STATEMENT OF DR. CLINTON W. STALLARD, JR.

Good Morning;

I am the Director of Medical Services, Department of Medicine and Biological Science of the Standard Oil Company of Ohio. I am appearing on behalf of the American Petroleum Institute.

I am a graduate of the University of Maryland, Chemistry and Medicine, certified by the American Board of Preventive Medicine in Occupational Medicine, Fellow of the American College of Preventive Medicine, and a past or present Fellow or Member of other professional associations of occupational health.

We welcome this opportunity to meet with the Environmental Health Advisory Committee of the Science Advisory Board to discuss with you our research into the medical and scientific evidence concerning the public health implications of benzene in ambient community air. The American Petroleum Institute's Division of Medical and Biological Sciences has over the past several years undertaken a thorough review of the medical and scientific evidence on benzene as well as sponsoring additional research in this area.

This effort has included preparation of a critical evaluation of benzene toxicity by the New York University Medical Center's Institute of Environmental Medicine under the direction of the late Dr. Sidney Laskin and Dr. Bernard D. Goldstein as well as the five expert reviews of EPA's draft benzene health risk assessment documents that have been submitted to this Committee. We hope that the findings of our study will be beneficial to your deliberations.

It is well documented that exposure to benzene has produced hematotoxic effects, including cytopenias, pancytopenia and the more severe variant of bone marrow suppression, aplastic anemia. However, our research, including particularly the review by Dr. James H. Jandl, Chief of the Department of Hematology of the Harvard Medical School, reveals clear evidence of a dose-response relationship for these effects with a well-established threshold of at least 40 to 50 ppm, and perhaps as high as 100 ppm. Moreover, as indicated in API's post-hearing submission to the Occupational Safety and Health Administration, this threshold for cytopenias has been confirmed in numerous toxicological studies on animals.

Further confirmation of this threshold is provided by the virtual disappearance of benzene-induced cytopenias in the United States in the post-World War II era during which occupational exposure to benzene has been sequentially reduced to the present limit of 10 ppm on an 8-hour time-weighted average, with a 25 ppm ceiling. The experience in other countries has been similar, including particularly Italy and Turkey, where occupational exposure to benzene has been more recently reduced to levels to 20 ppm or less.

Significantly, it is clear that benzene-associated aplastic anemias have a much higher recovery rate (87%) than do idiopathic aplastic anemias (19%).

Recently initiated regulatory efforts, including the ongoing proceedings by the Occupational Safety and Health Administration and the current inquiry by EPA, have been the result of an increasing concern about a possible relationship between benzene exposure and an increased incidence of acute myelogenous leukemia and its acute variants.

Over the years since the beginning of this century, a number of individual case studies and several studies of groups of individuals occupational exposed to very high concentrations of benzene -- generally exceeding 200 ppm in situations where reliable measurements have been taken -- have suggested an association of benzene exposure with an increased incidence of acute myelogenous leukemia. Most recently, a study by Infante et al. of pliofilm workers occupationally exposed to very high levels of benzene apparently ranging from 100 to over 600 ppm, has provided additional evidence of such an association. Although the authors have suggested an increased risk of acute myelogenous leukemia for benzene-exposed workers of from 5 to 10 fold, the validity of this estimate is subject to considerable doubt.

First, 404 "dry side" employees who were apparently exposed to benzene concentrations of up to 20 ppm and who otherwise fit the cohort definition, but among whom no

no leukemia deaths were discovered after 95% follow-up, were excluded from the cohort of 748 workers on the basis of an unconfirmed assumption of no exposure.

Second, the study combines data from two geographically separated plants without demonstrating any similarity of results. Indeed, as indicated by the analysis of Drs. Lamb and Tabershaw, neither of the two cases of leukemia identified from the second plant were acute myelogenous leukemia and the duration of exposure to benzene for those cases was one month and six months as compared with 6 to 18 years for the five cases in the other plant. Accordingly, only the five cases of acute non-lymphocytic leukemia identified from among workers at the first plant can be arguably attributed to benzene exposure. But, three of those five cases occurred among workers employed prior to 1944, yet all employees in the pre-1944 employed group whose employment terminated prior to 1944 were excluded from the cohort because of an absence of work history data.

These and other problems that have been detailed in the reviews provided to you cast considerable doubt on the conclusions of the Infante study.

Moreover, although there is an implication in the published Infante study that these workers were exposed to very low benzene concentrations, abundant evidence brought out

during the OSHA hearings this past summer indicates that the cases identified were related to unknown, but apparently very high (over 100 ppm) exposures. Accordingly, the authors themselves emphasized during the OSHA hearings that the study is not subject to quantitative interpretation. Rather, its usefulness is solely as a qualitative indication of an association between benzene exposure and acute myelogenous leukemia, and is thus simply additive to the previous literature already suggesting such an association.

Significantly, examinations of workers employed in the same plants during the 25 years since 1949 have revealed no deaths from leukemia beyond those identified by Infante et al. Specifically, there are no new leukemia deaths after 1962.

This information combined with evidence developed in a number of studies of employees exposed to benzene concentrations generally below 20 ppm, including several studies of petroleum refinery workers, strongly suggests the absence of any increased incidence of acute myelogenous leukemia among individuals exposed to benzene concentrations below 100 ppm. There is now clear evidence that benzene-associated leukemias are acute myelogenous leukemia, or one of its variant forces, erythroleukemia, myelomonocytic leukemia, which are increasingly known as acute nonlymphatic leukemias. In addition, the sequence which leads to the appearance of leukemia after

benzene exposure always includes a premonitory toxic response of bone marrow. Cytopenia leading to aplastic anemia is first present, and is largely reversible, even when severe. Recovery is permanent in most instances. Those leukemias which appear represent the end result in 4% to 5% of aplastic anemias. These results are similar to those found in pancytopenia or aplastic anemia due to other agents, such as chloramphenicol or phenylbutazone. "No well documented cases of acute nonlymphatic leukemia attributable to benzene exposure have occurred in which there was no prior period of cytopenia or pancytopenia." (Jandl critique, p. 2). Thus the well established threshold for benzene-induced cytopenia may well constitute the effective threshold for any acute myelogenous leukemia attributable to benzene.

Moreover, the high reversibility and complete recovery rates for even severe cases of benzene-induced aplastic anemia is evidence that benzene is not itself leukemogenic, but that some other primary or secondary factor may be involved in those cases of acute myelogenous leukemia following high level benzene exposures.

Apart from pancytopenia and leukemia, the other benzene-related health effect cited as significant in the draft benzene health assessment that has been submitted to this Committee is the evidence of chromosomal aberrations associated

with benzene exposure. However, as demonstrated in the reviews submitted to you and confirmed by numerous witnesses at the OSHA benzene hearings, no firm conclusions can be drawn that chromosomal changes associated with benzene exposure are true adverse health effects. Thus, no consistent chromosomal aberrations have been associated with benzene exposure, and the wide variety of largely self-correcting changes that have been observed are also associated with numerous other factors. Moreover, even these changes have not been observed at levels below 12 ppm.

The draft documents concerning human exposures to atmospheric benzene and the determination of population risks from ambient benzene exposures have been extensively critiqued in the materials submitted to this Committee. To summarize, it is unfortunate that the Stanford Research Institute's estimates were largely developed without the use of actual monitoring data, although such data is apparently available. Moreover, there are defects in the methodology used in the draft SRI report which indicate a significant over-estimation of both the size of the exposed population and ambient benzene concentrations. The SRI draft also fails to consider additional potentially significant sources of benzene, including especially benzene from natural sources.

Accordingly, all of the input data to the carcinogen assessment group's preliminary report is subject to considerable doubt. Nevertheless, and accepting at face value all of the extrapolative efforts of the carcinogen assessment group, a calculated benzene exposure of 1.03 ppb does not appear to represent a threat to public health in view of the well-established thresholds for adverse health of at least 40,000 to 50,000 ppb.

Although I have attempted to briefly summarize our medical and scientific assessment of the draft health effects risk assessment documents, I am accompanied today by four of our expert reviewers -- James H. Jandl, Stephen H. Lamb, Gerald E. Andersen, and Will M. Ollison -- who are prepared to answer questions or elaborate on their reviews to assist your determinations.

Thank you.