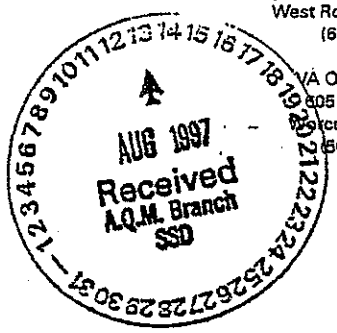
DEPARTMENT OF VETERANS AFFAIRS
Medical Center

VA Medical Center
940 Belmont Street
Brockton, MA 02401
(508) 583-4500

VA Medical Center
1400 VFW Parkway
West Roxbury, MA 02132
(617) 323-7700

VA Outpatient Clinic
605 Lincoln Street
Worcester, MA 01605
(508) 856-0104



August 11, 1997

Ms. Genevieve A. Shiroma
Chief, Air Quality Measures Branch
California Air Resources Board
Attention: Diesel Exhaust Draft Report
P.O. Box 2815
2020 L Street
Sacramento, California 95812

Dear Ms. Shiroma:

I am submitting my comments on the "Health Risk Assessment For Diesel Exhaust" public and scientific review panel review draft dated March 1997, and released May 9, 1997.

As you are aware, I am the lead author on a series of articles published in the 1980's regarding diesel exhaust exposure and lung cancer mortality in railroad workers. I have been extensively involved in the reassessment of the retrospective cohort data that OEHHA has been using to form the basis of its risk assessment for diesel exhaust. Although younger workers with the most potential exposure to diesel exhaust are more likely to die of lung cancer, the relationship between lung cancer mortality and exposure cannot be summarized by a positive slope as presented by OEHHA. This means that the current results cannot be summarized using a single number relating cumulative exposure to diesel exhaust to health outcome. The major limitations for the use of the study for risk assessment are (1) the need to truncate the study in 1976 due to under ascertainment of death in these years, thus eliminating important person-years of observation in workers with known exposure between 1977-1980, and (2) the assignment of past exposure since there is great uncertainty regarding the level of exposure, and which workers were actually exposed to diesel exhaust before 1959.

Previous communications that I have had with OEHHA have stressed the uncertainties of the shape of the exposure-response relationship in the retrospective cohort data, particularly in the setting of under ascertainment of death between 1977-1980. A letter that I wrote in 1994 is quoted in the ARB/OEHHA responses to public comment, but the letter is not quoted in its entirety. In the second paragraph I noted that the shape of the exposure-response relationship was not as positive as originally reported, with a reference to my 1991 letter to the EPA. I also stressed the need to obtain additional information regarding the mortality experience of this cohort. It was not my intention for my concluding paragraph of that letter to be interpreted as implicit approval for this version or any past version of the OEHHA risk assessment document Furthermore, in May 1995 I submitted my comments to the U.S. EPA

regarding the use of retrospective cohort study for risk assessment. The comments made in that letter mirror my previous and current comments to OEHHA. A copy of this letter was submitted previously to you at the public hearing on July 1. Although any governmental agency must be satisfied with assumptions made regarding assessing risk, there also should be general approval of the scientific community. I do not believe that your current document fully expresses the uncertainty of the estimates of risk that you have presented, nor does the current retrospective cohort data allow the calculation of unit risk with confidence.

Sincerely yours,

Eric Garshick, M.D., M.O.H.

Chapter 1: General Comments

Conclusions Regarding Causal Inference: I agree with the conclusions of the documents written by the World Health Organization, IARC, and the Health Effects Institute regarding the evidence for the carcinogenicity of diesel exhaust in humans. Based on the same data, you go beyond these conclusions in the current draft document The weight of the evidence does suggest that whole diesel exhaust is a human lung carcinogen, however the human studies have limitations. These limitations are mainly due to lack of exposure histories, and a short duration of follow-up (just over 20 years) of exposed workers in the best studies. However, based on the strong likelihood that diesel exhaust may cause lung cancer in humans, and that more additional definitive studies are expensive and time consuming, it still is important to regulate human exposure.

Use of Animal Data For Quantitative Risk Assessment: Since the most likely mechanism of lung cancer in rats exposed to diesel exhaust is attributable to particle overload, my opinion is that it is not possible to use the animal data to determine the human risk of lung cancer.

Differing Analyses Of the Railroad Worker Retrospective Cohort Study: In previous communications to the Office of Environmental Health Hazard Assessment, I have pointed out that there is considerable uncertainty in the slope in the relationship between cumulative exposure to diesel exhaust and lung cancer. Although the younger workers in the retrospective cohort study had the greatest risk of dying of lung cancer, based on our reanalysis of these data, it is not possible to use a positive slope to definitely describe the relationship between cumulative exposure and lung cancer mortality. I believe that the use of a slope as derived in the OEHHA assessment has not been justified. Using years of exposure (months of exposure unweighted for estimated exposure level) starting in 1959, the slope is not positive, and appears flat or negative. The lack of a positive slope between cumulative exposure does not imply the study is negative, but is due to weaknesses in exposure assignment, changing exposures over time, and the lack of exposure data pre-1959. In addition, contributing to the uncertainty of the slope are unrecognized deaths in the years 1977-1980 since relatively few "cells" contribute to the effects of 10-14 years and 15-17 years of exposure as originally presented. When the study is truncated in 1976, important person-years of follow-up are excluded and it is even more difficult to determine the true slope.

Two major differences in the development of the various analyses using the retrospective cohort data to examine lung cancer mortality has been the modeling of age (as noted in Appendix F), and the inclusion of a "background" level of particulate among the unexposed workers. However, in an examination of the analyses presented, it seems that both Dr. Stanley Dawson, the principal author of the California risk assessment, and Dr. Kenny Crump, a

principal critic, have used similar methods in adjusting for age despite the arguments offered in Appendix F that different methods are used. The remaining difference therefore is the method used to account for background exposure. The difference between these analyses should be more clearly examined since different assumptions are made by using "exposure" weights for workers without actual diesel exposure.

Chapter 6: Carcinogenic Effects

Page 6-49, 2nd paragraph: I agree that most human carcinogens have a latency of at least 10 years. However, it would be more complete to state that the latency for most human carcinogens is generally in the range of 20 years or more. A limitation of the epidemiological studies in humans is the lack of studies with many workers with long term exposure that is well characterized (more than 25 to 30 years).

Chapter 7, Section 7.3, Human Risk Estimates From Epidemiological Studies

Page 7-15, 4h paragraph: The coefficient for the risk of lung cancer attributable to work in a diesel exhaust job in the case-control study published by our group was for exposure that was assumed to start in 1959. It was not known which workers had exposure pre-1959 (up to an additional 10 to 15 years) since the railroad industry converted to diesel power after World War II, or the intensity of the exposure relative to exposure assessed in the early 1980's. A risk assessment done only using exposure post 1959 would assign an artificially high risk to each year of exposure and inflate the risk. However, the estimates of diesel exhaust exposure chosen (125 ug/m^3 and 500 ug/m^3) are high based on the measurements made in railroad workers, and also include background non-diesel particles. The use of these estimates of exposure would tend to lead to a lower risk per ug of presumed diesel exhaust exposure.

Page 7-18, and page 7-17: The relative risks obtained for the cohort excluding shopworkers are used to develop risk estimates by obtaining the slope of the relative risk plotted versus cumulative exposure. Although the major findings of our study have been replicated when attained age is used in the analysis when exposure is based job title held in 1959, we have shown based on our 1991 letter to EPA that the analysis using cumulative exposure based only on age in 1959 does not adequately control for attained age. The slope of the relative risk obtained based on years of exposure (with a 5 year lag) is not positive. Truncation of the study in 1976 due to under ascertainment of death between 1977-1980 even with adequate control of attained age leads to considerable uncertainty in the effects of 10-14 years of exposure, and eliminates the category of 15-17 years of exposure from analysis. Thus the use of these data as presented in Table 7.8 for risk

assessment is not justified.

Appendix D: Meta-Analysis

I would not use the relative risk of 1.82 for the results of retrospective cohort study, but would use a relative risk of for the workers age 40-44 in 1959.

Appendix E

Page E-3: It is not clear that attained age categories in 10 y age intervals adequately controls for attained age although this stated. The results with 5 year age intervals should be present It is reasonable to exclude the last 4 years of follow-up, and exclude the shopworkers for the reasons stated in the text.

Page E-4: The table on this page lists the models considered. Mod 3 includes terms for attained age and calendar year, whereas mod 4 includes terms for age cohort and calendar year. These 2 mode seem to be the main models of interest, since there is controver on how to adjust for age in the regression models. The exposu term is expressed as a continuous variable, but it is stated tha exposure was also expressed in several categorical variables in t same models to assess the fit of the slope.

The results, presented in Tables E-2 and E-3 show similar value for slope for most of the models tested, regardless of difference in fit. Figure E-2 shows a categorical analysis, demonstrating relative risk that initially rises, then decreases for the last points. The model fitting cumulative exposure as a continuous variable is "anchored" at zero, and assigned a relative risk of 1.0. Therefore, relative to this point, these other groups "drive" the slope of the line to be positive. In Figure E-3, 3 categorical data points are presented. Again, the slope of the line for cumulative exposure as a categorical variable is positive, largely because the origin is "anchored" at zero exposure, and the subsequent values are positive. The graphs presented do not prove that the models using a single slope adequately describes the relationship between cumulative exposure and lung cancer.

Page E-7: The Armitage-Doll model is used as an additional modeling tool. A ten year lag is assumed implying that exposure in the 10 years before death doesn't contribute to cancer. This excludes over half the years of documented exposure in a study that is only 18 years in duration, 1959-1976. Exposure pre-1959 is assigned based on the percentage of diesel engines in service, but since 10 years of actual exposure is discounted, assigned exposure is used substantially to predict lung cancer risk. Given the relatively short duration of known exposure and subsequent follow-up in this cohort, it is hard to justify the use of a 10 year lag to model exposure.

Appendix F

The discussion listed here recounts historical events, particularly relating to the use of age in various regression models. However, Dr. Dawson does use attained age in some of the models he presents in Appendix E. This should also be noted here.