CATERPILLAR®

Caterpillar Inc.
100 NE Adams Street
Peoria, Illinois 61629-1410

May 15, 1996

Ms. Diane Manning
National Institute for Occupational Safety and Health
Education and Information Division
Mail Stop C34
4676 Columbia Parkway
Cincinnati, OH 45226-1998

Dear Ms. Manning:

We welcome the opportunity to comment on NIOSH's draft publication, "Criteria for A Recommended Standard: Occupational Exposures to Metalworking Fluids." **Caterpillar is extremely committed to the health and safety of our workers. We certainly are committed to taking appropriate action to protect employees from excessive exposures to MWFs.**

Attached to this letter is a review and critique of the NIOSH document, prepared for Caterpillar by Philip Cole, M.D., Dr. P.H., professor at the University of Alabama School of Public Health, Department of Epidemiology. We hope that NIOSH finds this report to be of benefit as the final copy of the NIOSH publication is prepared.

Additional comments are listed below:

Epidemiology

1. Most of the published epidemiologic studies were conducted involving workers exposed to much higher levels of MWFs and at a time when MWF composition was different. Also, fluid maintenance was not as refined as it is today. These historically higher exposures could be expected to show a higher level of biological response that must be accounted for in establishing "safe" exposure limits in today's workplaces.

2. The draft criteria document discusses asthma as being associated with MWF aerosol exposure. We would like to point out that, overall, there is a world-wide increase in asthma, even in pediatric and teenage populations.

3. In the few cases where we have had employee medical complaints from "exposure" to machine cutting fluid mist, we have not been able to determine pre-shift vs. post-shift or beginning of week vs. end of week decrements in pulmonary function testing.

Complaints have been subjective and difficult to distinguish between other exposures, including smoking, viral respiratory tract infections, or "reactive airways" from unknown sources.

4. Based upon our review of the literature and our own experience, at this time we do not believe skin cancer from exposure to MWF to be a problem.

5. We feel that much more study is needed before an REL of 0.5 mg/m^3 should be established based upon non-malignant respiratory disease prevalence.

6. As alluded to in Epidemiology 5 , we support a detailed respiratory work-up for employees who have become symptomatic. We must keep in mind that a cause and effect relationship does not automatically exist because a person who works with MWFs develops respiratory symptoms.

Periodic Examination

1. Regarding dermatitis, it tends to occur in micro-epidemics associated with excessive tramp oil, bacterial or fungal over-growth, excess concentrations of MWF additives, and low humidity conditions (e.g., winter months in northern climates). Dermatological complaints should immediately be investigated by an industrial hygienist (or safety professional) along with those responsible for MWF management. The situation should be quickly evaluated and the appropriate corrective actions taken.

2. The only pre-placement medical test we believe could be beneficial would be a respiratory questionnaire and a methacholine challenge test, with follow-up by a physician if either is positive, and possibly exclusion of the person from exposure to machine cutting fluid mists. Methachlorine challenge may be too extensive a pre-placement evaluation. Prospective scientific studies published in reputable journals with peer review should be conducted to determine if this is a reasonable approach.

3. At most, the Criteria Document should call for a pre-placement screening which includes a respiratory questionnaire reviewed by a physician along with a baseline pulmonary function test. If an employee becomes concerned or symptomatic, he or she can report to the medical department of the employer or his or her own personal physician, at which time the respiratory evaluation can commence. Periodic screening would be expensive and useless.

4. Physician reports to workers and employers are probably in order: however, we should avoid a rush judgment regarding cause and effect until a thorough evaluation by a physician with training in occupational medicine has been completed. Items to be considered should include industrial hygiene monitoring results, a review of the MSDSs, a history of other respiratory complaints in the work area, and information regarding control measures for the MWF.

Recommended Exposure Limit

1. It is our understanding that one of the missions of NIOSH is to perform research projects, such as researching new methods of air sampling and analysis. It would appear that NIOSH has taken the position of using the easy and convenient total particulate method, rather than develop new methods of sampling and analysis which should be high on NIOSH's agenda. NIOSH should thoroughly evaluate this point from a valid scientific viewpoint, before arbitrarily setting an REL of 0.5 mg/m^3.

2. We question NIOSH's statement that, "it is technologically feasible to control exposures to MWF aerosols to a concentration of 0.5 mg/m^3 (total particulate) for many MW operations." The information contained in this report does not support this statement. We also question your definition of "many." Have you identified some operations where engineering controls will not reduce exposures to below a 0.5 mg/m^3 REL? Most of the information which NIOSH used to formulate this statement came from recent technology developed in the automobile industry. Has NIOSH considered machining operations which make much larger parts than are made in the auto industry?

3. We also question the origin and scientific validity of the 0.5 mg/m^3 limit. Reportedly, this is merely an *arbitrary* number selected by one member of the Occupational Health Advisory Board for GM/UAW in 1989, and there is no independent standard which would support this limit from a scientific or medical point of view.

4. Assuming an employer had 4,000 employees exceeding an action level of 0.25 mg/m^3, we estimate costs for the generic medical screening recommended in the document would be approximately $300,000/ year. If the use of respiratory protection is required, additional costs would be incurred due to medical exams for respirator usage and costs for a respiratory protection program. These costs would greatly exceed any potential benefit to be realized.

5. We believe that NIOSH should do an extensive scientific review to determine whether separate RELs should be developed for each major type of machine cutting fluid. We believe that there is a drastic difference in a straight cutting oil and a synthetic cutting fluid. Synthetic cutting fluids essentially are composed of ~95%

water. Clearly such drastically different compositions would have totally different metabolic pathways and toxicological effects.

Industrial Hygiene

1. Although the total particulate method of analysis is easy and convenient, quite obviously this method will measure other airborne contaminants in the work environment, such as welding fume, grinding particulate, and background airborne particulates. It would be entirely possible that in many industrial environments, even though wet machining was present, none of the measured airborne contaminants would be from machine cutting fluid mists.

2. ***We believe that it is extremely important to properly control the fluids contained in the machining systems***. NIOSH needs to thoroughly examine this issue. We would recommend machining fluid control standards such as listed in ASTM E 1497 - 94, "Standard Practice for Safe Use of Water-Miscible Metalworking Fluids." For example, if too much biocide is added to a system, employees may suffer from pulmonary and dermatological irritation. Even if an REL is established at 0.5 mg/m^3, this method only measures particulates and not volatile compounds of MWFs, thus employees may still suffer from irritation even if the particulate levels are "none detected." NIOSH spends only a very small portion of its criteria document discussing the most important issue regarding MWF. Ideally, one core group in a facility should have centralized control over management of MWF systems.

Very truly yours,

D. J. Crane, M.D.
Corporate Medical Director
Corporate Medical Department

G. E. Williams, CIH, CSP
Corporate Industrial Hygiene Manager
Corporate Auditing and Compliance Division

cc: Edward Stein, Ph.D. - OSHA - Washington, D.C.
nmc/djc/6137951.sam

A Critique of the NIOSH Document "Criteria For A Recommended Standard: Occupational Exposures to Metalworking Fluids"

Prepared for

Caterpillar, Incorporated

by

Philip Cole, M.D.

May 10, 1996

This report is a review and critique of parts of the National Institute of Occupational Safety and Health (NIOSH) document entitled, "Criteria for a recommended standard: occupational exposures to metalworking fluids." The authorship of the report is not provided. The sections evaluated include all those pertaining to epidemiologic studies of the possible association between metalworking fluids (MWF) and cancer and to epidemiologic studies of the possible association between MWF and nonmalignant respiratory disease, namely:

- Section 4.1 - Occupational health risks for workers exposed to MWFs. Cancer risks for workers exposed to MWFs (pp. 18-66)
- Section 4.2 - Occupational health risks for workers exposed to MWFs. Nonmalignant respiratory effects (pp. 67-119)
- Section 9.2.1 - Effects from exposure. Cancer (pp. 170-173)
- Section 9.2.2 - Effects from exposure. Nonmalignant respiratory effects (pp. 173-179)
- Section 9.3 - Rationale for the recommended exposure limit (REL) (pp. 184-190).

MWF AND CANCER

Overall Review

The criteria document reviews and summarizes twelve retrospective follow-up or proportional mortality ratio (PMR) studies of occupational groups with potential exposure to MWF, as well as more than thirty population-based case-control or cancer incidence studies. NIOSH concludes that there is "substantial" evidence that occupational exposure to MWF, occurring before the mid-1970s, caused several forms of cancer, including cancer of the stomach, rectum, pancreas, larynx, skin and bladder (pp. 48, 172).

In evaluating the epidemiologic evidence, NIOSH notes that consistency in results for several of the above cancers across studies was lacking but asserted that inconsistency did not preclude a causal interpretation of positive statistical associations. The rationale offered for this assertion is that different types of MWF (straight oils, soluble oils, synthetic fluids, semi-synthetic fluids) cause specific forms of cancer, that the occupational groups studied may have been exposed to different types of MWF (e.g., p. 48, paragraph 2), and that examination of cancer associations by type of MWF either was not done in most studies or was done inadequately.

Only one of the many investigations of MWF and cancer developed and analyzed quantitative cumulative exposure estimates for individual subjects. Thus, the cancer studies are inherently, and severely, limited in their usefulness for developing a standard for occupational exposure. NIOSH based its recommended exposure limit for MWF (0.5 mg/m^3 total particulate) not on evidence pertaining to cancer, but rather on evidence from studies of nonmalignant respiratory disease, which had comparatively good exposure measurements, at least for current exposure (p. 184).

Overall Critique

NIOSH's identification of the pertinent epidemiologic literature appears to be complete. The decision to emphasize the investigation by Eisen and coworkers is sound, as this study is large, is of relatively high quality and contains information on dose-response patterns. The latter information is important to consider when attempting to determine if observed associations are causal. NIOSH's presentation of data from the epidemiologic investigations is accurate for the most part, although not comprehensive. [The study by Eisen and coworkers has been reported in three publications, by Eisen et al. (1992), Tolbert et al. (1992) and Eisen et al. (1994). In the present review, this work is counted as one study and is referred to as the research of Eisen et al.]

Both the tabular material and the text in the criteria document would be improved by the inclusion of summary rate ratios for specific cancers for the overall cohort in the important retrospective follow-up study of Eisen et al., rather than for subgroups, only. In general, NIOSH's presentation of data from the studies of cancer and its evaluation of these data places undue emphasis on the statistical significance of results from individual studies. In addition, NIOSH's use of inaccurate terminology (e.g., "risk ratio" instead of "rate ratio") is regrettable.

The main shortcoming of the criteria document's sections on MWF and cancer is its causal interpretation of the positive statistical associations seen in some of the studies. External consistency is an important, perhaps the most important, criterion in judging whether or not results from a series of epidemiologic studies indicate a causal relationship. This is because epidemiologic research is observational, rather than experimental. Rarely can evidence from one or two epidemiologic studies be accepted as strongly supporting the presence of a causal relationship. The latter can occur only when the study is of high quality, with a low likelihood of error due to bias and confounding, when the study has observed a strong association and when the study is precise. None of the studies of MWF and cancer, taken alone, has these attributes. In fact, in addition to exhibiting inconsistent results for most of the cancers listed above, the relevant studies vary considerably with regard to quality, most do not control adequately for confounding, and none reports strong and precise positive associations. For these reasons, NIOSH's conclusion that "there is substantial evidence that MWF exposures prior to the 1980s are associated with cancer of the stomach, pancreas, larynx, rectum, skin, and bladder" (p. 48), in that the statement implies a causal association, is unwarranted for most of these cancers.

It could be contended that many of the subjects studied were exposed to most types of MWF (especially, to straight and soluble MWF) during their careers, bringing into question the rationale for lack of external consistency that was offered by NIOSH. Few quantitative data are available for addressing this issue. If, on the other hand, one accepts NIOSH's position that the workers included in the various studies were exposed to different MWFs and that exposure to different types of MWF might cause different forms of cancer, then one must conclude that the data on MWF and cancer are not sufficient for

evaluating external consistency and, therefore, are for the most part inadequate for causal inference.

In the aggregate, the epidemiologic evidence of a causal relationship with MWF is most convincing for squamous cell skin/scrotal cancer, for larynx cancer and for rectal cancer. For skin/scrotal cancer, the two studies with designs adequate for evaluating squamous cell cancer reported very high rate ratios (>10) for MWF exposure, and there is good biologic plausibility of a causal association with MWF. For larynx cancer, all but one of eight studies reported a positive association with exposure to MWF or with work in jobs likely to entail such exposure. The highest quality investigation, by Eisen et al. (1994), found some suggestion of a weak dose-response relationship with exposure to straight oils; and a relationship is biologically plausible. Yet, the observed association between MWF and larynx cancer is weak to moderate in strength (rate ratios of about 2.0). This weakness is a major problem because larynx cancer has potent nonoccupational causes that were not controlled for as potential confounders in the study by Eisen et al. or in some of the other investigations. In addition, the association between straight MWF and larynx cancer in the investigation of Eisen et al. was limited to only one of the three study plants (and was imprecise) when confounding by sulfur was controlled for. This result suggests that the apparent relationship between MWF and larynx cancer may be due, at least in part, to confounding by other occupational exposures. Because of the weakness of the association observed between MWF and larynx cancer, it may well be due to confounding, and exposure to straight oils used in metal working can not be viewed as an established cause of larynx cancer. For rectal cancer, six of eight studies report a positive relationship, but the association is weak, and most of the information available on dose-response comes from a single study, by Eisen et al. (reported by Tolbert et al., 1992).

The epidemiologic evidence that MWF in general or specific types of MWF are associated with stomach, pancreas or bladder cancer is less coherent than it is for squamous cell skin/scrotal cancer, for larynx cancer or for rectal cancer. Among thirteen studies reporting results for stomach cancer, overall rate ratios or proportional mortality ratios (PMRs) are close to 1.0 in four studies, between 1.2 and 1.5 in four studies and above 1.5 in five studies. More importantly, the study by Eisen et al. did not find any convincing association with stomach cancer in the overall study group or in subgroups specified on the basis of type of metal working operation or type of MWF. NIOSH concluded that the results reported by Eisen, Tolbert et al. "tend more towards suggesting a relationship between cutting oil exposure and stomach cancer, than arguing against it" (p. 27). This interpretation is unjustified. Data presented by Eisen et al. (1992) suggest that uncontrolled confounding may have been responsible for the small increase in the standardized mortality ratio (SMR) for stomach cancer seen in comparisons between the MWF cohort and the general United States population. The internal analyses conducted by Tolbert et al. (1992) found rate ratios of, at most, 1.2 (with upper bounds of 95% confidence limits of 2.1 or less) among subjects with the highest exposure to specific types of MWF compared to subjects with no exposure. Such results are supportive of the null hypothesis.

The evidence that MWF exposure causes pancreas cancer is weak. The positive findings come in large part from PMR studies. The retrospective follow-up studies also have reported some positive results, but these have been limited mostly to black workers, whereas results are null in whites. Such a pattern suggests that observed associations are due to chance or confounding by an unmeasured disease determinant. The analyses reported by Tolbert et al. (1992) found little evidence of dose-response relationships. The highest rate ratio for pancreas cancer in their many analyses was 2.0 for subjects with 8 or more years of exposure to synthetic fluids. This result was based on only nine exposed workers and was imprecise. The retrospective follow-up study of metal components manufacturing workers by Acquavella et al. provides no support for an association. Cohort members employed in the only three occupational groups identified by Acquavella et al. as having potential MWF exposure had 2 observed compared to 3.3 expected pancreas cancer deaths. This information is not included in the text or in the tables of the criteria document.

Most data on potential MWF exposure and bladder cancer are from population-based case-control studies. Again, reported associations are weak. In addition, exposure estimation in these studies is inadequate, and few data are available on dose-response patterns. The retrospective follow-up study by Eisen et al. was large enough to provide precise estimates of effect measures for fatal bladder cancers. The fact that Eisen et al. did not report results for bladder cancer implies that they did not observe any association with MWF. A causal interpretation of the case-control findings is unwarranted.

Additional Comments on Specific Sections

Section 4.1.1: The document refers to studies of broad occupational groups as intended to be "hypothesis-generating" (p. 20). The distinction between "hypothesis-generating" and other purposes of a study is not relevant. The document later identifies the major limitations of the research described.

Section 4.1.2: The criteria document briefly mentions, but does not present in detail, surveys of mortality among broad occupational groups, such as those based on the death certificate data of Washington State, California and other regions of the US. The document cites surveys which found a positive, statistically significant association between possible MWF exposure and a form of cancer. However, surveys with null, inverse or nonstatistically significant positive results are not identified. NIOSH summarizes the material included, stating that "the findings from these studies suggest an association between MWF exposures and certain cancers" (p. 20). The omission of data from reports that did not have statistically significantly positive cancer results for occupational groups potentially exposed to MWF precludes a balanced assessment of the material. Further, NIOSH's emphasis on statistical significance is not appropriate. The summary statement is unevaluable without a fuller presentation of the data.

Section 4.1.3: As mentioned, the procedure used by NIOSH to cite data from the reports by Eisen et al. (1992 and 1994) and Tolbert et al. (1992) (p. 21) is confusing and leads to the omission of important information. Some results can be summarized for all three plants and for whites and blacks, combined, and this would be useful. The analyses by type of MWF are not mutually exclusive, and this should be kept in mind in presenting and interpreting results. On page 23, the document states that for cancers other than skin, stomach, pancreas, larynx, rectum and bladder "statistically significant (positive and negative) findings will be briefly summarized." This statement is one of many examples of the unwarranted emphasis placed on statistical significance in the criteria document.

Section 4.1.3.1: In referring to the skin cancer results of mortality studies (p. 24 and table 4.1-2), it would be helpful for NIOSH to clarify whether or not the data pertain to squamous cell skin cancer, to melanoma or to unspecified skin cancer. In table 4.1-2, the cited skin cancer data from Silverstein et al. are incorrect (correct data: PMR=0.92, 95% CI=0.25-2.34).

Section 4.1.3.3: In interpreting data on MWF and pancreas cancer, NIOSH states, "the number of studies with statistically significant findings suggests that exposure to some MWF's (or less likely confounding exposure present in some work environments where MWF's are used) may increase the risk of pancreatic cancer" (p. 31). The meaning and rationale of this statement are unclear. As other occupational exposures are not mentioned as potential confounders of other MWF-cancer associations, does this statement indicate that special considerations apply to the interpretation of results for pancreas cancer?

Section 4.1.3.4: In commenting on larynx cancer, the document states, "Negative data from mortality studies must be interpreted with caution for this site, because of its high (>60%) 5 year survival rate" (p. 33). This remark is confusing and probably irrelevant. As noted above, results for larynx cancer are largely positive, despite the fact that three of the studies with larynx cancer results examined mortality, only. The authors of the criteria document probably have confused the issue of precision with the issue of "negative" results.

Section 4.1.3.5: The text on page 34 states that there are "5 PMR studies reporting data for rectal cancer", whereas the corresponding table (table 4.1-6) identifies only four PMR studies.

Section 4.1.3.6: In summarizing the section on bladder cancer, it is stated that, "The association between bladder cancer and MWF exposure is well supported by one large and well designed case-control study...as well as several other studies conducted in different geographic locations" (p. 38). This is an overstatement of the strength of the evidence. The case-control studies report odds ratios that are consistent with null or weakly positive associations with possible MWF exposure in diverse occupational settings. Dose-response data are not available in most studies. The "well designed" study by **Silverman et al**. also reported weak associations with jobs likely to entail MWF exposure,