing or repeated or prolonged immersion)
- Skin abrasion or cuts
- Individual susceptibility to irritants or allergens in MWFs
- Inadequate cleansing of the skin after contact
- The irritant nature of some soaps, detergents, and other cleansing materials used by the workers
- Reuse of MWF-soaked clothing or materials
- Use of personal protective equipment such as faceshields and clean, non-irritating, nonsensitizing gloves and aprons
- The cleanliness of the general work environment
- Climate (high or low humidity and hot, warm, or cold temperatures)
- Machine types and operations, and engineering control methods (e.g., tight-fitting machine enclosures)

Sufficient dermal exposure assessment and absorption studies have not been conducted for MWFs. In a variety of unguarded metalworking operations and situations in which

workers wear no personal protective equipment (e.g., gloves, aprons, and face and eye protectors), workers may be frequently splashed or may repeatedly dip their unprotected hands and arms into MWFs. High-speed, high-feed operations may produce aerosols that settle on the skin and mucosal surfaces. In addition, MWFs on the skin may not readily evaporate or be easily washed off. In these cases, the degree of skin contact may be underestimated [Rosenstock and Cullen 1986]. The amount of dermal absorption for many of the MWF components and additives is unknown for intact, abraded, irritated, or otherwise damaged skin.

Because of the poor prognosis for workers with MWF dermatitis [Pryce et al. 1989a], dermatitis prevention is important, and limiting the dermal exposure to MWF is the crux of preventive measures. Other preventive measures may include the following [Mansdorf and Lubs 1994; Tucker 1988; Zugerman 1986]:

- Substituting safe, less irritating, or nonallergenic additives or MWF constituents
- Using process modification, isolation, and ventilation to limit the dispersal of MWFs
- Using work practices and administrative controls to assure proper MWF maintenance and workplace cleanliness
- Properly using personal protective equipment such as protective gloves, aprons, and clothing
- Educating workers about the dermal effects of MWF contact and the importance of workplace personal hygiene
- Changing MWF-saturated clothing quickly
- Washing skin surfaces that have contacted MWFs as soon as possible with nonirritating and nonabrasive soaps

8.2.4 Effects of Microbial Contamination

Water-based and water-contaminated MWFs typically contain both bacteria and fungi. The organisms may be introduced as transients from the air, make-up water, or extraneous materials introduced into the tanks; or they may be disseminated from flocs of biomass that have sloughed from the biofilms growing on the system surfaces. Rossmoore [1981] reported aerobic bacterial counts of 10^5 to 10^7 colony-forming units/ml in MWFs; Salmeen et al. [1987] reported densities that consistently exceeded 10^9 colony-forming units/ml. These counts are similar to those obtained from untreated municipal sewage, but they still greatly underestimate the total extent of microbial contamination because they do not account for anaerobic and other nonculturable bacteria, nor do they include fungi. Microbial growth in MWFs is a long-recognized

problem, but the emphasis has generally been on maintenance of MWF processing characteristics [Hill 1983; Salmeen et al. 1987; Mattsby-Baltzer et al. 1989b, 1990] rather than on the possible health risks for exposed workers. Workers may be exposed to microbially contaminated MWFs by extensive skin contact with contaminated MWF [Salmeen et al. 1987] and by inhaling contaminated aerosols [Mattsby-Baltzer et al. 1989b]. Not surprisingly, researchers have suggested that some respiratory health effects seen in exposed workers may be related to contaminating microorganisms or their products (such as endotoxins, exotoxins, and mycotoxins) [Holdom 1976; Hill and Al-Zubaidy 1979].

The toxic effects of endotoxin inhalation are particularly well known; they include fever, obstructive pulmonary effects, and inflammation [Snella 1981; Kabir et al. 1978; Rylander and Vesterlund 1982]. Robins et al. [1995b] reported personal exposures of automotive workers to endotoxin concentrations ranging from 16.4 to 234 endotoxin units/m^3 [Robins et al. 1994]. For comparison, Rylander and Jacobs [1997] have suggested an occupational threshold concentration equivalent to 100 endotoxin units/m^3 to prevent airways inflammation [Rylander and Jacobs 1997]. Although endotoxins may contribute to adverse respiratory effects, the role of endotoxins in MWF-associated respiratory effects (including asthma) has not been determined.

One published report describes an MWF-aerosol-associated outbreak of a self-limiting nonpneumonic form of legionellosis with influenza-like symptoms [Herwaldt et al. 1984].

Exposure to MWF aerosols has been commonly assessed either as an aerosol mass (gravimetric measurement) or as mass obtained by solvent extraction of the sampling filter. Neither method specifically measures the microbial concentrations or toxins. Therefore, any measurement based on these sampling and analytical methods would not quantitatively or qualitatively assess microbiological and toxin exposure concentrations. Health data are currently insufficient to support an REL for bacterial or fungal concentrations in contaminated MWFs, but the potential of these contaminants as health hazards for exposed workers should be investigated. The emphasis should be placed on a total MWF system management program—including careful fluid monitoring, record-keeping, and maintenance; the judicious use of biocides only as a preventive measure and not as a treatment for microbial overgrowth; a system of mist control including close-capture ventilation and machine enclosures; and training for employees and management on the hazards and proper use of MWFs.

8.3 Rationale for the REL

The NIOSH REL for occupational exposures to MWF aerosol is 0.4 mg/m^3 (TWA) for thoracic particulate mass. Until thoracic samplers are more widely available and adopted, an acceptable substitute for the thoracic particulate mass is the total particulate

mass sample. To translate the thoracic particulate measurement into an equivalent total particulate measurement, divide the total concentration by a correction factor of 1.25* (or other factor experimentally measured for that operation). Thus the REL of 0.4 mg/m³ for thoracic particulate mass is equivalent to a 0.5 mg/m³ for total particulate mass.

The NIOSH REL of 0.4 mg/m³ for thoracic particulate mass (or 0.5 mg/m³ for total particulate mass) is based on four major considerations: (1) the adverse respiratory health effects of MWF aerosol exposure, (2) the selection of an index for measuring MWF aerosol exposure, (3) the applicability of the REL to all types of MWFs, and (4) the technological feasibility of the REL.

8.3.1 Respiratory Health Effects

Substantial evidence indicates that MWF aerosol exposure at concentrations above the REL adversely affects the respiratory systems of many workers. Serious adverse respiratory effects related to MWF aerosol exposure include nonspecific respiratory symptoms, acute impairment of lung function, asthma, and HP. In addition, some evidence suggests that long-term exposure to MWF aerosol can cause chronic lung function impairment even in the absence of overt clinical asthma or HP. By analogy to other occupational respiratory hazards, it is prudent to assume that chronic lung function impairment can result from repeated acute effects on lung function caused by MWF aerosol exposure.

Although some adverse respiratory effects occur at MWF aerosol exposures below the NIOSH REL, evidence indicates that acute impairment of lung function and asthma may be less severe at lower concentrations. However, no exposure-response studies have related HP to MWF aerosol concentration. In addition to reducing MWF aerosol exposures, improvements in the management of fluid systems and microbial contamination of water-containing MWF will most likely be required for most effective control of MWF-associated respiratory health effects, including HP.

8.3.2 Index for Measuring MWF Exposures

A major consideration in determining the REL was whether it should be based on the total particulate mass or the thoracic fraction of the total particulate mass. Since most specific MWF components linked with these effects are uncertain, a surrogate measure of exposure such as the thoracic or total particulate mass is necessary. If only the adverse respiratory effects are considered, an REL measured as thoracic particulate mass is preferable to one measured as total or inhalable particulate mass.

*Conversion factor adapted from data of Woskie et al. [1994].

Increasingly, industrial hygienists are adopting more precisely defined criteria for different size fractions of airborne particulates or aerosols [Soderholm 1993]. In simple terms, these new criteria separate airborne particulates into three fractions. Soderholm [1993] has specified the characteristics of the ideal sampler that would accurately collect these fractions. The concentrations measured by an inhalable particulate sampler and the older "total" sampler (such as the 37-mm, closed-face cassette used in the NIOSH Method 0500) are expected to be approximately equal in environments where the geometric median or mass median particle diameter is smaller than about 10 µm.

Observations from three plants suggest that MWF aerosols generally involve particles in the range of 2 to 8 µm when size is expressed either as geometric mean diameters or mass median diameters [Woskie et al. 1994]. Thoracic mass was strongly correlated (r=0.95) with inhalable mass [Woskie et al. 1994]. In most MWF environments, the correlation between the older "total" particulate mass and the thoracic fraction will be high. Although the thoracic fraction of the MWF aerosol is likely to be more strongly associated with respiratory effects, the inhalable or older "total" particulate mass may be more strongly associated with the risk of occupational cancer. The nonrespiratory cancers epidemiologically associated with some past MWF exposures may have resulted from ingestion of MWF particulates following deposition in the nose, mouth, or throat. Most of the recent epidemiologic studies of adverse respiratory effects measured the thoracic fraction rather than the older "total" particulate mass. NIOSH recommends an exposure limit for MWF aerosol based on thoracic particulate mass. However, until thoracic samplers are more widely available and adopted, NIOSH recommends the use of total particulate mass sampling for MWF aerosol. The methods for sampling thoracic particulates are discussed in Chapter 7. The recommendation for the thoracic particulate REL and sampler is based on the importance of adverse respiratory health effects and the ability of size-selective sampling to measure the particulates that reach the pulmonary airways [ACGIH 1997b; ISO 1995]. NIOSH recommends that samples collected by either method be analyzed gravimetrically by NIOSH Method 0500.

NIOSH considered proposing an REL based on a provisional method developed by the ASTM (ASTM E34.50) Committee for separation of MWF from co-sampled material. Samples are collected on polytetrafluoroethylene (PTFE) filters and extracted with a ternary solvent blend. The difference in the weight of the filter before and after collection yields the total mass sampled. The difference in the weight of the filter before and after extraction is the weight of the MWF. The technique is undergoing evaluation in a large-scale field test and is discussed in Chapter 7. NIOSH decided not to propose an REL based on this provisional method because it has not been fully evaluated. Currently, little or no scientific evidence suggests that "extractable" MWF is superior to thoracic or inhalable particulate aerosol as a predictor of adverse health effects from MWF aerosols. However, extractable MWF aerosol measurements may be useful in occupational environments where there are simultaneous exposures to nontoxic particulate materials and MWF aerosols.

8.3.3 Applicability of REL to All MWFs

NIOSH recommends that the MWF aerosol REL apply equally to all classes of MWFs because all have been associated with adverse health effects (although for some effects, limited evidence indicates variation in risk by class). The cancer study with the most statistical power [Tolbert et al. 1992] suggests that specific classes of MWFs are associated with cancer at certain sites. Within the Tolbert study, straight oil MWF exposure was associated with an increased risk for laryngeal and rectal cancer, and synthetic MWF exposure was associated with an increased risk for pancreatic cancer. NIOSH believes it is premature to conclude that all soluble classes of MWFs were free of past carcinogenic risks, since soluble MWFs contain many ingredients found in straight oil MWFs—but in different concentrations. Also, many of the epidemiologic studies with positive findings involved exposures to more than one class of MWF. The substantial evidence of carcinogenicity for some MWFs in commercial use before the mid-1970s and the possibility that some of the currently used MWFs continue to pose a carcinogenic hazard support the recommendation (based on respiratory disease risk) for reduced exposures to all types of MWFs. Removal of PAHs from MWFs began in the 1950s, and EPA regulations in the 1980s were directed at reducing nitrosamine exposures. These changes are likely to have reduced the risk of cancer in MWF-exposed workers, but only future epidemiologic research can determine whether the hazard has been totally eliminated.

Several different skin diseases can result from skin contact with MWFs and their contaminants. Straight oil MWFs are often reported to produce folliculitis, oil acne, and keratoses; the water-based oil emulsions (soluble oil and semisynthetic) and synthetic MWFs primarily cause irritant contact dermatitis and occasionally cause allergic contact dermatitis [Fisher 1986]. Skin carcinomas are historically associated with the PAH content of mildly refined base oils (previously used in straight oil and soluble oil MWFs). Skin diseases associated with MWFs suggest that all types of MWFs can have adverse health effects.

Substantial evidence indicates that adverse respiratory effects are associated with all classes of MWFs (straight oil, soluble oil, synthetic, and semisynthetic) and with related exposures from contaminants and additives (see Sections 5.1 and 8.2.1). Respiratory effects include symptoms consistent with airways irritation, chronic bronchitis, and asthma; acute reductions in pulmonary function; chronic impairment in pulmonary function; increased airways reactivity to methacholine challenge; asthma; and HP. Substantial evidence indicates that respiratory symptoms and acute reductions in pulmonary function occur with all types of MWF exposures (Tables 5–2 and 5–4). Limited epidemiologic evidence shows that all types of MWFs are associated with chronic reductions in pulmonary function (Table 5–3). Evidence also indicates that exposure to aerosols of microbially contaminated water-based (i.e., soluble, semisynthetic and

synthetic) MWFs is associated with risk of HP [Bernstein et al. 1995; Rose et al. 1996; Kreiss and Cox-Ganser 1997]. Substantial evidence exists for an increased risk of asthma in workers exposed to synthetic and soluble oil MWFs, and some evidence exists for an elevated risk with straight oil MWF exposures (Table 5–1) [Forbes and Markham 1967; Robertson et al. 1988; Savonius et al. 1994]. In addition to the evidence for asthma with MWF exposure, there is evidence of increased airway reactivity following methacholine challenge [Wild and Ameille 1997; Massin et al. 1996; Kennedy et al. 1995b,c]. As with other occupational exposures that cause respiratory symptoms, acute reductions in pulmonary function, and asthmatic disease, NIOSH believes that it is prudent to assume that MWFs cause chronic pulmonary function impairment even in the absence of overt clinical asthma. Reducing chronic MWF exposures to the NIOSH REL or lower should reduce the likelihood that these exposures will cause substantial reductions in pulmonary function. NIOSH recommends that the REL apply equally to all classes of MWFs. Additional research may make it possible to identify MWF formulations with substantially lower risks.

8.3.4 Technologic Feasibility of Controlling MWF Exposures

Keeping MWF aerosol exposures at or below the REL is technologically feasible for most metalworking operations. This assertion is supported by the following observations: (1) MWF aerosol concentrations have steadily declined over the last several decades, as indicated by the OSHA IMIS data set, NIOSH HHEs, and environmental measurements reported in the scientific literature; (2) the automation has increased for machining operations; and (3) engineering controls have been widely implemented and good work practices have been adopted. The most complete information available about the decrease in MWF aerosol exposures comes from the automotive manufacturing industry. Mean MWF aerosol concentrations were between 0.2 and 0.55 mg/m^3 (thoracic fraction) in most recent respiratory studies [Greaves et al. 1995a,b, 1997; Robins et al. 1994; Kriebel et al. 1994]. A recent engineering study found that median aerosol exposure concentrations (total particulate mass) were 0.5 mg/m^3 for older machines without retrofit enclosures, 0.44 mg/m^3 for older machines with retrofit enclosures, and only 0.21 mg/m^3 for enclosed new machines [Hands et al. 1996]. Presumably, machines without enclosures were those with inherently lower emissions. These data indicate that more complete and effective enclosure is possible when the machine is designed with an enclosure. Although the trend in the industry may be toward higher production rates and thus higher MWF aerosol production, these data show that aerosols can be controlled effectively by machine enclosure, ventilation, and air cleaning.

MWF aerosol exposures can be minimized by using the same basic principles of control in both small and large industries. Small metalworking operations may not employ large fixed automation such as transfer machines, but they may use smaller, more flexible machine tools. Older tools found in large and small industries may not be adequately enclosed. The lack of enclosures on older machines could be partially offset by their

lower production rates (turning speed, MWF application, machine utilization, etc.), which may reduce the generation of mists.

Between 1990 and 1995, OSHA compliance data collected from a wide variety of industries showed that 73% of the MWF aerosol concentrations were less than 0.5 mg/m³ (Table 3–3). These data indicate that MWF aerosol exposures are now being kept below 0.5 mg/m³ in many workplaces. Data are not limited on the feasibility of reducing exposures that exceed 0.5 mg/m³ (total particulate mass) at specific worksites. Worker exposures at nonautomated metalworking operations may be difficult to control. One study by Yacher et al. [1997] demonstrated a threefold reduction in exposures (from 0.3 to 0.1 mg/m³) after air-cleaning devices were installed on previously enclosed but nonventilated machines. Many nonautomated machines involve worker/machine interactions that place the worker close to (i.e., at arm's length of) the point of MWF aerosol generation and at risk for substantial dermal exposure. If the worker cannot be isolated from the machine, it may prove difficult to use local ventilation or enclosures to reduce the aerosol exposure.

Newer, automated metalworking machines allow work stations to be positioned to minimize aerosol exposures. With these machines, aerosol-generating operations can be effectively enclosed, and the aerosols can be exhausted and processed in air cleaners for recirculation or discharge to the environment.

8.4 Summary

NIOSH recommends that exposures to MWF aerosols be limited to 0.4 mg/m³ for thoracic particulate mass (which corresponds to approximately 0.5 mg/m³ for total particulate mass) as a TWA for up to 10 hr/day during a 40-hr workweek, measured according to NIOSH Method 0500. The NIOSH REL is intended to prevent the diverse respiratory effects associated with MWF exposure. Limiting MWF aerosol exposure is also prudent because of the association of past MWF exposures with various cancers. Measurement of MWF aerosol is generally a practical and reasonable surrogate of exposure data for nonbiological agents in MWFs that cause the adverse health effects. In most MWF operations it is technologically feasible to keep worker exposures at or below 0.4 mg/m³ (thoracic mass).

The NIOSH REL or lower concentrations can be readily achieved for operators of newer machines equipped with engineering controls. The NIOSH REL may not be technologically feasible for older machines that have inadequate engineering controls. In some metalworking operations, it is feasible to reduce exposures to concentratisons substantially below the NIOSH REL. Keeping exposures below the NIOSH REL is desirable because evidence indicates adverse respiratory effects in some workers exposed to MWF aerosol at the NIOSH REL. Further research may allow NIOSH to develop more protective future recommendations regarding recommended levels of

microbiological contaminants, other specific components of MWFs, and lower concentrations of MWF particulate exposure.

Keeping MWF aerosol exposures at or below the NIOSH REL will significantly reduce the risk of adverse health effects in exposed workers. To further minimize health risks, a comprehensive safety and health program should be implemented to provide for worker education and training, worksite analysis, fluid management, mist control, and medical monitoring. Reducing MWF exposures to concentrations below the REL is an important step in protecting workers, but the steps outlined in the occupational safety and health program described in Chapter 9 are also highly important. In particular, the prevention of dermal exposures to MWFs is critical in preventing MWF-related skin disorders.

CHAPTER 9

Recommendations for an Occupational Safety and Health Program

NIOSH has long recognized the value of comprehensive occupational safety and health programs to prevent occupational deaths, injuries, and illnesses. To be effective, a safety and health program needs to be developed and implemented as part of the employer's management system. Such a program must have strong management commitment and worker involvement. The major elements for a comprehensive, effective safety and health program are: (1) safety and health training, (2) environmental monitoring, (3) hazard prevention and control, and (4) medical monitoring of exposed workers. These elements are described in the following sections.

9.1 Safety and Health Training

Employers should establish a safety and health training program for all workers with MWF exposures. One important goal of training is to enable workers to identify workplace hazards. Instruction should be provided when changes occur in job duties, when a new job is assigned, and when new MWFs or hazardous chemicals are introduced. Both employees and contract workers should be informed about hazardous chemicals in their work areas and the availability of information from MSDSs and other sources.

Workers should be trained to detect and report hazardous situations (e.g., the appearance of bacterial overgrowth and degradation of MWFs). Instruction should include information about how workers can protect themselves (e.g., the use of appropriate work practices, emergency procedures, and personal protective equipment). Workers should be encouraged to maintain good personal hygiene and housekeeping practices to prevent MWFs from contaminating the workplace. In addition, workers should be instructed about the adverse health effects associated with MWF exposures.

9.2 Environmental Monitoring

An occupational safety and health program designed to protect workers from the adverse health effects of exposures to MWF and MWF aerosol should include the

means for thoroughly identifying all hazards. An important part of this program is sufficient environmental monitoring to determine the effectiveness of work practices, engineering controls, and personal protective equipment.

The goal of environmental monitoring is to ensure a more healthful work environment where worker exposures (as measured by full-shift samples) do not exceed the REL. However, as indicated earlier in this document, adverse health effects can occur at the REL, and thus lower exposures are desirable where feasible.

In work areas where airborne MWF exposures may occur, the initial environmental sampling survey should collect representative personal samples for the entire work shift. Surveys should be repeated at least annually and whenever any major process change takes place. Surveys should also qualitatively evaluate the workers' potential skin exposures. All routine personal samples should be collected in the breathing zones of the workers. More frequent monitoring should be undertaken in workers with higher exposure. Airborne exposure measurements should be taken at least every 6 months for workers whose exposures to MWFs are one-half or more of the REL. For workers exposed to MWF aerosols at concentrations above the REL, more frequent monitoring should be maintained until at least two samples indicate that the worker's exposure no longer exceeds the REL. All workers should be notified of monitoring results and of any control actions being undertaken to reduce their exposures. Those who develop an environmental sampling strategy should consider variations in work and production schedules and the inherent variability in most environmental sampling [NIOSH 1995].

When the goal of sampling is to determine whether worker exposures are below the REL, random sampling (without a systematic bias excluding high or low exposures for workers or sampling periods) is usually not included in the sampling strategy. Instead, the strategies should focus sampling efforts on workers with the highest exposures (i.e., the maximum-risk worker, a concept discussed by Leidel and Busch [1994]). Such targeted strategies can most efficiently identify exposures above the REL if maximum-risk workers and time periods can be accurately identified. However, all workers or worker groups should be periodically sampled to ensure that the targeted sampling includes all workers with exposure potentials above the REL.

Source and area samples may be useful supplements to personal monitoring. Area sampling can help determine the source of MWF aerosol exposures and assess the effectiveness of engineering controls.

9.3 Hazard Prevention and Control

First and foremost, management should be knowledgeable about the proper selection, application, and maintenance of MWFs for each operation in the plant or shop; selected

workers should also be trained in these areas. Worker exposures during metalworking operations can occur through inhalation of MWF aerosols and through contamination of the skin by settled mists, splashes, dipping of hands and arms into MWFs, or handling of parts coated with MWF. Most airborne exposures can be controlled by a combination of proper MWF use and application, MWF maintenance, isolation of the operation(s), ventilation, and other operational procedures. Dermal exposures may be reduced by the use of machine guarding, and protective equipment such as gloves, face guards, aprons, or other protective work clothes. Workers should be encouraged to clean MWF-contaminated skin periodically with gentle soaps, clean water, and clean towels. Workers should not need to place their unprotected hands and arms repeatedly into MWFs. Barrier creams may be useful for some workers, but their protective effects are controversial. The use of nonbarrier cream moisturizers may also be protective.

9.3.1 Work Practices

9.3.1.1 Fluid Selection, Use, and Application

Factors to be considered in reducing MWF exposure include operation, fluid type, ventilation, fluid flow rates, machine speed, machine guarding, placement of machines with respect to flumes, and mist collection devices [Ball 1997]. Splashing and mist generation can be minimized by the proper application of the MWF. MWFs should be applied at the lowest possible pressure and flow volume consistent with adequate part cooling, chip removal, and lubrication. To avoid unnecessary mist generation, the fluid should be applied at the interface of the tool and workpiece, thereby minimizing contact with other rotating equipment. Properly maintained filtration and delivery systems can provide cleaner fluids for use, reduce misting, and minimize splashing and emissions. Fluid delivery should stop when machining stops. MWFs should not be allowed to flow over the unprotected hands of workers loading or unloading parts.

If petroleum-containing MWFs are used, the base oil should be evaluated for potential carcinogenicity using ASTM Standard E1687–95: *Determining Carcinogenic Potential of Virgin Base Oils in Metalworking Fluids* [ASTM 1997b]. If soluble oil or synthetic MWFs are used, ASTM Standard E1497–94: *Safe Use of Water-Miscible Metalworking Fluids* [ASTM 1997a] should be consulted for safe use guidelines, including those for product selection, storage, dispensing, and maintenance. To minimize the potential for the formation of nitrosamines, nitrate-containing materials should not be added to MWFs containing ethanolamines. The use of antimisting additives may be considered to minimize the mist production.

The MWFs selected should be as nonirritating and nonsensitizing as possible and remain consistent with operational requirements. MWFs should be maintained by a careful management program and should be compatible with machines, tools, and workpieces. The National Center for Manufacturing Sciences (NCMS) has developed a

draft document *(Metalworking Fluid Evaluation Guide)* that presents MWF compatibility (including in-process compatibility) and performance issues to be considered during fluid selection [NCMS 1996]. Components of the MWF management program should include diligent maintenance of filtration and delivery systems. This maintenance includes the selection of appropriate filters and the consideration of ancillary equipment such as chip-handling equipment, dissolved-air flotation devices, belt skimmers, chillers or plate and frame heat exchangers, and decantation tanks. Coolant return trenches should be guarded to prevent the dumping of floor wash water and other waste fluids. Sumps or coolant tanks should be covered to prevent contamination with waste or garbage. Machines should be kept clean and free of debris. Parts washing before machining can be an important part of maintaining cleaner MWFs [Joseph 1991].

Since all additives will be depleted with time, the MWF and additives concentrations should be monitored frequently so that components and additives can be made up as needed. The MWF should be maintained within the pH and concentration ranges recommended by the formulator or supplier. MWF temperature should be maintained at the lowest practical level to slow the growth of microorganisms, reduce water losses and changes in viscosity, and—in the case of straight oils—reduce fire hazards.

9.3.1.2 Fluid Maintenance

Drums, tanks, or other containers of MWF concentrates should be stored appropriately to protect them from outdoor weather conditions and extremes of temperature, which may cause the fluid concentrates to be unstable because of chemical changes (especially in the case of concentrates mixed with water).

MWFs should be routinely monitored and a record should be kept of the fluid level in the sump or coolant tank, the MWF concentration (measured by refractometer or titration), the fluid pH, and the degree of tramp oil contamination (inspected visually). Monitoring may be more frequent during periods of hot weather or increased work output—both of which may result in increased fluid losses [HSE 1994]. The draft *Metalworking Fluid Evaluation Guide* developed by NCMS presents a list of MWF "symptoms" with possible causes, fixes, and fluid tests [NCMS 1996]. In addition, the guide presents test methods for determining the disposability of spent MWFs.

Insufficient data exist to determine what constitutes a "safe" level of microbial contamination in MWF—either in terms of species present or of absolute numbers of CFUs. Commercial tests are available to determine dissolved oxygen in MWFs (for an indirect measurement of biological activity). Routine microbiological plate counts or dipslides can be used to estimate the number of viable microorganisms. Neither the undiluted fluid concentrates nor the water used for making up the fluids is free of bacteria. However, because of concerns about safety and health as well as fluid

performance, the working solutions should be made with water of drinking quality and correct hardness. To maintain proper MWF concentrations, neither water nor concentrate should be used to top off the system. The MWF mixture should be prepared first by adding the concentrate to the clean water (in a clean container) and then adding the emulsion to that mixture in the coolant tank [HSE 1994]. MWFs should be mixed just before use; large amounts should not be stored, as they may deteriorate before use. Personal protective clothing and equipment should always be worn when removing MWF concentrates from the original container, mixing and diluting concentrate and preparing additives (including biocides), and adding MWF mixture, biocides, or other potentially hazardous ingredients to the coolant reservoir. Personal protective clothing should include eye protection or faceshields, gloves, and aprons that do not react with but shed MWF ingredients and additives.

Coolant systems should be regularly serviced, and the machines should be rigorously maintained to prevent contamination of the fluids by tramp oils (e.g., hydraulic oils, gear box oils, and machine lubricants leaking from the machines). Tramp oils can destabilize emulsions, cause pumping problems, and clog filters [HSE 1994]. Tramp oils may float to the top of MWFs, effectively sealing the fluids from the air and changing the bacterial flora of the fluids. The metabolic products such as volatile fatty acids, mercaptols, scatols, ammonia, and hydrogen sulfide are produced by the anaerobic and facultative anaerobic species growing in MWF with low levels of oxygen. A variety of methods may be used to remove tramp oils: centrifugal liquid or liquid separators, coalescers, oleophilic belts and ropes, skimmers, and vacuums [HSE 1994]. Continuous removal systems should be considered for work situations involving high lubrication losses.

When the fluids are not being agitated and circulated, oxygenation of the fluids can occur only by diffusion. If this process is restricted by a layer of oil, there may be little or no oxidation of the reduced molecules. When the pumps are restarted, malodorous and irritating gases may be suddenly released, causing the characteristic "Monday morning smell," so named because some operations are turned off over the weekend or other prolonged periods of inactivity. This smell generally does not occur in fluid systems that are in good condition. Leaving coolant circulation pumps running over the weekend or during downtime may not be practical, but it may be feasible to pump air through the fluid to produce movement and reduce anaerobic bacterial growth [HSE 1994].

MWFs are usually replaced over time as emulsion and additives are added to make up fluid losses. If it becomes necessary to replace the fluids, care should be taken that all parts of the system are thoroughly cleaned because microorganisms tend to grown on surfaces. Bacteria such as *Pseudomonas* and *Flavobacter* species secrete layers of slime and may grow in stringy configurations that resemble fungal growth. Many bacteria secrete polymers of polysaccharide or protein, which form a glycocalyx and cement cells together much as mortar holds bricks. Fungi may grow as masses of hyphae that form

mycelial mats. The attached community of microorganisms is called a biofilm and may be very difficult to remove by ordinary cleaning procedures. Cleaning methods include the use of steam, vacuums, disinfectant solutions, or commercial chemical cleaners. The cleaning method selected should be compatible with the MWFs [HSE 1994]. Special cleaning precautions are needed for entry into confined spaces [29 CFR 1910.146].

Biocides are used to maintain the efficacy of MWFs by preventing microbial overgrowth. These compounds are often added to the stock fluids as they are formulated. Over time, chemical and biological demands may consume the biocides and cause the concentrations to fall below those needed to inhibit microbial growth. However, biocide concentration should not exceed that needed to meet fluid specifications, as overdosing could cause workers to experience dermal effects, respiratory irritation, or other adverse health effects. Treatment with biocides may eliminate the predominant bacterial species and permit the emergence of previously subordinate, slower-growing species. Therefore the spectrum of biocidal activity should be broad enough to suppress the growth of a highly diverse contaminant population. A single-dose shock treatment may kill the fluid phase (planktonic) organisms without reaching the cells buried within the biofilm. Rapid regrowth from the undisturbed biofilm may be incorrectly interpreted as biocide failure.

Biocides should be added judiciously to *prevent* microbial growth and not as a remedy for grossly contaminated fluids—particularly if large numbers of gram-negative bacteria are present. Even though the numbers of viable cells might be reduced, killed bacterial cells can release large amounts of endotoxins and other microbial products. Currently, no feasible way exists to remove endotoxins, which are soluble and heat-stable. Conscientious monitoring and prevention of microbial proliferation is the best approach for preventing the buildup of endotoxins and other hazardous biological substances and for preserving fluid quality and function.

9.3.1.3 Sanitation and Hygiene

Workers should keep personal items such as food and cosmetics away from the work environment. Eating and applying make-up should not be permitted in work areas. A no-smoking policy should be established, since cigarette smoke may exacerbate the respiratory effects of MWF aerosols for all workers. Employers should support smoking cessation efforts [NIOSH 1991].

Workers should be instructed in personal hygiene to reduce potential dermal exposures to MWFs. Workers should be encouraged to clean MWF-contaminated skin promptly and should be allowed time during the work shift to do so. Workers should change from contaminated work clothes into street clothes before leaving work. If onsite shower facilities are available, workers should be encouraged to shower and change into clean clothes at the end of the work shift.

Good housekeeping includes keeping the floors, equipment, and general work environ- ment clean. Wastes (including floor wash water) should not be dumped or swept into MWF sumps or coolant return trenches.

9.3.2 Labeling and Posting

Workers should be trained to be aware of labeling practices in accordance with the OSHA hazard communication standards [29 CFR 1910.1200 and 29 CFR 1926.59]. Warning labels and signs should be posted on or near hazardous metalworking processes. Depending on the process and MWF exposure concentration, warning signs should state the need to wear protective clothing or an appropriate respirator for exposure to MWF aerosol concentrations exceeding the REL. If respiratory protection is required, the following statement should be posted:

RESPIRATORY PROTECTION REQUIRED IN THIS AREA

All labels and warning signs should be printed in both English and the predominant language of workers who do not read English. Workers unable to read the labels and signs should be informed verbally about the hazards and instructions printed on the labels and signs.

9.3.3 Engineering Controls

9.3.3.1 Isolation

Skin and inhalation exposures to MWF and MWF aerosol can be minimized by using mechanical parts handling equipment and machine enclosures to isolate the workers. Simple splash-guarding may suffice for low-production machines, but complete enclosure (with ventilation) is required for high-production machines. Plant layouts should be such that transfer machines are isolated from other operations. Workers should be provided with isolation booths or fresh air showers.

Machine enclosures are an effective method of reducing worker exposures. Johnston and White [1995] have described the features that are important in designing effective enclosures. ANSI B11 [1997] contains detailed enclosure and mist control designs as well as considerations for installation and use. Hands [1995] examined exposure data collected at an automobile parts manufacturing plant to determine the effect of enclosures on MWF aerosol exposures. This study suggests that enclosures (particularly manufacturer's enclosures that are original equipment) effectively reduce MWF exposures. Retrofitting enclosure structures may also reduce exposures.

9.3.3.2 Ventilation

The ventilation system should be designed and operated to prevent the accumulation or recirculation of airborne contaminants in the workplace. The ventilation system should include a positive means of bringing in at least an equal volume of air from the outside, conditioning it, and evenly distributing it throughout the exhausted area. Principles for the design and operation of ventilation systems are presented in the following publications:

Industrial Ventilation: A Manual of Recommended Practice [ACGIH 1995]

American National Standard: Fundamentals Governing the Design and Operation of Local Exhaust Systems [ANSI 1979]

Recommended Industrial Ventilation Guidelines [Hagopian and Bastress 1976]

Ventilation of operations that produce MWF aerosols is most readily achieved if the machine tool and machining operation are enclosed. The ventilation rate should be selected based on the size of the enclosure openings and the overall size of the enclosure. Air velocity through all openings must be sufficient to prevent the escape of mist. The air velocity depends on the proximity of the opening to the point of mist generation, the energy of the generated mist, and any airflow induced by the rotating machinery or elevated temperature. Guidelines for the selection of this indraft or capture velocity can be found in *Industrial Ventilation: A Manual of Recommended Practice* [ACGIH 1995]. The total exhaust flow rate must also be adequate to purge the enclosure after machining has ceased and before the enclosure is opened. Exhaust duct takeoffs should be located near the point of mist generation and away from enclosure openings to ensure complete purging of the enclosure. Appropriate ventilation rates for purging can be determined by using the procedures outlined in *Industrial Ventilation: A Manual of Recommended Practice* [ACGIH 1995].

Local exhaust ventilation may be used where the machining operations do not permit the use of an enclosure. Design criteria for exhaust hoods are found in *Industrial Ventilation: A Manual of Recommended Practice* [ACGIH 1995].

Air exhausted from machine tool enclosures is often cleaned and recirculated in the workplace. Criteria to ensure the safe recirculation of exhaust air are discussed in *The Recirculation of Industrial Exhaust Air* [NIOSH 1978], and general guidelines for recirculating exhaust air are presented in *Industrial Ventilation: A Manual of Recommended Practice* [ACGIH 1995]. Current industrial practice employs either filtration or precipitation to remove mist particles from the recirculated exhaust air. Selection of appropriate air cleaning equipment (either filtration or electrostatic precipitation) for exhaust from metalworking operations is based on the concentration and size distribution of the particles present in the exhaust stream. Vapors may also be produced in the process, but they are not removed by the filters and precipators typically

employed in metalworking operations. The NIOSH REL is directed at reducing MWF aerosols; researchers have not studied the role MWF vapors play in causing adverse health effects. If unfiltered exhaust air is vented outside the work environment, local air pollution authorities should be contacted regarding the relevant regulations.

In addition to local ventilation of machining operations, general ventilation systems inside plants, manufacturing or processing enclosures, or buildings may be used to control worker exposures to aerosols, vapors, mists, and dust. General ventilation systems are designed to maintain either heated or cooled airflow throughout the plant or building, and airborne hazards are controlled by dilution or removed by exhaust. Air quality is maintained by designing a general ventilation system that minimizes air stagnation and excess humidity, prevents short-circuiting of the fresh air supply to the exhaust, and directs clean air across the workers to carry airborne contaminants to the exhaust.

9.3.4 Protective Clothing and Equipment

Engineering controls are used to reduce exposure to MWF aerosols. But in the event of airborne exposures that exceed the NIOSH REL or dermal contact with the MWFs, the added protection of CPC and equipment such as respirators should be provided. Maintenance staff may also need CPC because their work requires contact with MWFs during certain operations. All workers should be trained in the proper use and care of CPC. After any item of CPC has been in routine use, it should be examined to ensure that its effectiveness has not been compromised. The following recommendations should be used as a guide to selecting CPC.

9.3.4.1 Protective Clothing

Protective clothing for workers exposed to MWFs should protect wearers from chemicals as well as punctures, cuts, and abrasions. Workers should wear faceshields or goggles, protective sleeves, aprons, trousers, and caps as needed to protect their skin from contact with MWFs. The use of gloves may increase the risk of injury from entanglement with moving tools or workpiece parts. If gloves are required, special attention should be given to guarding the equipment and ensuring that the gloves will tear easily if entangled. Workers should also wear safety shoes with slip-resistant soles.

Types of dermal protection should be determined by assessing the identity, concentration, and toxicity of the chemicals to which workers are exposed, the state of these chemicals (solid, liquid, or gas), and the body parts potentially affected. Three interactive parameters must be evaluated to determine the performance of protective materials and their properties:

- Chemical resistance of the materials

- Physical properties of the materials
- Human factors

Chemical resistance

CPC is constructed from plastic and elastomeric materials and functions as a protective barrier to the skin. This clothing is conveniently categorized by body part to be protected (type of dermal protection) and by the performance (properties) of the garment materials. Selecting CPC involves choosing both the type of dermal protection needed (e.g., gloves to protect hands) and the material from which the clothing should be constructed (e.g., butyl rubber for gloves).

Chemical resistance testing evaluates the interaction between challenge chemicals and the garment material. Three interactions are possible: (1) chemical degradation—a breakdown of the garment's physical structure as a result of garment/chemical incompatibility, (2) chemical penetration—the bulk chemical flow through garment imperfections or through discontinuities such as seams and closures, and (3) chemical permeation—the molecular flow of chemicals through garment material.

Where feasible, selection of CPC should be based on permeation data. Furthermore, the permeation properties of chemical mixtures must be determined by testing, not inferred from the permeation properties of the components.

Physical properties

Physical properties of CPC are important to barrier performance. Key physical properties for gloves are resistance to flexing, tearing, abrasions, cuts, and punctures. Ergonomic evaluations such as dexterity and grip involve physical properties that are governed by glove thickness. Surface texture is another important property, since grip is enhanced by a rough surface. The physical requirements of the task must be balanced against the chemical resistance requirements and human factors. Although CPC should protect the worker, it must not unduly restrict worker performance.

Selection criteria

The physical and chemical properties of CPC should be determined from tables, charts, and general references used to select appropriate CPC. Chemical resistance data for a brand of CPC and its physical properties may be available from the manufacturer. Since only a few studies have been published on CPC for MWFs, material selection is based on limited data for one cutting oil and one emulsifiable cutting fluid.

Data indicate that nitrile affords the most chemical resistance of chemical protective materials [Forsberg and Mansdorf 1993]. The physical properties of nitrile are also rated as excellent for flexibility and resistance to abrasion, tears, and punctures. In

addition, Silvershield™ and 4H™ material are believed to afford protection similar to that of nitrile. Approximate service life is 4 hr for these materials.

9.3.4.2 Respiratory Protection

Respirators should not be used as the primary means of controlling worker exposures. Instead, effective engineering controls (such as machine enclosures or local exhaust ventilation) should be implemented to minimize routine exposures to MWF aerosol. However, workers may use respirators when engineering controls are being implemented and when intermittent tasks expose them to concentrations that cannot be kept below REL by engineering controls alone.

The primary goal of a respiratory protection program is to reduce MWF aerosol exposures to concentrations below the REL. The secondary goal is to reduce these exposures further to protect workers who may experience adverse respiratory effects at concentrations below the REL. Depending on the nature and severity of their conditions, some workers with asthma or HP will develop clinical symptoms even when exposures to MWF aerosols are substantially below the REL. In these workers, personal respiratory protection may not prevent adverse health effects. Respiratory protection for these workers should be based on the individual recommendation of a qualified physician or health care provider. A possible (but unevaluated) use of personal respiratory protection might be to protect unaffected workers who are not exposed at concentrations above the REL, but who work in a facility with recent disease outbreak (e.g., HP) associated with MWF aerosol.

When respirators are used, the employer should establish a comprehensive respiratory protection program as outlined in the *NIOSH Respirator Decision Logic* [NIOSH 1987b] and the *NIOSH Guide to Industrial Respiratory Protection* [NIOSH 1987a] and as required in the OSHA respiratory protection standard [29 CFR 1910.134]. Important elements of the OSHA respiratory protection standard are (1) an evaluation of the worker's ability to perform the work while wearing a respirator, (2) regular training of personnel, (3) periodic environmental monitoring, (4) respirator fit-testing, and (5) respirator maintenance, inspection, cleaning, and storage. The program should be evaluated regularly by the employer. Respirators should be selected by the person who is in charge of the program and knowledgeable about the workplace and the limitations associated with each type of respirator. Without a complete respiratory protection program, workers will not receive the protection anticipated.

Selection of the appropriate respirator depends on the operation, chemical components, and airborne concentrations in the worker's breathing zone. Table 9–1 lists the NIOSH-recommended respiratory protection for workers exposed to MWF aerosol. Guidance on the selection of appropriate respirator filters is presented in the *NIOSH Guide to the Selection and Use of Particulate Respirators Certified Under 42 CFR 84* [NIOSH 1996].

Table 9–1. NIOSH-recommended respiratory protection for workers exposed to MWF aerosols*

Concentration of MWF aerosol (mg/m^3)	Minimum respiratory protection†
≤0.5 mg/m^3 (1 × REL)‡	No respiratory protection required for healthy workers§
≤5.0 mg/m^3 (10 × REL)	Any air-purifying, half-mask respirator including a disposable respirator**,†† equipped with any P- or R-series particulate filter (P95, P99, P100, R95, R99, or R100) number
≤12.5 mg/m^3 (25 × REL)	Any powered, air-purifying respirator equipped with a hood or helmet and a HEPA filter‡‡

*Only NIOSH/MSHA-approved or NIOSH-approved (effective date July 10, 1995) respiratory equipment should be used.

†Respirators with higher assigned protection factors (APFs) may be substituted for those with lower APFs [NIOSH 1987a].

‡APF times the NIOSH REL for total particulate mass. The APF [NIOSH 1987b] is the minimum anticipated level of protection provided by each type of respirator.

§See text for recommendations regarding workers with asthma and for other workers affected by MWF aerosols.

**A respirator that should be discarded after the end of the manufacturer's recommended period of use, or after a noticeable increase in breathing resistance, or when physical damage, hygiene considerations, or other warning indicators render the respirator unsuitable for further use.

††An APF of 10 is assigned to disposable particulate respirators if they have been properly fitted.

‡‡High-efficiency particulate air filter. When organic vapors are a potential hazard during metalworking operations, a combination particulate and organic vapor filter is necessary.

Additional guidance on the selection of more protective respirators is presented in the *NIOSH Respirator Decision Logic* [NIOSH 1987b]. The REL is directed at reducing exposure to MWF aerosol—not to vapors from MWFs and MWF aerosols. Thus the recommended respirators were selected for their ability to reduce particulate exposure—not MWF vapor exposure.

9.4 Medical Monitoring of Exposed Workers

Medical monitoring (together with any intervention based on the results of medical monitoring) represents secondary prevention and should not supplant primary prevention efforts to control inhalation and skin exposures to MWF aerosol. However, as indicated by evidence reviewed in this document, the 0.4 mg/m^3 REL for thoracic particulate mass does not remove all risk for the development of skin or respiratory disease among exposed workers. A major objective of the medical monitoring recommended here is the early identification of workers who develop symptoms of MWF-related conditions such as asthma, HP, and dermatitis. If identified early, affected workers can have their exposures controlled to minimize their risk of recurring conditions (such as acute asthma and irritant contact dermatitis) and chronic effects (such as significant, irreversible impairment of lung function and allergic contact dermatitis).

Another important objective of medical monitoring is to provide standardized data that can be used to identify work areas that need additional primary prevention efforts.

All workers who are exposed to MWF aerosol or have skin contact with MWF may benefit from inclusion in an occupational medical monitoring program. However, priority should be given to workers at highest risk. For example, all workers exposed to MWF aerosol above a designated concentration (e.g., half the REL) should be included. Medical monitoring should be conducted in work areas where (regardless of exposure concentration) one or more workers have recently developed asthma, HP, or another serious condition apparently related to MWF exposure. Medical monitoring should be more intense in work areas with high exposures or with severe adverse health effects among workers. HP is infrequent but often severe.

All exposed workers should be provided with appropriate education and training—particularly with respect to self-referral for further medical evaluation if they develop symptoms suggestive of asthma, HP, other respiratory conditions, or dermatitis. All workers in the medical monitoring program should be provided with information about the program purposes, potential health benefits of participation, and program procedures (how routine test results are used, what actions may be taken on the basis of these results, who has access to individual results from routine medical monitoring and from more detailed medical evaluations, and how confidentiality is maintained [Matte et al. 1990]).

The employer should assign responsibility for medical direction and supervision of the program to a qualified physician or other qualified health care provider (as determined by appropriate State laws and regulations) who is informed and knowledgeable about the following:

- The respiratory protection program and types of respiratory protection devices available at the workplace
- The identification and management of occupational asthma, HP, and other work-related respiratory effects or illnesses (including pre-existing asthma exacerbated by occupational exposures)
- The identification and management of occupational skin diseases

Anyone who administers spirometric tests as part of an occupational medical monitoring program should have completed a NIOSH-approved training course in spirometry or other equivalent training. Spirometry equipment and procedures should comply with American Thoracic Society guidelines [ATS 1979, 1987, 1995, and future updates] that are current at the time of the testing.

9.4.1 Information Provided to Program Director

The employer should provide the program director with the following specific information for each worker covered by the medical monitoring program: a list and description of current and previous job assignments, hazardous exposures, exposure measurements, personal protective equipment provided or used, relevant MSDSs, and applicable occupational safety and health standards [Matte et al. 1990]. If a worker is referred to others for periodic examinations or detailed evaluations, the examiners should be provided with the appropriate information.

9.4.2 Initial or Preplacement Examination

The employer should provide an initial medical examination for each worker included in the medical monitoring program. For newly hired workers and for workers transferred from work areas where they were not exposed to MWFs, this examination should be provided before assignment to a job associated with such exposures. At a minimum, the initial examination should consist of (1) administration of a standardized questionnaire about symptoms and medical history of asthma, other serious respiratory conditions, and skin diseases, and (2) an examination of the skin. Baseline spirometric testing may also be useful for comparisons with subsequent tests of individual workers.

9.4.3 Periodic Examination

All workers included in the medical monitoring program should be provided with periodic health examinations. These should include a brief standardized questionnaire to determine the presence or absence of respiratory symptoms (e.g., shortness of breath, wheezing, chest tightness, or cough) and skin disorders as well as their temporal relationship to work. In addition, the questionnaire should determine the use of medications for these conditions. The frequency of periodic examinations (e.g., semiannual, annual, or biannual) for a given worksite should be dictated by the frequency or severity of health effects in that worker population. In the absence of a case of likely disease associated with MWF or MWF aerosol at a particular metalworking facility, annual examinations would be reasonable.

If an employer's resources permit, routine periodic examinations should include examination of the skin and spirometric testing. The addition of spirometric testing will improve the sensitivity and specificity of screening programs, but it will increase the cost. The skin examination should emphasize screening for dermatitis and skin cancer. The spirometric testing should emphasize measurement of FEV_1 and FVC. Spirometry should be performed preshift on the first day back to work after a weekend off and postshift on the same day. Each worker's preshift values should be interpreted with respect to predicted normal values and in comparison with each worker's previous test results. Cross-shift differences should also be evaluated to indicate any acute adverse effect of

work exposure [NIOSH 1974; Robins et al. 1994]. Such objective examination and testing complement information obtained from questionnaires. As observed in workers exposed to cotton dust [Imbus and Suh 1973], acute symptoms correlated with cross-shift lung function decline in individual workers. In one study of workers exposed to MWF aerosol, only 13 of 28 cross-shift FEV_1 declines exceeding 10% were accompanied by work-related symptoms [Robins et al. 1994].

9.4.4 Detailed Medical Examinations for Selected Workers

Any worker should undergo additional or more frequent medical evaluations if the worker

- — is identified by periodic questionnaire (or spirometry testing) or by self-referral as having respiratory symptoms (or physiologic effects) suggestive of asthma or other respiratory conditions possibly related to MWF aerosol exposure, or
- — is identified by periodic questionnaire, skin examination, or self-referral as having recurrent or chronic dermatitis, or
- — is judged by the program director to have any medically significant reason for more detailed assessment.

Robins et al. [1994] have proposed more specific guidance about medical monitoring for respiratory effects of MWFs.

Detailed pulmonary evaluations should include a careful history and appropriate physiologic testing. Physiologic testing may be used to document (1) hyperresponsive airways (e.g., a comparison of pre- and post-bronchodilator spirometry or methacholine challenge testing) and (2) airway effects associated with workplace exposure to MWF aerosols (e.g., a comparison of pre-and post-shift spirometry testing on the first day of the workweek or serial peak flow testing over several days) [Balmes 1991]. Laboratory-based specific inhalation challenge testing should be left to highly specialized laboratories and experienced clinical investigators [ACCP 1995]. Chest radiography, measurements of pulmonary gas transfer (e.g., diffusing capacity tests and blood gases before and during exercise), or other clinical testing may be indicated in workers with symptoms or findings that suggest lung parenchymal involvement (e.g., HP).

Dermatological evaluations should include a full medical and occupational history, a medical examination, a review of exposures, and complete followup to note the clinical course of the individual's skin condition. The work-relatedness of skin diseases may be difficult to prove. The accuracy of the diagnosis is related to the skill level, experience, and knowledge of the medical professional who makes the diagnosis and confirms the relationship with a workplace exposure. Guidelines are available for assessing the work-relatedness of dermatitis [Mathias 1989], but the diagnosis may be difficult

nonetheless. The diagnosis should be based on the medical and occupational histories and physical findings. In some situations, diagnostic tests are useful—for example, skin patch tests to detect causes of allergic contact dermatitis. In irritant contact dermatitis, patch tests or provocation tests are discouraged because of a high false-positive rate. In many instances, allergic contact dermatitis can be confirmed by skin patch tests using standardized allergens or, in some circumstances, by provocation tests with nonirritating dilutions of industrial substances [Fisher 1986]. False-positive and -negative patch tests occur even with allergic contact dermatitis [Nethercott 1990]. The lack of a standard case definition and the difficulty of diagnosis can lead to misclassification of occupational contact dermatitis, and incorrect estimates of disease frequency.

9.4.5 Physician's Reports to the Worker

Following the initial and each periodic or detailed examination, the physician should provide a written report to the worker. This report should include the following:

- The results of any medical tests performed on the worker
- The physician's opinion about any medical conditions that would increase the worker's risk of impairment from exposure to MWF or MWF aerosol (or any other agents in the workplace)
- The physician's recommended restriction of the worker's exposure to MWF or MWF aerosol (or any other agents in the workplace) and of the worker's use of respiratory protective devices or protective clothing
- The physician's recommendations about further evaluation and treatment of medical conditions detected

9.4.6 Physician's Reports to the Employer

Following the initial and each periodic or detailed examination, the physician should provide a written report to the employer. This report should include the following:

- The physician's recommended restrictions of the worker's exposure to MWF aerosols (or any other agents in the workplace) and of the worker's use of respiratory protective devices or protective clothing.
- A statement that the worker has been informed about the results of the medical examination and about medical condition(s) that should have further evaluation or treatment.

To protect confidentiality, the report provided to the employer should not reveal specific findings or diagnoses without a signed authorization from the worker.

9.4.7 Employer Actions

The employer should assure that the physician's recommended restrictions of a worker's exposure to MWF or MWF aerosol or to other workplace hazards are not exceeded without the use of personal protective equipment. Workers are likely to delay self-referral or deny symptoms on periodic questionnaires if the reporting of symptoms leads to involuntary transfers or loss of income. Thus efforts to encourage worker participation and prompt, accurate reporting of symptoms are important to the program's success. Medical monitoring and followup medical evaluations should be provided without cost to the participating workers.

The employer should ensure that the program director regularly collaborates with the employer's safety and health personnel (e.g., industrial hygienists) to identify and control work exposures and activities that pose a risk of adverse health effects. Aggregate analyses of medical monitoring data can be useful for identifying risks while maintaining the confidentiality of the results for individual workers.

9.4.8 Followup Medical Evaluations

Workers who are transferred as a result of the physician's opinion should be reevaluated later to document that the intended benefit (e.g., reduced symptoms or reduced physiologic effects) has been achieved. Transferred workers should continue to be monitored periodically until they have been asymptomatic for at least 2 years. If symptoms persist, the responsible physician should carefully consider any continuing exposures (e.g., irritants or allergens) that may be exacerbating the worker's condition.

In addition, workers who have negative physiologic test results despite symptoms suggestive of asthma should be carefully followed with repeat medical evaluation during an episode of acute symptoms.

CHAPTER 10

Research Needs

Substantial research has been conducted on the health effects of acute and chronic exposures to MWFs and to MWF aerosol, but additional information about current exposure risks would be very useful. NIOSH recommends the following research to determine the magnitude of potential health effects, to improve our understanding of their etiology, and to evaluate the effectiveness of prevention strategies:

- Provide additional epidemiologic and industrial hygiene evaluations for workers exposed to MWFs in current use. Include HP, asthma, and chronic obstructive airways disease in these studies.
- Investigate and evaluate potential worker exposures and health effects from bacterial and fungal contamination, endotoxins, and other metabolic products in MWFs.
- Develop methods of biomonitoring exposed workers and using biomarkers to measure worker exposures to MWF contaminants and hazardous ingredients and additives.
- Accurately assess dermal exposures to MWFs and their absorption through normal or damaged skin.
- Determine whether contaminants are concentrated or removed during the refining and recycling of used MWFs. Examine the health risks of using recycled or reprocessed MWFs.
- Examine and evaluate worker protection and engineering controls in various work situations to determine better ways to eliminate or reduce exposures to MWFs and to MWF aerosols. Document effective control strategies.
- Test representative mixtures of MWF components to evaluate the potential synergy of typical MWF mixtures.
- Develop bioassays or other methods to measure respiratory or dermatologic irritation.
- Investigate possible substitutes for hazardous MWF ingredients and additives to identify those that are the safest.

- Conduct research on acute and chronic exposures that lead to irritation, sensitization, and lung or skin injury. Models should be developed for assessment of exposure to multiple agents.
- Develop sensitization and irritation bioassays for biocides in MWFs.
- Develop sampling and analytical methods to detect and monitor MWFs contaminated with N-nitrosamines. Investigate current conditions on the worksite that lead to nitrosamine formation.
- Conduct further research to determine concentrations of MEA, DEA, and TEA exposures during metalworking operations and their adverse health effects.

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