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BEFORE THE
UNITED STATES DEPARTMENT OF LABOR
OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION

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COMMENTS OF THE CHEMICAL MANUFACTURERS ASSOCIATION ON OSHA'S PROPOSED STANDARD FOR OCCUPATIONAL EXPOSURE TO BENZENE

Occupational Exposure to Benzene: Proposed Rule, 50 Fed. Reg. 50512 (December 10, 1985)	Docket No. H-059-C

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Introduction

These Comments are submitted by the Chemical Manufacturers Association ("CMA") in response to the Notice of Proposed Rulemaking on Occupational Exposure to Benzene published in the Federal Register of December 10, 1985. 50 Fed. Reg. 50512. CMA is a non-profit trade association whose member companies represent more than 90 percent of the productive capacity for basic industrial chemicals in the United States. Many of CMA's member companies produce, use, or market benzene, and the petrochemical facilities of CMA's members would be subject to the revised benzene standard that OSHA has proposed.

Because of the substantial interest that CMA's member companies have in regulatory determinations and actions relating to benzene, CMA participated extensively in the 1977 rulemaking proceeding, which eventuated in a standard that was set aside by the courts. CMA also has participated in the activities that

OSHA has undertaken or sponsored over the course of the past several years to consider whether the existing benzene standard should be revised. Thus, CMA provided information and views in response to OSHA's Request for Information published in the Federal Register of July 8, 1983 (48 Fed. Reg. 31412) and participated actively in the discussions held under the auspices of the Institute for Environmental Mediation. We welcome the opportunity to present our views on the present proposal and hope that they will be reflected in the final action that OSHA takes in this proceeding.

The rulemaking proposal raises a wide variety of issues, many of which are of great concern to CMA. In these Comments, we will begin by addressing the critical health effect and risk assessment issues, and will then proceed to deal with questions of feasibility and other matters raised in the rulemaking notice.

I. Health Effect Issues

A. Non-Malignant Health Effects

1. Central Nervous System and Hematotoxic Effects

The preamble to OSHA's rulemaking proposal quite properly focuses on the cancer risk (more particularly, the leukemia risk) that has been associated with exposure to benzene in various occupational settings in the past. It is true, of

course, that exposure to elevated levels of benzene also has been associated with non-malignant health effects, such as central nervous system effects, aplastic anemia, bone marrow depression and cytopenias. However, these non-malignant health effects are not ones that would be found at occupational exposure levels of 10 ppm and below. For that reason, they are not relevant to the present proceeding.

For example, while exposures to benzene at levels of 50-150 ppm have been reported to produce headache, lassitude, and weakness, exposures at levels of 25 ppm have no such effect.1/ As EPA has observed: "Lower levels of benzene [i.e., below 50 ppm] do not seem to elicit these [central nervous system] responses no matter how long the exposure."2/

Similarly, long-term exposure to moderate or high levels of benzene (i.e., 40 ppm - 500 ppm) can produce signs of hematotoxicity, including bone marrow depression, pancytopenia, aplastic anemia and less severe blood abnormalities.3/ However, the evidence does not indicate that these non-malignant

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1/ See EPA, Draft Criteria Document for Benzene (February 1984) at 51. Moreover, the mild central nervous system effects that may occur at benzene levels of 50-150 ppm "appear to be rapidly reversible following cessation of expsoure." Id.

2/ Id. at 52.

3/ See, e.g., 42 Fed. Reg. 27467 (May 27, 1977); Testimony of Dr. Robert Snyder in OSHA Docket H-059, Ex. 156, Tab 2, pp. 1-3.

hematological effects will result from short- or long-term exposure to benzene at levels of 10 ppm and below. Thus, in the 1977 benzene proceeding, Dr. Robert Snyder stated that "[i]n both animals and man the lowest level [of exposure] demonstrated to produce bone marrow depression was approximately 40 ppm."4/ Other witnesses in the 1977 proceeding expressed the same view.5/

These conclusions are supported by the findings of a recent study conducted at a coke oven by-product recovery plant.6/ In that study, hematological data -- including red blood cell counts, white blood cell counts, and hemoglobin -- from benzene exposed workers were compared to comparable data from a non-exposed reference group of supervisory employees. The benzene-exposed workers, who had an average exposure of 10.5 ppm, were divided into three groups having cumulative exposures equivalent to 20-year occupational exposures of less than 1 ppm, 1-10

4/ Testimony of Dr. Robert Snyder in OSHA Docket H-059, Ex. 156, Tab 2, p. 8; Transcript ("Tr.") in OSHA Docket H-059 at 3224-3225.

5/ See Testimony of Dr. Hervey B. Elkins, Tr. 3210 (threshold for injury to the blood-forming system is between 25 and 50 ppm); Testimony of Dr. Robert E. Olson, Tr. 2925 (most people put the threshold for blood dyscrasias at 50 ppm); Testimony of Dr. Robert E. Eckardt, Tr. 2088 (unaware of any reports of blood dyscrasias below 35 ppm); Testimony of Dr. Irving R. Tabershaw, Ex. 149A, p. 6 (cytopenia has not been demonstrated to occur below 25 ppm). All citations in this footnote are to OSHA Docket H-059.

6/ Hancock, et al., "Hematological Findings Among Workers Exposed to Benzene at a Coke Oven By-Product Recovery Facility," 39 Archives of Environ. Health 414 (1984).

ppm and more than 10 ppm, respectively. No statistically significant differences among the various exposure and comparison groups were found for the hematological parameters examined.7/ The authors concluded that "the estimated cumulative exposures examined . . . [appear to] represent doses which fall below the threshold at which non-leukemogenic, hematotoxic effects on humans are manifested . . . ."8/ They noted that their findings are consistent with the results of an earlier chemical industry study9/ and observed that the results of their study "provide no evidence that the current OSHA permissible exposure level of 10 ppm is inadequate to protect employees against the non-leukemogenic chronic effects of benzene on the hematopoietic system . . . ."10/

In short, as Dr. Bernard Goldstein recently observed: "The available evidence suggests that the current 10 ppm TWA OSHA standard is sufficient to protect against overt symptomatic pancytopenic effects."11/ And, Dr. Goldstein notes, even if

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7/ See id. at 416.

8/ Id. at 417.

9/ Id., citing Townsend, et al., "Health Exam Findings Among Individuals Occupationally Exposed to Benzene," 20 J. Occup. Med. 543 (1978).

10/ Id. at 417.

11/ Goldstein, "Clinical Hematotoxicity of Benzene," in Mehlman, ed., Carcinogenicity and Toxicity of Benzene, 51, 57 (1983).

there is "variation in the individual response to benzene . . . the extent of variation in susceptibility to the pancytopenic effects of benzene does not appear to be great."12/

2. Teratogenic and Reproductive Effects

Exposures to benzene even at levels well in excess of 10 ppm have not been shown to present a teratogenic or reproductive hazard. Thus, EPA has concluded that "it is unlikely that benzene administered by inhalation during the principal period of organogenesis constitutes a teratogenic hazard."13/ Other experts in the field have reached a similar conclusion. Thus, Dr. Bernard Schwetz has reported that

> developmental toxicity studies conducted in three species . . . using three different routes of administration, are in agreement that teratogenic effects are not associated with exposure to levels of benzene that are not maternally toxic . . . . Even at levels of benzene sufficiently high to cause maternal toxicity [in the inhalation study], there was little or no evidence of a teratogenic effect.14/

12/ Id. at 52.

13/ EPA, Ambient Water Quality Criteria for Benzene (October 1980) at C-42. See also EPA's Response to Public Comments on Regulation of Benzene, 49 Fed. Reg. 23478, 23481, col. 2 (June 6, 1984) ("EPA agrees . . . that the available data do not implicate benzene as a potential teratogen or embryotoxin in test species.").

14/ See Schwetz, "A Review of the Developmental Toxicity of Benzene," in Mehlman, ed., Carcinogenicity and Toxicity of Benzene (1983) at 17, 20. Maternal toxicity generally has not been reported to occur at concentrations below about 300 ppm.

He concludes that based on these teratologic studies, "exposure to levels of benzene which do not cause other forms of toxicity would not be expected to cause adverse developmental effects."15/

* * * * *

In short, non-malignant health effects of benzene are not a matter of concern at exposure levels of 10 ppm and below, the levels that are of interest in the present proceeding. The current 10 ppm standard, as OSHA acknowledges, was designed to protect against risks of "aplastic anemia and other blood dyscrasias as well as acute and chronic health effects."16/ The decision to propose a 1 ppm standard was not based on new evidence showing a risk of aplastic anemia and other blood

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15/ Id. at 21. Other investigators who have reviewed the literature agree with this conclusion. See Lee, et al., "Assessment of Benzene Health Effects in Ambient Water," in Mehlman, ed., Carcinogenicity and Toxicity of Benzene (1983) at 91, 102 ("In summary, there is general agreement among scientists that teratogenic effects are not associated with exposure to levels of benzene that are not toxic to the pregnant animal. Even at levels of benzene sufficiently high to cause maternal toxicity, there was little or no evidence of teratogenic effect."). Accord, European Chemical Industry Ecology & Toxicology Center, Technical Report No. 16: A Review of Recent Literature on the Toxicity of Benzene (December 12, 1984) (hereinafter "ECETOC Report") at 2 ("There is no reliable evidence to suggest any association between exposure to benzene and adverse effects on human reproduction."). The ECETOC Report is submitted herewith as Appendix A.

16/ OSHA, Preliminary Regulatory Impact and Regulatory Flexibility Analysis for the Benzene Standard (December 1985) ("Regulatory Impact Analysis") (Ex. ___) at I-1.

dyscrasias at 10 ppm but on studies published since 1974 which OSHA interpreted as suggesting a need to lower the standard in order to provide adequate worker protection against a perceived risk of leukemia.17/ Since non-malignant hematological effects such as aplastic anemia and pancytopenia will not be caused by occupational exposure to benzene at levels of 10 ppm, there is no basis for suggesting that lowering the permissible exposure limit ("PEL") from 10 ppm to 1 ppm would reduce the incidence of aplastic anemia and other blood dyscrasias.18/

17/ Id. at I-1, I-20.

18/ See 50 Fed. Reg. 50512, 50539, col. 2, 50541, cols. 1-3. Thus, even if the Vigliani study did indicate a ratio of deaths from benzene-induced non-malignant blood dyscrasias to deaths from benzene-induced leukemia of 0.42 (see id. at 50541, col. 2), it would be entirely irrelevant to the questions at issue in the present proceeding, since the benzene exposure levels in the Vigliani study were far in excess of 10 ppm. By contrast, the exposure levels at issue in this proceeding are below the threshold for the production of non-malignant blood dyscracias. Accordingly, OSHA's "Benefits Analysis," which estimates specific numbers of aplastic anemia deaths that would be avoided under alternative regulatory proposals, misses the mark, since it is "[b]ased on the assumption that the Vigliani case study is typical . . . ." Regulatory Impact Analysis at III-8. The Ott and Rinsky studies, to which OSHA refers for support (see id.) do not demonstrate an increased risk of aplastic anemia associated with occupational exposure levels of 10 ppm and below. Consequently, they do not support OSHA's unjustified use of the Vigliani study to predict the avoidance of aplastic anemia deaths through a reduction in the PEL from 10 ppm to 1 ppm.

B. Carcinogenicity

1. The Qualitative Evidence of Benzene-Related Leukemia Does Not Demonstrate an Increased Risk at Occupational Exposure Levels of 10 ppm and Below.

As OSHA points out in the Notice of Proposed Rulemaking, there are a variety of epidemiological studies and clinical reports associating occupational exposure to benzene in various contexts with an increased risk of leukemia, principally of the acute myeloid variety.19/ For the most part, the exposure levels involved in these studies and reports were very high -- in excess of 100 ppm. For example, the shoeworkers studied by Aksoy and co-workers were estimated to have average exposures of 150-210 ppm, with excursions between 210 and 640 ppm.20/ Similarly, the workers studied by Vigliani were exposed to benzene concentrations that were mostly around 200-500 ppm, with peaks up to 1,500 ppm.21/ While certain other studies may suggest the possibility of an increased risk of leukemia at benzene exposure levels below 100 ppm, no study conclusively demonstrates that

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19/ See 50 Fed. Reg. 50512, 50516-50524.

20/ See id. at 50517.

21/ See id. at 50512, 50518, col. 1; Brian MacMahon, Epidemiologic Evidence on the Possibility that Risk of Leukemia May Be Increased by Exposure to Benzene at Low Concentrations (April 23, 1985) at 45 (hereinafter referred to as "MacMahon Report"). A copy of the MacMahon Report is submitted as Appendix B to these Comments.

occupational exposures of 10 ppm and below present a significantly increased risk of leukemia.

a. The Rinsky Study

In its rulemaking proposal, OSHA relies extensively upon the NIOSH study by Rinsky, et al. of rubber hydrochloride (Pliofilm) workers at two manufacturing facilities in Ohio (hereinafter referred to as the "Rinsky Study") as direct evidence that benzene is a human leukemogen. Whatever that study may demonstrate about an association between benzene exposure and leukemia, it certainly does not constitute direct evidence of an increased risk of leukemia at levels of 10 ppm and below. As Dr. Brian MacMahon points out, a "major difficulty with this study is the poor information on the level of exposure with which the excess of leukemia was associated -- a matter about which there has been a great deal of debate."22/ Dr. MacMahon goes on to observe that "every one of the 8 leukemias in the cohort, and 4 other cases which were not eligible for the cohort, occurred after exposures substantially higher than 10 ppm."23/ Based upon his extensive review of the epidemiologic literature and the debate that has surrounded the interpretation of the Rinsky study, Dr. MacMahon concludes that the excess leukemias found in

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22/ MacMahon Report at 2.

23/ Id. at 2, 27.

the Rinsky study are associated with average exposure levels that are five to ten times the current 10 ppm standard.24/

OSHA's discussion of the exposure data for the Rinsky cohort provides no basis for reaching a contrary conclusion. OSHA appears to accept the suggestion that worker exposures in the study "were generally within the recommended limits in effect at the time of employment, that is, they were between 100 ppm and 10 ppm during the years 1941-1975."25/ Even if that conclusion were correct, it would mean that the average exposures were considerably in excess of 10 ppm. Exposures of the workers who actually contracted leukemia would have been considerably higher, since they all were employed during the 1940s and 1950s, when the recommended limits (to the extent they existed at all) were 35 ppm-100 ppm.26/

Moreover, there is good reason to believe that exposures of the Rinsky cohort often exceeded the recommended limits. OSHA itself refers to a 1955 report in which workers at one of the two Pliofilm plants entered areas where benzene exposures ranged from 19 - 680 ppm, at a time when the

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24/ Id. at 3.

25/ 50 Fed. Reg. 50512, 50518, col. 2.

26/ See JRB Associates, Technological Feasibility and Economic Impact Study of Alternative Standards for Benzene (1984) ("JRB Report") (Ex. 153), Table 1-2.

recommended exposure limit was 35 ppm.27/ Although respirator usage allegedly was required in such high exposure areas, the fact is that, even as late as 1973-74, workers at the same facility often did not wear respirators when they entered areas of high benzene concentrations that were well above the 10 ppm exposure limit in effect at the time.28/ During the 1930s and 1940s (when many members of the Rinsky cohort were exposed to benzene) industrial hygiene practices and the awareness of occupational health problems were far less developed than is the case today (or was the case in 1973-1974) -- with the result that employees exposed to unacceptably high levels of benzene often might not have worn respiratory protection.29/

Moreover, exposure information was severely limited for the Pliofilm plant at which most of the leukemia cases were found.30/ At that facility, benzene levels ranging up to 100 ppm were measured in 1957, when the recommended exposure limit was 25 ppm.31/ At the plant for which more exposure information is

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27/ See 50 Fed. Reg. 50512, 50519, col. 2.

28/ See id.

29/ See Supplementary Statement of Dr. Hervey B. Elkins, filed in OSHA Docket H-059. A copy of Dr. Elkins' Statement is submitted herewith as Appendix C.

30/ The fact that the incidence of leukemia was so much higher at the facility having very little exposure data suggests that exposure levels may have been significantly higher at this facility than at the plant for which more exposure data are available.

31/ See 50 Fed. Reg. 50512, 50519, col. 3.

available, 73 percent of the 15 measurements taken from 1946-1950 were above the permissible exposure limit in effect at the time.32/

In sum, average benzene exposures of the Pliofilm cohort studied by Rinsky, et al., were far in excess of the exposure levels that are of interest in the present proceeding. Furthermore, all of the leukemia cases were found in workers first exposed to benzene prior to 1963, when a Threshold Limit Value ("TLV") of 25 ppm was proposed by ACGIH.33/ No leukemia deaths have been found among cohort members first exposed after 1963. [Check the accuracy of these statements.]

In addition, the numerically low incidence of leukemia in the study and "the marked heterogeneity of benzene exposure in the work force studied" further complicate the effort to attribute the increased leukemia incidence to particular exposure levels.34/ For these and other reasons, Dr. Bernard Goldstein, like Dr. MacMahon, has concluded that "the Rinsky et al. data, and the original findings of Infante et al., do not provide significant direct support for leukemogenesis occurring at levels of

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32/ See Letter from Dr. H.G.S. van Raalte, et al. to the editor of Risk Analysis, June 9, 1983. A copy of Dr. van Raalte's letter is submitted herewith as Appendix D.

33/ See 50 Fed. Reg. 50512, 50514, col. 3.

34/ See Bernard D. Goldstein, Benzene Toxicity: Review of Recent Literature (February 3, 1983) (Ex. ___) at 5.

benzene at or near the present OSHA standard."35/

b. The Wong Study

The rulemaking notice also devotes considerable attention to the study by Wong, et al., of chemical industry workers.36/ That study also should not be interpreted as demonstrating an increased risk of leukemia or lymphopoietic cancer among workers exposed to benzene levels below 10 ppm. The standardized mortality ratio ("SMR") for all cancers among benzene-exposed members of the Wong cohort was 102.3 -- barely elevated and certainly not statistically significant.37/ Similarly, although the SMR for lymphatic and hematopoietic cancer was slightly elevated among the benzene-exposed workers, the increase was not statistically significant.38/ This also was true of the various subcategories of lymphatic and hematopoietic cancer, including leukemia, and of lung cancer.39/ In short,

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35/ Id. It also should be noted that the most recent update of data on the Rinsky cohort shows that the Standardized Mortality Ratio ("SMR") for leukemia has declined from the level of 560 reported by OSHA (see 50 Fed. Reg. 50512, 50519, col. 1) to 328. See Rinsky, et al., "Benzene and Leukemia: An Epidemiologic Risk Assessment," August 9, 1985 (Ex. 176A) at 12.

36/ See 50 Fed. Reg. 50512, 50522-23. This study (Ex. 151-A) will hereinafter be referred to as the "Wong Study."

37/ See Wong Study, Table 22.

38/ See id., Table 22.

39/ See id., Table 22. In the case of lung cancer, the insignificant excess found among the exposed workers was largely

[Footnote continued next page]

overall cancer mortality among the benzene-exposed workers in the Wong Study was comparable to the rate in the general U.S. male population, while the rate for lymphatic and hematopoietic cancer was only slightly, but not significantly, higher than the national norm.

A statistically significant increase in the relative risk for lymphatic and hematopoietic cancer was found in the Wong Study only when workers occupationally exposed to benzene were compared to an internal control group of workers who did not have such exposure at the plants studied (although they may have been exposed to benzene when working for other employers). However, as Dr. Wong and various peer reviewers and other investigators point out, this increased relative risk is attributable primarily to the unexplained and unusually low mortality rate experienced by the internal control group.

This is particularly evident in the case of leukemia, where there were seven deaths among the exposed workers and none in the control group, even though 3.4 leukemia deaths would have been expected among the controls based upon the age- and

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[Footnote continued from preceding page]

attributable to a single plant which (i) was located in a county having an above average lung cancer rate, and (ii) contributed a large percentage of the exposed cohort members and a disproportionately small percentage of the unexposed cohort members to the study.

sex-adjusted experience of the general population not exposed to benzene.40/ As EPA's Carcinogen Assessment Group observes, the carcinogenic potency of benzene estimated from the Wong Study "can be attributed to the fact that the non-exposed group had no cases of leukemia. As a result, the increase in risk over controls may be due to an artifact in the data rather than to a true carcinogenic response."41/ Dr. Wong himself noted that the significant mortality deficit among the control group magnifies the

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40/ See Wong Study at ii and Table 23; B. MacMahon, "Review of 'An Industry-Wide Mortality Study of Chemical Workers Exposed to Benzene'" at 2, 4 (October 12, 1983) (submitted herewith as Appendix E) (The difference in leukemia and lymphatic cancer between the exposed and unexposed workers "results primarily from a deficit of both leukemia and lymphatic cancers among unexposed workers, not from an excess among exposed employees . . . . I do not think that one can conclude from these data that there is an excess of leukemia in the exposed group."); P. Enterline, "Review of Draft Report 'An Industry-Wide Mortality Study of Chemical Workers Exposed to Benzene'" at 6 (November 1, 1983) (submitted herewith as Appendix F) ("[T]he absence of leukemia deaths in the control group is most unusual and statistically significant . . . . If the control group is inappropriate, then comparisons with this group are invalid."); Letter from Kenneth J. Rothman to R. T. Richards, January 13, 1984, at 4 (submitted herewith as Appendix G) ("most striking feature . . . is the lower-than-expected mortality in the occupational cohort lacking benzene exposure. . . . The unusual mortality experience of the comparison group inevitably raises doubt about the validity of the data on the exposed cohort as well.").

41/ EPA Carcinogen Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985 at 23-24. The cancer mortality deficit among the non-exposed workers cannot be explained by the so-called "healthy worker effect." As Dr. Brian MacMahon points out: "Cancer in general tends to have a less marked 'healthy worker effect' than other causes of death, and it is difficult to understand how any of the known mechanisms of such an effect could apply to leukemia." MacMahon Report at 57.

apparent relative risk of the exposed workers.42/

In addition, the size of the cohort as a whole "was small for a number of specific analyses,"43/ resulting in a high degree of statistical variability. In the case of leukemia particularly, the number of deaths was very small, the statistical variability was very large, and the dose-response relationship was not monotonic -- i.e., the incidence of leukemia did not increase steadily as increasing cumulative exposure levels were examined.44/ In a quantitative risk assessment based on the Wong Study, Dr. Frank Carlborg concluded that because the data set in the study is relatively meager, it fits a variety of dose-response models, including "the no-effect model which assumes that an exposure to benzene does not affect the incidence of lymphopoietic cancer. . . ."45/ Since the no-effect model "fits the data very well in the statistical sense,"46/ the data from the Wong Study "are consistent with the hypothesis that the incidence of lymphopoietic cancer in the exposed group is

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42/ See Wong Study at 54.

43/ Id. at 64.

44/ See id. at 64 and Figure 2.

45/ F. Carlborg, A Quantitative Cancer Risk Assessment for Benzene Based on Data from an Industry-Wide Mortality Study of Chemical Workers at 7. Dr. Carlborg's report is submitted herewith as Appendix H.

46/ Id. at 4.

age-dependent and not related to the benzene exposure."47/

Two basic conclusions emerge from the Wong Study. First, the overall cancer rate and the rates of lymphatic and hematopoietic cancer (including leukemia) among the benzene-exposed workers were not significantly elevated when compared to the general population. Second, the increase in relative risk for lymphatic and hematopoietic cancer among the benzene-exposed workers when compared to the internal control group is of questionable relevance. The increase must be considered in light of the low number of deaths in the cohort as a whole, the unexplained and dramatic mortality deficit among the internal controls, and the absence of any leukemia in the control group.48/

For these reasons, Dr. MacMahon has concluded that "it is unclear whether leukemia risk is or is not increased in the [Wong] study group . . . ."49/ Indeed, because the most "striking and statistically significant feature of [the Wong] data is the deficit of leukemia in the unexposed workers," Dr. MacMahon finds it "difficult to accept these data at face value."50/ He

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47/ Id.

48/ It also is important to note that none of the seven leukemia deaths in the Wong cohort were of the acute myelogenous cell type, the type that has generally been associated with benzene related leukemia. See 50 Fed. Reg. 50512, 50523, col. 1.

49/ MacMahon Report at 8.

50/ MacMahon Report at 57.

824 also notes that "the small numbers make the SMRs for leukemia
825 consistent with almost any hypothesis,"51/ and he "decline[s] to
828 accept the estimated SMRs as reliable evidence either for or
829 against association of leukemia with the reported cumulative
830 exposures."52/ Dr. Kenny Crump has expressed a similar view,
831 stating that "the significant findings [in the Wong study] are
832 due in large measure to the deficits in cancer in the unexposed
833 group . . . . Therefore, without some explanation for the cancer
835 deficit in the unexposed group, this study by itself does not
836 provide strong evidence of a relationship between occupational
837 exposure to benzene and lymphatic and hematopoietic cancer."53/

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842 c. The Dow Study

843
844 OSHA preliminarily suggests that the study by Ott, et
845 al., of Dow Chemical Company workers54/ "represents direct
849 observation of a leukemogenic risk from low level benzene
850 exposure."55/ For a variety of reasons, such an interpretation

851 _____
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826 51/ Id. at 38. Cf. the discussion of Dr. Carlborg's report
827 at p. ___, supra.

830 52/ MacMahon Report at 58.

838 53/ See Crump & Allen, Quantitative Estimates of Risk of
839 Leukemia From Occupational Exposure to Benzene (May 1984) (Ex.
840 152) (hereinafter referred to as "Crump Report") at 14.

845 54/ Ott, et al., "Mortality Among Individuals
846 Occupationally Exposed to Benzene," Archives of Environ. Health
847 (January/February 1978) 3-10 (Ex. 128-33) (hereinafter referred
848 to as the "Dow Study").

850 55/ 50 Fed. Reg. 50512, 50520, col. 1.

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of the Dow Study is not justified.

In the Dow Study as originally reported, two cases of leukemia were found in an occupational cohort where 0.8 cases were expected. When a third worker (whose cause of death was recorded as bronchopneumonia, with myeloblastic leukemia listed under "other significant conditions") is treated as a case of leukemia, the incidence rate is three cases of leukemia where 0.8 were expected.56/ Several points must be made about this finding.

First, it is questionable whether this study, which was denominated and structured as a mortality study, should be analyzed as an incidence study.57/ Even when it is so analyzed, the finding of three leukemias where 0.8 were expected (p=0.047) is only "of borderline statistical significance."58/ Moreover, the

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56/ See Dow Study at 9.

57/ See MacMahon Report at 4. As EPA observes, "reclassification generally is not appropriate in mortality studies that must rely on death certificates, since the same reclassification is not applied to the group from which expected numbers are derived." EPA, Health Assessment Document for Nickel (EPA-600/8-83-012F, September 1985) at 8-31.

58/ Goldstein, "Clinical Hematotoxicity of Benzene," supra, n.11 at 55. As Dr. MacMahon observes: "The statistical significance of the excess based on three cases is in question." MacMahon Report at 22. Thus, it is a "fine judgment" as to "whether or not there is a statistically significant increase in these data . . . ." Id. at 4. See also EPA, Ambient Water Quality Criteria for Benzene (October 1980) at C-59 (the leukemia incidence in the Dow Study "is only of marginal statistical significance").

data, as EPA has observed, "are too few to provide an independent stable estimate of the relation between benzene and leukemia."59/

Second, there was a distinct possibility of confounding exposures among the Dow cohort, including confounding exposures at other places of employment. For example, one of the employees who developed leukemia had only 18 ppm-months of benzene exposure at Dow and had earlier been employed in a saw mill which manufactured veneer, an occupation for which an increased incidence of myelocytic leukemia has been reported.60/ Observing that "workers in benzene-related occupations [in the Dow Study] typically were exposed to other chemicals," the National Academy of Sciences ("NAS") concluded that "extrapolation of benzene-induced cancer risk from such data as these would be tenuous."61/

Third, as Drs. Crump and Allen point out, in the Dow Study:

> No dose response trend is apparent for any cancer type. There is no particular indication from the dose response analysis that

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59/ EPA, Draft Criteria Document for Benzene (February 1984) at VI-16.

60/ See Milham, "Neoplasia in the Wood and Pulp Industry," 271 Ann. N.Y. Acad. of Science 294-300 (1976); Dow Study at 8-9. See also Environ Corporation, Review of Benzene Risk Assessments (November 11, 1983) (Ex. ___) (hereinafter referred to as "Environ Report") App. A at 23-24 ("In addition to benzene, workers at the Dow plant were exposed to a large variety of chemicals, some of which may have carcinogenic potential . . . .").

61/ NAS, Drinking Water and Health: Vol. 3 (1980) at 85.

> leukemias are related to [benzene] exposure 62/

As noted in a review of the Dow Study by Environ Corporation, the fact that the workers who developed leukemia had relatively low cumulative benzene exposures compared to the large number of cohort members who did not develop leukemia despite having moderate or high benzene exposures makes it difficult to attribute the leukemias to the benzene exposures.63/ As a general proposition: "An increase in the amount of exposure should be associated with an increased risk of developing the disease, if the exposure is of causal importance."64/

For the foregoing reasons, the authors of the Dow Study observed that "a retrospective assessment of the possible relationship [of leukemia] to benzene exposure [of cohort members is] very judgmental."65/ And they concluded: "No mortalities

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62/ Crump Report at 10.

63/ See Environ Report, App. A at 25.

64/ Id. at 25-26. Dr. Philip Cole also has commented on this point. He states that the fact that the three leukemia cases among the Dow cohort "experienced an exposure that was less than the overall average is persuasive evidence of a lack of 'dose-response' in this data set [which] in turn, detracts appreciably from the prospect that the data reflect a cause-effect relationship." Cole, "A Quantitative Estimate of Leukemia Mortality Associated with Occupational Exposure to Benzene: A Critique," p. 3 (submitted as an attachment to March 22, 1983 letter of R.T. Richards to Leonard Vance, Ex. 137). Hereinafter this document will be referred to as the "Cole Critique."

65/ Dow Study at 9.

directly attributable to benzene exposure were observed."66/ EPA has characterized the study in the same fashion, stating: "No association with benzene exposure was detected,"67/ and concluding that the Dow Study taken alone cannot be viewed "as conclusive evidence of an association between low-level (2-9 ppm) occupational exposure to benzene and leukemia . . . ."68/ The United States Supreme Court has expressed a similar view.69/

Recently, the Dow Study was updated to cover the mortality experience of an expanded cohort through 1982.70/ The Dow Study Update identified two additional cases of leukemia among the expanded cohort, both of whom died at age 80. The authors noted a non-significant excess of leukemia deaths which became

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66/ Id. at 3.

67/ EPA, Ambient Water Quality Criteria for Benzene (October 1980) at C-59.

68/ Response to Public Comments on the Regulation of Benzene, 49 Fed. Reg. 23478, 23483, col. 2 (June 6, 1984).

69/ Industrial Union Department AFL-CIO v. American Petroleum Institute, 448 U.S. 607, 633 (1980) ("The authors of the study . . . concluded that it could not be viewed as proof of a relationship between low-level benzene exposure and leukemia because all three workers had probably been occupationally exposed to a number of other potentially carcinogenic chemicals at other points in their careers and because no leukemia deaths had been uncovered among workers who had been exposed to much higher levels of benzene.").

70/ Bond, et al., Executive Summary of Report "An Update of Mortality Among Chemical Workers" (hereinafter referred to as "Dow Study Update"). A copy of the Dow Study Update is submitted herewith as Appendix I.

statistically significant when the focus was narrowed to myelogenous leukemia.71/ As in the earlier study, no cumulative dose-response relationship was found.72/

The authors explained that the "limited available industrial hygiene survey data" made it difficult to estimate "chronic and acute exposure levels for individual employees . . . ."73/ They noted, however, that most of the leukemia cases "were likely to have had possible exposures to intermittent, short-term, high levels of benzene measured in excess of 250 ppm in some samples."74/ Mirroring the comments that had been made with respect to the original study, the authors identified

> a number of factors [that] complicate use of these data for risk assessment. These include the small number of leukemias observed, the lack of an apparent dose-response relationship, competing exposures to other potentially hazardous materials, and the uncertain contribution of brief high exposures [up to 250 ppm and more] which most likely occurred during the time period of these individual's [sic] employment.75/

71/ See id. at 3.

72/ See id.

73/ Id. at 4.

74/ Id.

75/ Id. at 4-5.

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In sum, the available studies do not demonstrate a significantly increased risk of leukemia at occupational benzene exposure levels of 10 ppm and below. As Dr. Cesare Maltoni recently observed,

> the available epidemiological and experimental data at present do not provide precise information on the risk of doses around or below 10 ppm.
>
> In such a situation, any decision can only be based on social and political considerations rather than on scientific ones.76/

Thus, in 1985, as in 1978, any decision OSHA might make to reduce the current PEL would not rest on a demonstrated human health risk at occupational exposure levels of 10 ppm and below. Rather, it would be based on the presumption that there is no threshold for the leukemogenic effects of benzene and on the application of a highly conservative linear extrapolation model to estimate increased leukemia risks down to a benzene concentration of zero. As discussed below, both the no-threshold presumption and the assumption of dose-response linearity down to zero are subject to serious question in the case of benzene.

76/ Maltoni, et al., "Experimental Studies on Benzene Carcinogenicity at the Bologna Institute of Oncology: Current Results and Ongoing Research," 7 Am J. Indus. Med. 415, 418 (1985).

For these reasons, OSHA should, at the very least, explicitly recognize the uncertainty that exists on the question whether there is any leukemia risk at all at the occupational exposure levels that are of interest in this proceeding. Furthermore, it should be emphasized that the cancer risks OSHA predicts at exposures below 10 ppm not only are likely to be overstated (because of OSHA's conservative approach to estimating risk), but are frankly hypothetical in nature.

2. Epidemiological Studies Do Not Show an Association Between Occupational Benzene Exposures and Cancers Other Than Leukemia.

As discussed in the previous section, the association between exposure to benzene in certain occupational settings and an increased risk of leukemia rests upon a variety of epidemiological studies and clinical reports in which the leukemogenic response appears to be associated with benzene exposure levels well in excess of 10 ppm. There also have been "occasional suggestions of other tumors - lymphoreticular, prostate, stomach, lung and multiple myeloma - being associated with benzene exposure . . . ."77/ However, as Dr. Brian MacMahon observes, "the evidence [for such non-leukemogenic tumors] is anecdotal or weak and, generally speaking, not replicated."78/

77/ MacMahon Report at 1.

78/ Id.

For example, DeCoufle, et al., suggest that the results of their study may indicate a possible association between benzene exposure and multiple myeloma.79/ But, as Dr. MacMahon points out, these suggestions "are no more than speculation."80/ Moreover, as OSHA notes, DeCoufle et al. "did not present any information on benzene exposure levels for [the cohort studied.]"81/ Thus, because of "the absence of any objective benzene-in-air measurements, . . . the possible concomitant exposure of the workforce to other chemicals and the small size of the study population . . . [it is] difficult to place any reliance on . . . [the] conclusions" of the DeCoufle study.82/

The most recent update of the Rinsky Study83/ does not demonstrate a causal relationship between benzene exposure and multiple myeloma either. Although an excess incidence of multiple myeloma was found in the study, several factors call the significance of the finding into question. For one thing, there was no dose-response relationship. As the authors note, "SMRs for multiple myeloma . . . did not increase with increasing

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79/ See 50 Fed. Reg. 50512, 50520, col. 1.

80/ MacMahon Report at 18.

81/ 50 Fed. Reg. 50512, 50520, col. 1.

82/ ECETOC Report at 25.

83/ Rinsky, et al., "Benzene and Leukemia: An Epidemiologic Risk Assessment," August 9, 1985 (Ex. 176A).

exposure."84/ Moreover, cumulative benzene exposures of the multiple myeloma cases were quite low, with three of the four cases having less than 40 ppm-years of exposure and one of the cases being exposed for only four days.85/ Furthermore, for two of the cases, no corroborating medical reports were available.86/ Understandably, the authors of the study concluded that the observations of multiple myeloma "must . . . be interpreted cautiously in the absence of further corroboration."87/

In short, as one review of the benzene literature concludes, reports of non-leukemogenic cancers "are too few in number, and the evidence quoted in their support is insufficient, to make a convincing case that cancers other than leukemia can be causally associated with excessive exposure to benzene."88/ OSHA itself has recognized this point, stating:

84/ Id. at 13.

85/ See id. at 13 and Table 5.

86/ See id., Table 5.

87/ Id. at 19. Nor does the Wong Study, in the words of the author, "offer any firm data on the relationship between benzene exposure and multiple myeloma." Wong Study at 62.

88/ ECETOC Report at 21-22. Drs. Robert Snyder and Debra Laskin have expressed a similar view, stating that "the total body of evidence suggests that . . . the expression of the carcinogenic activity [of benzene] in man [takes] the form of one of several types [of] leukemia." R. Snyder & D. Laskin, A Review of Recent Developments in the Study of Benzene Toxicity (October 4, 1985) ("Snyder Review") at 28. A copy of the Snyder Review is submitted herewith as Appendix J.

> Although suspicion of types of cancers other than of the lympho-hematopoietic system has been raised, these have not been adequately evaluated from epidemiologic cohort or case-control studies of workers exposed to benzene.89/

At the present time, then, there is no justification for associating non-leukemogenic tumors with exposure to benzene, and speculation as to any such possible association cannot serve as a basis for reducing the current standard.

3. Animal Bioassays

At the time of the 1977 hearings, an animal model for benzene carcinogenicity had not been demonstrated. In the intervening years, studies conducted at the University of Bologna, New York University, and the National Toxicology Program have shown that benzene is a carcinogen in animals through the oral and inhalation routes. In the preamble to the proposed Benzene Standard, OSHA suggests that "[t]hese findings add support to evidence that benzene is a human carcinogen and suggest that cancers other than of the lympho-hematopoietic system also may be involved in humans."90/

89/ 50 Fed. Reg. 50512, 50516, col. 3.

90/ 50 Fed. Reg. 50512, 50527, col. 1.

The absence of an animal model for benzene carcinogenesis in earlier years had been a puzzling phenomenon, since in virtually all cases, a substance found to cause cancer in humans (as was the case for benzene) also has been shown to cause cancer in animals. As Dr. Robert Snyder observes, the fact that animal models for benzene carcinogenesis now have been demonstrated "add[s] further assurance to the conclusion derived from epidemiological and clinical studies that in a qualitative sense benzene poses the potential to produce leukemia in humans."91/ The development of an animal model for benzene-related neoplasia is important, since it "may help us to understand the molecular events underlying leukemogenesis in man."92/

However, the results of the animal bioassays do not provide a basis for concluding that benzene exposure is likely to produce cancers other than of the lympho-hematopoietic system in humans. As Dr. Snyder notes, "the total body of evidence suggests that benzene is indeed carcinogenic, with the expression of the carcinogenic activity in man taking the form of one of several types of leukemia."93/ The fact that solid tumors have been produced in animal studies "should not be interpreted to predict that benzene will cause solid tumors in man, because this is

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91/ See Snyder Review at 28.

92/ Id.

93/ Id.

. . . an example of differences in response among species."94/ As Dr. Snyder explains,

> The animal studies do not provide a basis for concluding that exposure of humans to benzene either at the doses and routes to which the animals were exposed or through other routes of exposure and at other doses is likely to lead to the production of forms of cancer other than leukemia.95/

After reviewing the recent literature on benzene toxicology, the Benzene Task Force of the European Chemical Industry Ecology & Toxicology Center concluded that there is adequate evidence to categorize benzene as an animal carcinogen.96/ However, the Task Force emphasized

> that the types of neoplasm (hepatomas, oral carcinomas) reported in the recent animal studies are rare in humans. In view of the long period over which workers exposed to benzene have been under observation, the Task Force believes that if a causal association existed between human exposure to benzene and the onset of such neoplasms, it would have been detected. Benzene is carcinogenic to rats, mice and man, but the substantial differences in the responses makes [sic] the qualitative and quantitative extrapolation of the animal results to man uncertain.97/

94/ Id.

95/ Id.

96/ ECETOC Report at 14.

97/ Id. at 14-15.

In sum, the recent animal studies provide qualitative confirmation of benzene's carcinogenic potential in humans, but they do not provide a basis for concluding that benzene will cause non-lymphopoietic cancers in humans. Nor, as discussed below, is it appropriate to use the animal data for purposes of quantitatively estimating the risk of leukemia that occupational exposures may present to workers.98/

C. Mutagenicity, Cytogenetic Effects, and Hematological Effects at the Cellular Level

1. Mutagenicity

Until very recently, benzene had not been found to be mutagenic in short-term tests of mutagenicity.99/ Thus, in December 1984, a review of recent literature on the mutagenicity of benzene concluded: "It is well established that benzene does not induce point-mutations in chromosomes."100/ While benzene or its metabolites are known to bind to DNA, this binding "has not been linked to the transformation of the affected cell to a cancer cell."101/

98/ See pp. __ - __, infra.

99/ See Snyder Review at 30; International Agency for Research on Cancer ("IARC") Monographs Volume 29: Benzene (1982) ("IARC Monograph") (Ex. 128-8) at 114.

100/ ECETOC Report at 15.

101/ Snyder Review at 30.

In the rulemaking notice, OSHA states "that benzene was found to be mutagenic in human cells in a recently developed gene-locus mutation assay utilizing a metabolically competent human lymphoblastoid cell line."102/ It is difficult for us to comment on this report (by Crespi and Penman), since the document in the OSHA docket (Ex. 159-19A) is simply a one paragraph abstract. Nonetheless, the brief description we have seen leads us to question whether this report should be taken as establishing that benzene is mutagenic in the face of a host of negative test results over the years.

The assay employed by Crespi and Penman (measuring the induction of mutations at the hypopxanthine guanine phosphoribosyl transferase or "HGPRT" locus in human lymphoblastoid cells) is relatively new and is not a well validated assay for studying point mutations at this locus.103/ Moreover, the abstract reports mutagenic activity at one dose only, and nothing is said about the percentage of cell survival at this dose. In most short-term mutation tests, a cytotoxicity screen is done, various dose levels are selected, and the assay is run at several doses corresponding to an anticipated range of

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102/ 50 Fed. Reg. 50512, 50528, col. 2.

103/ The HGPRT point mutation assay using Chinese hamster ovary cells is favored by genetic toxicologists and frequently is included in a mutagenicity test battery performed on a specific chemical.

percent cell survival, so that the existence of a dose-response relationship can be investigated. The absence of dose-response information in the Crespi and Penman abstract further detracts from the significance that can be attributed to the report.

In sum, the brief abstract of the novel assay to which OSHA refers does not appear to provide a sufficient basis for reaching a conclusion regarding the mutagenicity of benzene that is contrary to the results of studies performed by a variety of investigators in other laboratories.

2. Cytogenetic Effects

The rulemaking notice refers to the fact that benzene has been found to induce various types of cytogenetic effects, including aberrations and other chromosomal damage in humans, and increased production of sister chromotid exchanges ("SCEs") and micronuclei in experimental animal test systems.104/

a. Chromosome Aberrations in Human Studies

Most of the human studies of chromosome aberrations involved relatively high benzene exposures or limited information about benzene exposure levels. The study by Picciano (Ex. 144-118) on which primary reliance is placed, found that at

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104/ See 50 Fed. Reg. 50512, 50524-25, 50527-28.

exposure levels estimated to average less than 10 ppm, "[c]ells with marker chromosomes (rings, dycentrics, translocations and exchange figures) were significantly more common in benzene exposed workers compared to controls" and that "[c]ells with chromosome breaks were also more common among exposed workers . . . ."105/ The Picciano study, however, must be interpreted with caution.

Apart from the question of what clinical significance, if any, these chromosomal effects may have,106/ "the implication of the chromosome changes," as Dr. MacMahon notes, "is not as certain as Picciano suggests, and these 52 workers were exposed to a variety of other aromatic hydrocarbons, including toluene, styrene, ethylene and diethylbenzene which may have played a role."107/ Dr. Robert Snyder expresses similar reservations about the Picciano study, stating that "it is unclear if smoking, recent illness, other occupational clastogens and other confounding factors were carefully excluded."108/ Moreover, other

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105/ Snyder Review at 14.

106/ See pp. ___ - ___, infra. As Dr. Brian MacMahon observes: "The clinical significance of chromosome aberrations of these types [is not] clearly established." MacMahon Report at 24. Similarly, EPA states that "no direct evidence of a casual [sic] link[redacted] between chromosomal aberrations and leukemia exists." Response to Public Comments on the Regulation of Benzene, 49 Fed. Reg. 23478, 23481, col. 3 (June 6, 1984).

107/ MacMahon Report at 6.

108/ Snyder Review at 14.

factors have been identified which "may have affected the apparent significance of the results, particularly the unusually low overall incidence of aberrations in the controls."109/

b. Increased Production of SCEs and Micronuclei in Experimental Animal Test Systems

The rulemaking notice points to a variety of studies in which benzene exposures (including low cumulative exposures) have resulted in a significant increase of SCEs and micronuclei in experimental animal test systems.110/ The fact that benzene can induce these cytogenetic effects even at relatively low levels of exposure seems clear. However, as Dr. Robert Snyder points out, "it is not clear what the relationship, if any, is between these effects and leukemia at low doses of benzene."111/ The metabolites responsible for the clastogenic effects of benzene may be different from the metabolites responsible for its leukemogenic effects. Thus, clastogenic changes may be "parallel but independent of leukemogenesis,"112/ in which case "the dose effect relationships would be different, and the pharmacokinetics would be different."113/ Accordingly, as Dr. Snyder observes:

109/ Id. at 14-15.

110/ See 50 Fed. Reg. 50512, 50527.

111/ Snyder Review at 30.

112/ Id.

113/ Id.

> It can be said that in given test systems, benzene can be shown to be clastogenic but not mutagenic, and it can be shown to induce some types of cancer. However, there is as yet no direct link between clastogenic effects and carcinogenic effects of benzene."114/

In short, at the present time, as the President's Office of Science and Technology Policy ("OSTP") points out, "the association between an increase in the frequency of SCEs in cells in vitro or in vivo and heritable changes has not been clearly defined."115/ Nor is it clear "that the induction of micronuclei

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114/ Id. at 30-31. Dr. Snyder points out that benzene-exposed workers with increased chromosome aberrations have been found to have no significant increase in SCEs. See id. at 15. These discrepancies have led Tice, et al., to suggest that different molecular mechanisms and metabolites of benzene may underlie the induction of SCEs and chromosomal aberrations. See id. at 16, 30. Gebhart has demonstrated a significant lack of correspondence between SCEs and other cytogenetic changes. Gebhart, "Sister Chromatid Exchange (SCE) and Structural Chromosome Aberration in Mutagenicity Testing," 58 Hum. Genet. 235-254 (1981). The Congressional Office of Technology Assessment ("OTA") has noted that "the fundamental way in which a particular chemical interacts with the DNA to produce SCEs may be different from the mechanism that produces chromosomal aberrations." OTA, The Role of Genetic Testing in the Prevention of Occupational Disease at __ (April 1983). Even if a mechanistic link between the clastogenic and carcinogenic effects of benzene did exist, low level benzene exposures capable of producing clastogenic effects might not result in carcinogenic effects, for "thresholds for carcinogenesis may be different from the thresholds for clastogenic effects of the same chemical." Snyder Review at 33.

115/ See OSTP, "Chemical Carcinogenesis; A Review of the Science and Its Associated Principles," 50 Fed. Reg. 10372, 10404, col. 3 (March 14, 1985). As stated by one authority relied on by OSHA, "SCEs . . . are not, as far as we know, mutational agents in the strict sense." Bloom, et al., "Guidelines for Studies of Human Populations Exposed to Mutagenic and Reproductive Hazards," (Ex. 159-12) at 3.

is related to heritable changes in cellular phenotypes."116/ Our present state of knowledge simply does not allow us to conclude that there necessarily exists "a sequential series of events leading from one or more forms of clastogenic changes to the production of leukemia."117/

c. The Significance of Subclinical Cytogenetic Effects

The fact that relatively low cumulative exposures to benzene may induce various cytogenetic effects (including chromosomal aberrations and increased production of SCEs and micronuclei) in humans or experimental animal test systems does not demonstrate the existence of material health impairment resulting from low level benzene exposures. These subclinical cytogenetic effects have not been shown to be precursors of actual illness; nor can they appropriately be used as a basis for making clinical predictions.

The fact that benzene exposure could increase the incidence of chromosomal aberrations was considered during the 1977 Benzene Standard proceeding. At that time, OSHA, as the Supreme Court noted, "took no definitive position as to what these aberrations mean in terms of demonstrable health effects

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116/ OSTP, "Chemical Carcinogenesis," supra, 50 Fed. Reg. 10372, 10404, col. 2.

117/ Snyder Review at 30.

. . . ."118/ There is still no evidence indicating that these cytogenetic effects have any clinical importance.119/ Thus, a study on which OSHA relies in evaluating the significance of clastogenic effects acknowledges that "[w]e are aware of no health consequences of SCEs per se" and states that the presence of chromosomal aberrations and other "cytogenetic changes cannot be used to predict specific health effects in an individual."120/ As Bloom, et al., explain,

> In human populations, no associations have been definitively drawn between those individuals with induced [chromosomal] breakage and the subsequent development of cancer. This is true even in Japan, where thousands of persons have been shown to have chromosomal aberrations of radiation origin . . . . Thus . . . the presence of . . . chromosome breakage . . . is not . . . a harbinger of cancer for the carrier individual.."121/

NIOSH has expressed a similar view, stating that it "knows of no data that correlates [chromosomal abnormalities and

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118/ Industrial Union Department, AFL-CIO v. American Petroleum Institute, 448 U.S. 607, 633 (1980).

119/ In a recent decision, the Appellate Division of the Superior Court of New Jersey refused to accept subclinical cellular damage as a precursor of actual illness or as a basis for recovery. See Ayers v. Township of Jackson, __ A.2d __ (June 4, 1985).

120/ Bloom, et al., "Guidelines for Studies of Human Populations Exposed to Mutagenic Reproductive Hazards," (Ex. 159-12) at 3.

121/ Id. at 31.

increased frequencies of sister chromatid exchanges] . . . to the manifestation of cancer or adverse reproductive effects in an individual."122/ Thus, according to NIOSH "the presence of detectable chromosomal damage does not appear to provide a firm basis for predicting the likelihood of an individual demonstrating a tumorigenic response."123/

Various scientific organizations and individual commenters echoed this same theme in OSHA's Ethylene Oxide proceeding. Thus, the American Academy of Industrial Hygiene pointed out that "although SCEs and chromosome aberrations are indices of DNA damage, the end points are different, they are not necessarily correlated, and the relevance of one or the other in a given application is not obvious."124/ The Academy noted that there is "no current concensus [sic] concerning the relationship between DNA damage and the liklihood [sic] of an ultimate clinical outcome such as cancer."125/

122/ NIOSH Comments to OSHA Proposed Rule on Occupational Exposure to Ethylene Oxide (Ex. 11-146 in Docket H-200) at 4 (June 22, 1983).

123/ Id.

124/ American Academy of Industrial Hygiene Position Paper on a STEL for Ethylene Oxide (Ex. 175 in Docket H-200) at 2 (July 21, 1984).

125/ Id.

Other experts commenting in the Ethylene Oxide proceeding expressed similar views. For example, in discussing the significance of an increase in SCEs following chemical exposure, Vernon L. Carter observed that "no relationship has been established between this response and effects of concern such as cancer and reproductive problems."126/ Dr. J. W. Grisham stated that neither chromosomal aberrations nor SCEs "have been correlated with any disease outcome and, indeed, there is evidence suggesting that SCE may not represent a pathological (toxic) cellular reaction."127/ And, after describing the mechanism by which chromosome aberrations and SCEs are induced, Dr. R. Julian Preston of the Oak Ridge National Laboratory concluded that

> there is no evidence to suggest that an increase in SCE is responsible for any other cellular change . . . . The important point is that increases in SCE are not representative of chromosomal changes that themselves can cause adverse health effects.128/

126/ Letter of Vernon L. Carter, Jr., DVM to R. Leonard Vance (Ex. 178 in Docket H-200) at 3 (July 19, 1984). Dr. Betty Dabney has charactrerized the SCE assay as "highly experimental" and not now appropriate for use in setting occupational exposure standards. See Dabney, "The Role of Human Genetic Monitoring in the Workplace," 23 J. Occup. Med. 626-31 (1981).

127/ Letter of J. W. Grisham, M.D. to Mr. Robert C. Barnard (Ex. 49 in Docket H-200) at 3 (June 24, 1983).

128/ Preston, "The Induction of Chromosome Aberrations and Sister Chromatid Exchanges in Human Peripheral Lymphocytes by Ethylene Oxide, and the Use of Such End Points for Establishing Exposure Standards" (Ex. 189-16; Appendix A in Docket H-200) at 3.

Accordingly, Dr. Preston cautioned that "measurement of SCE in peripheral lymphocytes is not known to be a predictor of subsequent adverse health effects, and data obtained cannot be used for setting exposure standards."129/ The same is true, Dr. Preston stated, of measurements of chromosome aberrations in peripheral lymphocytes.130/

In short, as a recent review of benzene toxicity concluded,

> no relationship between the types of chromosome damage observed [in connection with benzene exposure] and effects on human health can be established at present. The observations have to be taken as indicating a response to exposure to benzene of unknown biological significance.131/

In EPA's words, "no direct evidence of a [causal] linkage between chromosomal aberrations and leukemia exists."132/

OSHA itself has acknowledged the limited and uncertain significance of these cytogenetic effects, stating that findings of "chromosomal damage do not provide direct evidence for a genetic or carcinogenic effect"133/ and contending in court that

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129/ Id. at 4.

130/ Id.

131/ ECETOC Report at 20.

132/ Response to Comments on the Regulation of Benzene, 49 Fed. Reg. 23478, 23481, col. 3 (June 6, 1984).

133/ 50 Fed. Reg. 50512, 50538, col. 2.

there is no evidence linking cancer or other adverse health effects to sister chromatid exchanges.134/ As pointed out by the Congressional Office of Technology Assessment, the fact is that "no occupational studies directly relate positive findings for any chromosomal endpoint with increased risk for any disease."135/ Thus, the fact that relatively low cumulative exposures to benzene may increase the incidence of various cytogenetic markers does not show that a risk of material health impairment exists at those levels of exposure. Regulatory action cannot properly be predicated upon the potential occurrence of such subtle cytogenetic effects.

3. Hematological Effects at the Cellular Level

In recent years, several investigators have studied the effects of benzene inhalation on bone marrow and splenic progenitor cells, using the spleen colony forming unit ("CFU-S") technique and the erythroid progenitor cell colony forming unit

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134/ See BNA Occupational Safety and Health Reporter, January 30, 1986 at 915-16.

135/ OTA, The Role of Genetic Testing in the Prevention of Occupational Disease at __ ___ (April 1983). Investigators from the Centers for Disease Control, Brookhaven National Laboratory and Oak Ridge National Laboratory have expressed a similar view. In the conclusions to a cytogenetic study of persons living near the Love Canal, they stressed that it is still impossible to know whether findings of increased chromosome damage "might predict later clinical illness in individuals." Heath, et al., "Cytogenetic Findings in Persons Living Near the Love Canal," 251 J.A.M.A. 1437, 1440 (1984).

("CFU-E") assay.136/ In these tests, benzene exposures as low as 10 ppm have been found to produce hematologic responses at the cellular level. These hematologic responses, however, are not examples of aplastic anemia or leukemia.137/ While they may possibly indicate the early stages of a disease process, it is equally likely, as Dr. Robert Snyder points out, that they are reversible biological responses which will not lead to hematological diseases such as aplastic anemia or leukemia "because the dose is too low and normal repair mechanisms would not permit progression of the disease process."138/

Rather than predicting potential bone marrow disease, these subtle hematologic responses may simply reflect the sophistication and sensitivity of the assays.139/ Accordingly, as Dr. Snyder observes, the responses seen in these assays must be interpreted with caution.140/ They "do not, in themselves, predict a significant adverse health effect. Nor do these data reflect a potential risk of cancer."141/

136/ See 50 Fed. Reg. 50512, 50528, col. 1; Snyder Review at 18-20.

137/ See Snyder Review at 34.

138/ Id. at 34-35.

139/ See id. at 35.

140/ See id.

141/ Id. at 35.

II. Risk Assessments for Benzene

The rulemaking notice devotes considerable attention to quantitative risk assessments for benzene. On the basis of these assessments, OSHA preliminarily concludes that the risk of leukemia mortality "from a working lifetime exposure to benzene at 10 ppm is 44-152 cases per 1,000 exposed employees."142/ On the assumption that the dose-response relationship is linear down to zero, the risk assessment preferred by OSHA143/ estimates that the risk of leukemia mortality from a working lifetime exposure to 1 ppm of benzene is 5-16.144/ In the pages that follow, we discuss various issues relating to the risk assessments for benzene and show that the likely risks are smaller than OSHA has assumed, particularly at exposure levels in the neighborhood of 1 ppm.

A. Animal Versus Human Data

One question raised in the rulemaking notice is whether animal data should be used to derive a quantitative estimate of the cancer risk to benzene-exposed workers and, if so, how this should be done. The short answer to this question is that a risk

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142/ 50 Fed. Reg. 50512, 50538, col. 3.

143/ White, et al., A Quantitative Estimate of Leukemia Mortality Associated With Occupational Exposure to Benzene (Ex. 127) (1982).

144/ 50 Fed. Reg. 50512, 50532, col. 3.

assessment for benzene should be based on human epidemiological data rather than on animal studies.

In the preamble to the proposed rule, OSHA states that "[t]he underlying epidemiological studies which provide a basis for the quantification of risk are in general of reasonable quality . . . and provide a basis for risk assessment."145/ In these circumstances, the human data should be preferred over the animal data for estimating the cancer risk that may be associated with exposure to benzene in the workplace.

The preference for human data has been expressed by a variety of authoritative sources and can be considered a guiding principle in quantitative risk assessment. Thus, EPA's Proposed Guidelines for Carcinogen Risk Assessment state clearly and unequivocally: "If available, estimates based upon human epidemiologic data are preferred."146/ And, in its most recent risk assessment for benzene, EPA points to "a number of factors [which] strongly suggest that animal studies are less reliable than those based upon human responses."147/ OSHA's risk

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145/ Id. at 50538, col. 2.

146/ EPA, Proposed Guidelines for Carcinogen Risk Assessment, 49 Fed. Reg. 46294, 46298, col. 1 (November 23, 1984).

147/ EPA Cancer Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985 at 18. See also id. at 24 (unit risks derived from animal studies are "intrinsically less reliable than those based upon the human response").

assessment contractors in the present proceeding have expressed the same view, emphasizing that while "comparisons between estimates made from human and animal data are instructive, in the case of benzene, estimates made from human data should take precedence over those from animal data."148/

The reasons for this preference for human data are easy to discern. As Sir Richard Doll recently explained, human epidemiological studies showing a relationship between disease and estimated cumulative exposure

> are better guides to control measures than attempts to extrapolate from the results of animal experiments. For not only are animal experiments unlikely to reflect the exact conditions of human exposure, but we also do not know how to allow for species differences in reaction. Nor, most importantly, do we have any means of predicting quantitative[ly] an effect in animals with a long life like Man from the relationship between life-time exposure to unit dose and cancer incidence in animals with lives measured in weeks rather than years.149/

Thus, while animal data "may help us to understand the molecular events underlying leukemogenesis in man," and may provide an interesting perspective on risk estimates derived from human epidemiological studies, the animal data

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148/ Crump Report at 33.

149/ Doll, "Epidemiological Discovery of Occupational Cancers," 13 Annals of the Singapore Academy of Medicine 331, 332 (April 1984).

are not appropriate for use in a quantitative risk assessment until such time as we can be certain that the mechanistic progression involving pharmacokinetics, metabolism, DNA, alkylation, DNA repair or the lack thereof, promotion, etc., at the exposure levels used in the animal studies are an accurate reflection of the course of human benzene-induced leukemia.150/

In short, risk estimates for benzene based on human data should take precedence over those based on animal studies. It should be recognized, however, that even if the animal data were used, the resulting risk estimate would not be higher than estimates based on human data. This fact has been recognized both by EPA and by OSHA's own risk assessment contractors.

Thus, in its most recent estimate of cancer risks associated with exposure to benzene, EPA concluded that risk estimates for benzene based on the preferred animal studies "are an order of magnitude lower" than risk estimates based upon human epidemiological data.151/ Drs. Crump and Allen, OSHA's own outside experts on this issue, reached a similar conclusion. After performing a variety of risk assessments on both human and animal data, Drs. Crump and Allen found that their estimates of human leukemia risk derived from animal inhalation studies were "all

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150/ Snyder Review at 28-29.

151/ EPA Carcinogen Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985, at 24-25.

considerably less than those made from human data."152/ Their estimates of human risk based upon the NTP gavage study were higher than the risks estimated on the basis of the animal inhalation studies.153/ However, even "the largest estimates of human risk from the animal studies, derived from all squamous cell carcinomas in male mice in the NTP study," were found by Crump and Allen to be lower than those based upon human data.154/

In short, animal data should not be used to perform a quantitative risk assessment for benzene, but if such data were used, the result would provide no basis for concluding that risk estimates derived from human epidemiological studies are understated.

B. Selection of Epidemiological Data

Although a variety of epidemiological studies purporting to indicate an association between benzene exposure and leukemia are available, the studies by Rinsky, Ott, and Wong appear to provide more complete exposure data than the others. Accordingly, recent risk assessment efforts for benzene have focused on those studies.155/ While the Rinsky and Ott Studies

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152/ Crump Report at 33.

153/ Compare id., Table 25, with id., Table 26.

154/ Id. at 33 and Tables 21 and 26.

155/ See, e.g., id. at 15.

may be appropriate for quantitative risk assessment, we believe that the Wong Study should not be used for that purpose.

As discussed at some length at pages ___ - ___ above, the Wong Study does not show a significantly increased incidence of lymphatic and hematopoietic cancer (including leukemia) among the benzene-exposed workers when compared to the general population, and the apparent increase in relative risk among the benzene-exposed workers as compared to the internal control group is highly questionable. Because of the significant and unexplained deficit in leukemia mortality among the internal controls, the apparent increase in risk in the exposed workers, as EPA acknowledges, "may be due to an artifact in the data rather than to a true carcinogenic response."156/

This unexplained leukemia deficit among the non-exposed workers in the Wong Study has been described as the most "striking and statistically significant feature of [the Wong] data."157/ It has led Dr. Brian MacMahon and others to question whether the study can serve as reliable evidence of even a qualitative association between leukemia and exposure to benzene.158/

156/ EPA Carcinogen Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985 at 23-24.

157/ MacMahon Report at 57.

158/ See id. at 58; pp. ___ - ___, supra.

1813 But whatever may be the case regarding possible qualitative
1814 inferences, the enormous uncertainty surrounding the study
1815 results (particularly the mortality experience of the unexposed
1816 workers) makes it inappropriate to use the Wong Study for pur-
1817 poses of quantitative risk assessment.

1819
1820 A particularly telling consideration in this regard is
1821 that the mysterious absence of any leukemia at all among the
1822 internal control group has an enormous impact on estimates of
1823 risk based on the Wong Study. Thus, Drs. Crump and Allen found
1825 that the leukemia deficit among the internal controls more than
1826 doubles the dose-response slope that would exist if the leukemia
1829 experience of the controls in the Wong Study had been normal.159/

1837
1838 A proportional mortality analysis of the Wong Study
1839 performed by Professor Robert Sielken Jr. confirms this
1840 point.160/ Prof. Sielken's analysis shows that if the
1846 lymphopoietic mortality experience of the non-exposed workers in
1849 the Wong Study had been closer to what normally would have been

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1829 159/ Compare Crump Report, Table 12, Data Set VII, with id.,
1830 Data Set VIII. In fact, the mortality deficit among the internal
1831 control group has an even bigger impact than Table 12 suggests,
1833 since the effect of the deficit is moderated in Table 12 by the
1834 fact that the results of the Wong Study are aggregated with those
1836 of the Rinsky and Ott Studies.

1840 160/ R. Sielken Jr., A Quantitative Risk Assessment Based on
1841 an Industry-Wide Mortality Study of Chemical Workers
1843 Occupationally Exposed to Benzene, February 1985 (hereinafter
1844 referred to as the "Sielken Report"). A copy of the Sielken
1845 Report is submitted herewith as Appendix J.

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expected, the estimated cause of death probabilities associated with benzene exposure would change exponentially. According to Prof. Sielken:

> If the number of non-exposed workers whose death was assumed to have been caused by lymphatic or hematopoietic cancer was changed from its observed value of 3 to either 6, or 9, or 12 then the increases in the estimated probabilities due to durations at positive dose levels were divided by approximately 1.5 or 3 or 50, respectively. Thus, the estimated increases [in the probability of mortality from lymphatic or hematopoietic cancer] decreased rapidly as the number of non-exposed workers whose cause of death was assumed to be lymphatic or hematopoietic cancer increased.161/

Based on his analysis, Prof. Sielken concluded that

> the estimated increases in the probability of a worker's death being caused by lymphatic or hematopoietic cancer associated with non-zero durations at non-zero doses [of benzene] could easily be several times too large if the number of deaths caused by lymphatic or hematopoietic cancer was unusually low among the non-exposed workers in the study due to chance.162/

Indeed, when Prof. Sielken tested the assumption that the number of lymphatic and hematopoietic cancer deaths among the non-exposed group was normal (i.e., 13 such deaths), the best-fitting model

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161/ Sielken Report at ii.

162/ Id. at 27.

> indicated no dose-response relationship: that is, for the exposures reported in the study the probability of an exposed worker's death being caused by lymphatic or hematopoietic cancer would be estimated to be the same as it is for a non-exposed worker.163/

In sum, use of the mortality results for the unexposed workers in the Wong Study significantly distorts any effort to develop a quantitative risk assessment for benzene. Unless and until the significant and highly unusual cancer deficit among the unexposed workers is explained, the Wong Study, as Drs. Crump and Allen observe, "does not provide strong evidence of a relationship between occupational exposure to benzene and lymphatic and hematopoietic cancer."164/ For that reason, the Wong Study should not be used for quantitative risk assessment. If it is used, however, the data relating to the unexposed workers should be omitted from the analysis, which would produce risk estimates that "are not much different from those [that Crump and Allen derive] from the Rinsky et al. and Ott et al. combined data."165/

163/ Id.

164/ Crump Report at 24.

165/ Id. Alternatively, the unexposed workers in the Wong study should be assumed to have had an SMR of 100, which would produce essentially the same result as excluding them from the analysis.

As noted above, Dr. Frank Carlborg developed a quantitative risk assessment based on data sets for all workers and for exposed workers only in the Wong Study. He concluded that, from

[Footnote continued next page]

C. The Crump and Allen Risk Assessment Should Be Preferred Over the Risk Assessments by White, et al. and IARC.

The rulemaking notice discusses three risk assessments for benzene -- the analysis performed by White, et al.,166/ the summary presented by IARC (Ex. 159-58) and the risk assessment performed under contract to OSHA by Drs. Crump and Allen (Ex. 152). For the reasons discussed below, the risk assessment performed by Drs. Crump and Allen should be preferred over the IARC and White Risk Assessments.

To assert, as OSHA does, that IARC "conducted a quantitative risk assessment of workers exposed to benzene"167/ surely is a classic misnomer. What OSHA describes as a "quantitative risk assessment" is no more than one and one-half pages in an

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a statistical standpoint, the data from the study are consistent with a "no-effect model which assumes that an exposure to benzene does not affect the incidence of lymphopoietic cancer and that all the variation among the observed response proportions can be attributed to age differences among the workers." Carlborg Report at 7. Only one model tested by Dr. Carlborg provided a statistically significant improvement in fit over the "no-effect model." Under that model, which assumes that the lymphopoietic cancer response depends upon exposure but not upon age, "a worker having 45 ppm-years of occupational exposure to benzene would have an estimated excess risk from lymphopoietic cancer of about one to two in one thousand, regardless of his age." Id. at 7-8.

166/ White, et al., "A Quantitative Estimate of Leukemia Mortality Associated with Occupational Exposure to Benzene," 2 Risk Analysis 195 (1982) (Ex. 128-37) (hereinafter referred to as the "White Risk Assessment").

167/ 50 Fed. Reg. 50512, 50531, col. 1.

Annex to the IARC Monograph on Benzene. It does not reflect an examination and analysis of exposure levels, and treats two of the studies discussed in no more than one or two sentences. Moreover, IARC does not draw all of the implications that OSHA itself has tried to draw from the page-and-a-half discussion. In short, the casual discussion of relative risk contained in the Annex to the IARC Monograph cannot seriously be treated as a quantitative risk assessment when compared to the lengthy, careful and detailed analysis presented by Drs. Crump and Allen.168/

The analysis by White, et al., can with more justification be described as a quantitative risk assessment. However, the White Risk Assessment has been completely superseded by the much more thorough and detailed risk assessment that was performed for OSHA by Crump and Allen.

From the outset, the White Risk Assessment has been seriously criticized. For example, White, et al., based their risk assessment solely upon workers who had been employed for five or more years, since they found that "most of the elevated leukemia risk was observed in this group."169/ They then applied the results of that analysis to derive risk estimates for workers

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168/ Moreover, as Dr. Robert Snyder observes, the risk estimate presented by IARC appears to be radically inconsistent with practical experience with the heavy industrial use of benzene during this century. See Snyder Review at 35.

169/ White Risk Assessment, 2 Risk Analysis at 198.

at all levels of exposure. Various peer reviewers criticized this statistical manipulation, calling it "indefensible" (Dr. Phillip Cole)170/ and pointing out that it amounts to using "the same set of data both to formulate and test [the] hypothesis."171/ As Dr. Brian MacMahon points out,

> there was no a priori hypothesis that such employees would be at greatest risk and there is no justification for selecting this particular group post hoc as most representative of the truth. Had the SMR been higher for persons exposed 1 or more years or 10 or more years, such subgroups could, with equal lack of justification, have been chosen for the risk assessment.172/

OSHA now recognizes that the approach taken by White, et al., was inappropriate, but attempts to excuse it with the observation that the leukemia mortality experience of workers having less than five years' exposure appears to be consistent with the risk estimate developed on the basis of workers with more than five years' exposure.173/ But such post hoc gerrymandering does not remove the suspicion, expressed by Dr. Philip Cole, that the White Risk Assessment was a biased attempt "to make benzene appear as hazardous as possible."174/ As Dr. Cole

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170/ Cole Critique, supra, (Ex. 137) at 3.

171/ March 30, 1984 letter of Professor Norman Breslow to R. Leonard Vance, Ex. 137.

172/ MacMahon Report at 47.

173/ See 50 Fed. Reg. 50512, 50533, cols. 2-3.

174/ Cole Critique, supra, Ex. 137 at 3. Dr. Charles Brown also described the exclusion of workers exposed less than five

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points out, the White Risk Assessment "appears to have been written to advocate a particular position rather than to represent a serious and unbiased attempt to develop a meaningful risk assessment for leukemia in relation to benzene."175/ In the words of Dr. Charles C. Brown, "it appears to be one-sided in its evaluation. The presentation is not as balanced as it should be to serve as the basis for regulatory decisions."176/

Even if the objectivity of the White Risk Assessment were not subject to question, it clearly could not be deemed as

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years as being "an incorrect, biased decision." May 16, 1983 letter of Charles C. Brown, Ph.D. to Ralph E. Yodaiken, Ex. 137.

175/ Cole Critique, supra, Ex. 137 at 2. In this regard, Professor Norman Breslow stated that "the paper cannot be regarded as good science." March 30, 1983 letter of Prof. Norman Breslow to R. Leonard Vance, Ex. 137.

176/ May 16, 1983 letter of Charles C. Brown, Ph.D. to Ralph E. Yodaiken. The risk estimates that White, et al., make for the Rinsky and Ott studies add to the suspicion of a lack of objectivity. Thus, as Dr. Brian MacMahon states:

> Given the gross assumptions regarding exposure and small numbers on which the estimates of risk are based, the similarity of the estimates of excess risk derived from the data of Rinsky, et al, and of Ott, et al, just have to be contrived or the result of the most extraordinary coincidence. Much of the exposure data in the Rinsky study are assumed and one cannot escape the suspicion that the assumptions have been made with the desired outcome in mind.

MacMahon Report at 46-47.

reliable as the more recent risk assessment performed by Drs. Crump and Allen. Apart from the fact that their risk assessment is far more objective, detailed, comprehensive and careful than the analysis of White, et al., the critical fact is that Drs. Crump and Allen obtained and utilized far more extensive exposure information than White, et al.

The White Risk Assessment rests on the assumption that all members of the Rinsky and Ott cohorts were subject to the same average benzene exposure. The authors simply calculated what they believed to be a representative average exposure for the cohort taken as a whole and drew a line from that point through zero to create a dose-response curve. As Dr. Irving Kessler observes, however:

> Averaging of exposures over numbers of workers and time represents only a first -- and very poor -- method of dealing with deficient information.177/

This approach is particularly susceptible to producing unreliable estimates when applied to studies, such as the Rinsky study, where the incidence of leukemia is small and the range of exposure levels within the workplace and among the work force is wide.178/ In such cases, the average benzene exposure of the

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177/ March 8, 1983 letter of Irving E. Kessler, M.D. to R. Leonard Vance, Ex. 137.

178/ See B. Goldstein, "Benzene Toxicity: Review of Recent Literature" (February 3, 1983) (Ex. ___) at 4-6; EPA, Ambient

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cohort as a whole (even if properly determined) may not be reasonably representative of the exposures of those workers showing a leukemogenic response.179/ Thus, if we are to have any confidence at all in the reliability of the risk assessment, it is critical that an attempt be made to develop individual exposure profiles, rather than arbitrarily assigning a single average exposure value to the entire cohort.

That is precisely what Drs. Crump and Allen did in developing a risk assessment for OSHA. In contrast to the White Risk Assessment (not to mention the brief IARC discussion), Crump and Allen have performed a comprehensive, detailed and worker-specific analysis of the occupational benzene exposures of the Rinsky cohort. They did not simply attribute a single average benzene exposure to all members of the cohort and assume that the increased leukemia risk found among members of the cohort (or among members of a subgroup within the cohort) was attributable to the average exposure value for the cohort as a whole. Instead, Crump and Allen obtained the underlying data tapes from the Rinsky study and developed a complete exposure profile for each worker in the cohort.180/ They were thus able to evaluate

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Water Quality Criteria for Benzene (October 1980) at C-59 and C-60.

179/ See B. Goldstein, "Benzene Toxicity," supra (Ex. ___) at 6.

180/ See Crump Report at 11 and Appendix B.

the increased risk on the basis of a more highly refined data set with a larger number of risk-exposure points than previous investigators, including White, et al. and IARC.

In sum, quite apart from questions about its objectivity, the White Risk Assessment (and, a fortiori, the IARC discussion of risk) is far less reliable and less suitable for regulatory decisionmaking than the risk assessment developed by Drs. Crump and Allen because, as the authors of the Rinsky study recently observed, the IARC and White Risk Assessments are "based on estimates of group exposure rather than on estimates of the exposure of individual workers. The resultant risk estimates were subject, therefore, to wide variances."181/ By contrast, the Crump and Allen risk assessment, as EPA points out, "contains much better human exposure estimates in the epidemiologic studies than has been previously available."182/ Accordingly, OSHA's quantitative evaluation of the potential cancer risk presented by occupational exposure to benzene should be based on the Crump and Allen risk assessment rather than on previous reports.

181/ Rinsky, et al., "Benzene and Leukemia: An Epidemiologic Risk Assessment," August 9, 1985 (Ex. 176A) at 4.

182/ EPA Carcinogen Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985 at 2.

D. The Crump and Allen Risk Assessment Conservatively Indicates That the Increased Risk of Leukemia From a Working Lifetime Exposure to 1 ppm Benzene Is Approximately An Order of Magnitude Lower at Exposure Levels of 1-10 ppm Than OSHA Has Assumed.

In the rulemaking notice, OSHA preliminarily estimates that the increased risk of leukemia from a working lifetime exposure to 10 ppm benzene is approximately 44-152/1,000 workers and that at an exposure level of 1 ppm, the increased risk is approximately 5-16/1,000.183/ By contrast, even when various conservative assumptions are made, the Crump and Allen risk assessment indicates that the increased risk of leukemia is almost an order of magnitude lower than OSHA suggests.

Although Drs. Crump and Allen analyzed the epidemiological data for benzene using a variety of exposure models, they prefer the weighted cumulative exposure model, since it fits the data somewhat better than the other models tested and is more consistent with the latency pattern of leukemia.184/ Crump and Allen analyzed the weighted cumulative exposure data under relative risk and absolute risk forms of the dose-response model.185/ They found that, under an absolute risk model, the

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183/ See 50 Fed. Reg. 50512, 50532.

184/ See Crump Report at 23-24.

185/ The relative risk model assumes that the increased risk of benzene-related leukemia mortality is proportional to the background leukemia mortality -- i.e., it assumes that the carcinogenic potency of benzene increases with age. The absolute risk model assumes that the increased risk of benzene-related leukemia mortality is the same at all ages, given equal doses. See id. at 16.

increased risk of leukemia mortality after a working lifetime exposure to 10 ppm benzene is 15/1,000, while under a relative risk model, it is 29/1,000.186/ The comparable risk values after a working lifetime exposure to 1 ppm benzene were found to be 1.5/1,000 under the absolute risk model and 3/1,000 under the relative risk model.187/

The weighted cumulative exposure models favored by Crump and Allen do not include data from the Wong Study, since weighted cumulative exposure data were not available from that study. As discussed at pages ___ - ___ above, the Wong Study is not appropriate for use in performing quantitative risk assessments for benzene. Accordingly, the fact that the risk estimates based on the weighted cumulative exposure model do not reflect data from the Wong Study makes those estimates more reliable than estimates which include the Wong data.

Even if the Wong Study were included, however, the risk estimates would not be significantly different, as long as the unexposed workers from the study are excluded or assumed to have a normal leukemia experience (i.e., to have an SMR for leukemia mortality of 100).188/ Moreover, as discussed above,189/ Dr.

186/ See id., Table 21.

187/ See id.

188/ Compare Crump Report, Table 12, Data Set IV (dose-response slope of 0.13 for the Rinsky and Ott studies

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Frank Carlborg found that a quantitative risk assessment of data from the Wong Study would produce an estimated increased leukemia risk of approximately 1-2/1,000 after 45 years of occupational exposure to 1 ppm benzene, a level of risk that is almost precisely the same as the increased risk estimated by Crump and Allen under the absolute risk-weighted cumulative exposure model.

The increased risk of 1.5-3/1,000 after a lifetime exposure to 1 ppm benzene estimated by Crump and Allen also is in close agreement with the most recent risk estimate for benzene developed by EPA's Carcinogen Assessment Group ("CAG"). In that document, CAG developed a composite unit risk estimate of 0.026/ppm (i.e., an increased risk of 26/1,000) after 70 years of continuous exposure to 1 ppm benzene.190/ This continuous 70-year lifetime exposure risk estimate equates to an increased risk of slightly under 3/1,000 for 40 years' occupational exposure to 1 ppm benzene.191/ This composite CAG risk

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alone), with id., Data Set VIII (dose-response slope of .016 for the Rinsky, Ott and Wong studies assuming SMR=100 for unexposed workers in the Wong Study).

189/ See p. ___ n._, supra.

190/ See EPA Carcinogen Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985 at 22-23.

191/ The increased risk of 0.026 which CAG estimates for 70 years' continuous exposure to 1 ppm benzene can be translated

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assessment, which is in such close agreement with the weighted cumulative exposure model estimates of Crump and Allen, gives equal weight to cumulative dose and weighted cumulative dose data, as well as to relative and absolute risk models.192/

Thus, the best available evidence193/ in this proceeding indicates that, taking a conservative approach to risk assessment, the increased risk of leukemia after a working lifetime exposure to 1 ppm benzene would be in the neighborhood of 1-3/1,000. It must be emphasized, however, that, for a variety of reasons, this estimate almost certainly overstates the true risk -- if, indeed, any risk whatsoever exists at exposure levels below 10 ppm.

First, as discussed above, no increased risk of benzene-related leukemia has been demonstrated at levels of 10 ppm and below.194/ To the contrary, as shown in the Comments of

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into a risk from 40 years' occupational exposure by multiplying by a factor of 0.111 to account for the fact that a worker is exposed only 8 hours per day, approximately 210 days per year for 40 years. Thus, 210/360 x 8/24 x 40/70 = .111. Multiplying 0.026 x 0.111 = 0.0029 -- or an increased risk of 2.9/1,000 after 40 years of occupational exposure to 1 ppm benzene.

192/ See EPA Carcinongen Assessment Group, Interim Quantitative Cancer Unit Risk Estimates Due to Inhalation of Benzene, February 15, 1985 at 22.

193/ See Section 6(b)(5) of the Occupational Safety and Health Act of 1970 (occupational health standards should be set "on the basis of the best available evidence").

194/ See pp. ___ - ___, supra.

Exxon Company, U.S.A. submitted in this proceeding, epidemiological studies of workers exposed to low levels of benzene (including a recently published study of 21,698 employees and retirees of the Exxon Company, U.S.A.) indicates that no increased risk of leukemia exists at low exposure levels.

The absence of a demonstrated increased risk of leukemia at exposures of 10 ppm and below is consistent with the possibility that there is a threshold for benzene-related leukemia above 10 ppm. Although OSHA has presumed, as a matter of policy, that no threshold exists for the carcinogenic effects of benzene, the fact is, as Dr. Bernard Goldstein points out, that a "major question" is whether the dose-response for benzene-related leukemia is "in fact, a linear relationship extrapolating back to zero . . . or whether there [is] some no effect level, which is inadequate to cause leukemogenesis."195/ EPA also has recognized that the question whether the non-threshold presumption should be applied to benzene "is not without uncertainty."196/

Dr. Robert Snyder points out that "[t]he data strongly indicate that one or more metabolites of benzene mediate benzene

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195/ B. Goldstein, "Clinical Hematotoxicity of Benzene," in Mehlman, ed., Carcinogenicity and Toxicity of Benzene at 57.

196/ Response to Comments on the Regulation of Benzene, 49 Fed. Reg. 23478, 23479, col. 3 (June 6, 1984).

toxicity."197/ He goes on to explain:

> Because of the need for a complex metabolic intervention . . . the concentration of benzene necessary to produce these [toxic] changes [and binding to DNA] must be real and measurable. In other words, there must be a threshold level of benzene which can be metabolized to a toxic metabolite. Enzyme kinetics teach us that the lower the concentration of substrate the slower the reaction and, below critical levels, reaction rates may be insufficient."198/

Dr. Snyder concludes that the "empirical evidence does not permit us to reach firm conclusions one way or the other" regarding the existence of threshold levels for carcinogens."199/ However, he points to a variety of biochemical and molecular factors which support the hypothesis that a carcinogenic threshold for substances such as benzene may indeed exist. In Dr. Snyder's words,

> it is apparent that the process of carcinogenesis can be interrupted at several stages both during initiation and promotion. It is reasonable, therefore, to assume that each of these stages represents a threshold level for carcinogenesis. Thus, there are many threshold levels for carcinogenesis rather than a single threshold. Moreover, these thresholds for carcinogenesis may be different from the thresholds for clastogenic effects of the same chemical.200/

197/ Snyder Review at 22.

198/ Id. at 31.

199/ Id.

200/ Id. at 33.

In the case of benzene, there are some special reasons to suspect that a carcinogenic threshold may exist. For one thing, as EPA points out, "the weight of evidence as a whole [makes] it . . . evident that benzene may exert its carcinogenic effect via non-genotoxic mechanisms."201/ Moreover, as Dr. Snyder reminds us, "an underlying question which has yet to be adequately dealt with is:

> Must frank bone marrow damage preclude a leukemogenic response to benzene? . . . If aplastic anemia or other severe bone marrow damage is a precursor to benzene-induced leukemia it would appear that reasonably high exposure to benzene, i.e., doses high enough to produce severe bone marrow depression, would be necessary to induce leukemia, even tehough some clastogenic responses could be produced at lower doses.202/

As the preceding discussion shows, there is good reason to believe that benzene exposures at levels of 10 ppm and below will not be associated with any increased risk of leukemia. But even if they were, the risk existing at exposure levels in the neighborhood of 1 ppm is likely to be considerably lower than the value of 1.5-3/1,000 estimated by Crump and Allen. Crump and

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201/ EPA, Draft Criteria Document for Benzene (February 1984) at XI-16.

202/ Snyder Review at 34. In this regard, Dr. Bernard Goldstein makes the point that "[i]f leukemia is a conseqeunce solely of significant pancytopenia, then a more stringent standard [than the current 10 ppm lmit] is unnecessary." B. Goldstein, "Clinical Hematotoxicity of Benzene," in Mehlmen, ed., Carcinogenicity and Toxicity of Benzene at 57.

Allen used a linear model to extrapolate risks to exposure levels of 1 ppm. However, it is far from clear that the dose-response for benzene-related leukemia is linear, particularly at dose levels in the range of 1-10 ppm.

Linear extrapolation models were developed to reflect the apparent dose-response relationship observed in radiation carcinogenesis. Chemical carcinogenesis, however, differs from radiation carcinogenesis in several significant respects, including the following:

- Chemical agents are inhibited by physical transport barriers, while radiation reaches cell nuclear material without such inhibitions.

- Many chemical agents, such as benzene, require metabolic activation; radiation does not.

- In contrast to radiation, the body has various detoxification, excretion and repair processes that operate on chemical agents. As OSHA acknowledges, a linear model "cannot take into account repair, detoxification reactions and metabolic activation."203/

- The high level of energy ion radiation can break chemical bonds; by contrast, chemical reactions are modulated by the limited molecular energies available from the reactants to overcome activation energy.

Thus, radiation derived extrapolation models reflecting linearity may not be appropriate for chemical carcinogenesis even if they accurately reflect the effects of radiation. However,

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203/ 50 Fed. Reg. 50512, 50530, col. 3.

questions have been raised as to whether linear models are appropriate even in the case of radiation when low doses are involved. Thus it has recently been reported that at radiation doses below 10 rad., the carcinogenic effect per rad. diminishes markedly, thus throwing into question assumptions of low dose linearity even in the case of radiation.204/

In short, the assumption of low dose linearity for benzene-related leukemia may not be well founded. As EPA acknowledges, there are data suggesting that dose-response curves for carcinogens are nonlinear, and the data for benzene "do not conclusively support either [a linear or nonlinear] hypothesis."205/ Dr. Bernard Goldstein also points to the assumption of low-dose linearity as one of the major questions and difficulties with risk assessments for benzene.206/ And Dr. Irving Kessler observes that a no-threshold linear model for benzene-related leukemia "is not very likely."207/

204/ See Kohn and Fry, "Medical Progress -- Radiation Carcinogenesis," 310 New Eng. J. Med. 504-511 (1984).

205/ Proposed Withdrawal of Proposed Benzene Standards, 49 Fed. Reg. 8386, 8387, col. 3 (March 6, 1984).

206/ See B. Goldstein, "Clinical Hematotoxicity of Benzene," in Mehlman, ed., Carcinogenicity and Toxicity of Benzene at 55, 57.

207/ March 8, 1983 Letter of Irving I. Kessler, M.D., to R. Leonard Vance, Ex. 137. See also December 13, 1982 letter of Bruce W. Karrh, M.D. to Leonard Vance, Ex. 137.

Further evidence for non-linearity in the dose-response curve for benzene-related leukemia at levels between 1 and 10 ppm is provided by the most recent update of the Pliofilm workers study. After analyzing additional exposure and mortality information for an expanded Pliofilm cohort, the authors of that study concluded that "the association between cumulative benzene exposure and leukemia" was explained best by a log-linear model, under which the incidence of benzene-induced leukemia decreases exponentially between exposure levels of 10 ppm and 1 ppm.208/ Under this analysis, the increased leukemia risk would decline by a factor of 130, rather than by a factor of 10, as exposures decline from 10 ppm to 1 ppm.209/ If the dose-response curve for benzene-related leukemia does follow this particular log-linear relationship between 10 ppm and 1 ppm, the increased risk of 1.5-3/1,000 at 1 ppm estimated by Crump and Allen could be high by more than an order of magnitude, and the true risk might be in the neighborhood of 0.1-0.3/1,000. Of equal importance is the fact that, based on the latest update of the Rinsky study, the additional health benefit of reducing exposures below 1 ppm would be negligible.210/

208/ Rinsky, et al., "Benzene and Leukemia: Epidemiological Risk Assessment," August 9, 1985 (Ex. 176A) at 2, 18.

209/ Id. at 20.

210/ Thus, while the study estimates a 13,000 percent reduction in risk from 10 ppm to 1 ppm (a reduction in the odds ratio from 221.4 to 1.7), it predicts only a 38% reduction in risk (from 1.7 to 1.06) as exposure are reduced form 1 ppm to 0.1 ppm. See id. at 20.

In sum, Crump and Allen's assumption of low-dose linearity was extremely conservative. They themselves recognize that their estimates based on linear models "should be regarded [as] 'plausible upper bounds' to the risk," particularly at a dose level of 1 ppm.211/ EPA has noted that use of a linear model may overestimate benzene-related leukemia risks substantially -- perhaps by as much as one or two orders of magnitude.212/ The most recent update to the Rinsky study, as discussed above, suggests that this may indeed be the case with respect to benzene exposures in the neighborhood of 1 ppm. Thus, at the very least, the assumption of linearity may have had an important effect on the risk estimates for exposure to 1 ppm benzene.213/ Since "the risks under non-linear models decrease rapidly with decreasing dose,"214/ the fact that Crump and Allen used only linear models means that the risks they have estimated at exposures of 1 ppm are on the high side.

Furthermore, it is important to bear in mind that the risk assessments performed by Crump and Allen, as well as the one

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211/ Crump Report at 35.

212/ See Proposed Withdrawal of Proposed Benzene Standards, 49 Fed. Reg. 8386, 8387, col. 3; Proposed Recommended Maximum Contaminant Levels for Volatile Synthetic Organic Chemicals in Drinking Water, 49 Fed. Reg. 24330, 24348, col. 2 (June 12, 1984).

213/ See Crump Report at 8.

214/ Id. at 34.

performed by White, et al., assume that members of the cohorts that were studied did not have any other occupational exposure to benzene apart from their experience in the work operation being studied. If, for example, workers in the Pliofilm cohort in the Rinsky Study worked in tire building operations as well, they might have had significant additional benzene exposure both through inhalation and as a result of dermal absorption.215/ Needless to say, if the SMRs in the Rinsky study really were associated with significantly higher cumulative benzene exposures than Crump and Allen assumed (because of additional exposures during tire building), the dose-response relationship and resulting risks would be much lower than Crump and Allen calculated.

Finally, it is important to bear in mind that the leukemia risk of 1.5-3/1,000 estimated by Crump and Allen is a risk projected to occur at age 60, after 40 years of occupational exposure to 1 ppm benzene have been accumulated. Increased risk levels would be smaller at earlier stages of the worker's career.

215/ OSHA estimates that approximately 32 mg of benzene per day could be absorbed through the skin as a result of building tires with a solvent containing 0.5 percent benzene. See 50 Fed. Reg. 50512, 50528, col. 3 - 50529, col. 1. OSHA also estimates that 8-hour exposure to 1 ppm benzene results in an intake through inhalation of 14 mg of benzene. See id. at 50529, col. 1. On that basis, if members of the Rinsky cohort also had worked in tire building operations and if, for example, the percentage of benzene in the solvents used during the 1940s and 1950s were 5 percent, the potential daily intake of benzene through dermal absorption alone would have been 320 mg, or the equivalent of an 8-hour inhalation exposure to 22 ppm benzene (320 mg divided by 14 mg = 22 ppm).

Moreover, a worker who has attained 60 years of age would be subject to significant risks from a large number of competing causes of death. This further emphasizes the speculative and hypothetical nature of the risks estimated by Crump and Allen, as well as in all of the other risk assessments that OSHA has considered.

E. Some Perspective on the Significance of the Risk.

In the preceding pages, we have shown that, using a variety of conservative assumptions, the increased risk resulting from a working lifetime exposure to 1 ppm benzene would be no higher than 1.5-3/1,000. Moreover, because

- the Rinsky cohort may have had additional occupational exposures to benzene that are not reflected in the underlying epidemiological studies,
- there may well be a threshold for benzene-related leukemia above 10 ppm, and
- in any event, there is good reason to believe that the dose-response relationship for benzene-related leukemia is non-linear in the dose range of 1-10 ppm,

the risks estimated by Crump and Allen on the basis of non-threshold linear models are likely to be greatly overstated. The best available evidence suggests that, if any risk of benzene-related leukemia exists at all at exposure levels in the neighborhood of 1 ppm, the increased risk after a working lifetime of such exposure is likely to be well below 1/1,000.

We do not believe that a hypothetical occupational risk of this size should be considered significant, particularly since the true risk, if any, is likely to be substantially lower. As OSHA recognizes, occupations such as firefighting and mining involve increased mortality rirks in the neighborhood of 20-30/1,000 employees, while the lifetime mortality risk for manufacturing occupations overall is 2.7/1,000.216/ Even in service employment, the increased mortality risk is 1.62/1,000.217/ An increased mortality risk of approximately 1/1,000 after a working lifetime exposure to 1 ppm benzene compares favorably to mortality risks in these other occupations. It also is instructive to note that the increased cancer mortality risk of 1/1,000 is only 0.6 percent of the background lifetime risk of fatal cancer in the United States.218/

In sum, whatever may be said about the potential increased risk of leukemia mortality after a working lifetime exposure to 10 ppm benzene, there simply is no basis for concluding that the hypothetically increased risk of 1/1,000 or less after a working lifetime exposure to 1 ppm benzene is significant. Given the enormous uncertainty surrounding the

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216/ See 50 Fed. Reg. 50512, 50539, col. 1.

217/ Id.

218/ See Radionuclide Standards, 49 Fed. Reg. 43906, 43910, col. 3 (October 31, 1984) (background lifetime risk of cancer mortality in the U.S. is about 165/1,000).

estimation of any increased risk of leukemia at benzene exposures in the neighborhood of 1 ppm, OSHA should studiously avoid any suggestion that ~~the~~ a significant health risk that would ~~remain~~ exist under its proposed standard ~~would still be significa~~nt.219/

III. Feasibility Issues

OSHA's preliminary determination that the proposed standard would be feasible in the petrochemical industry is based on a report prepared for OSHA by JRB Associates, entitled "Technological Feasibility and Economic Impact Study of Alternative Standards for Benzene" (Ex. 153) (hereinafter referred to as the "JRB Report"). The JRB Report, as supplemented by an Addendum prepared by Meridian Research, Inc. (Ex. 155), provides a profile of the industry and of current employee exposures, identifies the assumed baseline controls and additional controls that JRB asserts would be sufficient to achieve compliance with a 1 ppm standard, estimates the cost of compliance, and assesses the impact that such costs would have on the industry, its customers, and employees. In the following pages, we discuss various of these points and show that JRB's analysis is flawed or incomplete

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219/ The fact that of 16 countries listed in the JRB Report, only 2 (Switzerland and the USSR) have established permissible exposure limits or guidelines below 5 ppm further supports the view that no significant health risk exists at benzene concentrations of 1-5 ppm. See JRB Report, Table 1-4. It should be noted that 8 of the 16 countries are reported by JRB to have permissible exposure limits of 10 ppm or higher. Id.

in a variety of respects and that OSHA's preliminary conclusions regarding feasibility are, therefore, inadequately supported and subject to serious question.

A. Profile of Current Petrochemical Industry Operations

Table 3-3 in the JRB Report shows the number of petrochemical units using benzene as a feedstock by type of major benzene derivative or coproduct produced. According to the table, there are a total of 117 such petrochemical units, which JRB divides into seven categories. We have examined Table 3-3 and the accompanying notes and find that it does not present an accurate profile of the petrochemical industry today. CMA Table 3-3 below shows JRB's profile and a corrected profile prepared by CMA.

CMA Table 3-3

Number of Petrochemical Units Using Benzene as a Feedstock
By Type of Major Benzene Derivative or Coproduct Produced

Benzene Derivative/Coproduct	Number of Petrochemical Units	
	JRB	CMA
Ethylene	46	37
Ethylbenzene/Styrene	16	10
Alkylbenzene	5	5
Nitrobenzene/Aniline	8	3
Cyclohexane	11	8
Monochlorobenzene	5	4
Cumene/Phenol	26	12
Other	0	2
Total Number of Units	117	81

The explanation for CMA's corrections is as follows.

1. Ethylene Units -- JRB assumed that there are 35 ethylene-producing facilities in the United States, with an average of 1.3 ethylene units per facility.220/ CMA has gathered information on each individual ethylene facility. We find that rather than the 35 ethylene-producing facilities asssumed by JRB, there presently are only 31. The ethylene units at the Arco facility at Wilmington, California, the Cities Service facility at Lake Charles, Louisiana, the Koch facility at Corpus Christi, Texas, and the Texaco facility at Port Neches, Texas, have been shut down.221/ Seven of the remaining 31 facilities have two

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220/ See JRB Report, Table 3-3, Note a.

221/ When we use the term "shut down," we mean either that the unit has been dismantled or that there are no current plans to place it back in operation.

operating units each,222/ thus bringing the total number of ethylene units to 38.

2. Ethylbenzene/Styrene Units -- Benzene is present in ethylbenzene units, where benzene and ethylene are combined to make ethylbenzene. Virtually no benzene is present in styrene units, where ethylbenzene is dehydrogenated to make styrene. Therefore, in a styrene plant where ethylbenzene is supplied as a feedstock rather than being manufactured, occupational exposure to benzene will be minimal.223/ JRB assumes that benzene is used at all ethylbenzene and styrene plants and that all of the plants are in operation and have one unit per facility. These assumptions should be corrected as follows: Five of the ethylbenzene units do not use benzene.224/ The ethylbenzene and styrene units at two of these plants (American Hoechst at Baton Rouge, Louisiana and U.S. Steel at Houston, Texas) have been shut down. The Cosmar facility at Carville, Louisiana has two units rather

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222/ These facilities are Amoco at Chocolate Bayou, Texas; Arco at Channelview, Texas; Dow at Plaquemine, Louisiana; DuPont at Chocolate Bayou, Texas; Tennessee Eastman at Longview, Texas; Phillips Petroleum at Sweeny, Texas; and Shell at Norco, Louisiana.

223/ See JRB Report at D-18.

224/ These are Charter at Houston, Texas; Conoco at Chocolate Bayou, Texas; and Tenneco at Chalmette, Louisiana (all of which recover "native" ethylbenzene rather than synthesizing ethylbenzene from benzene); Arco at Beaver Valley, Pennsylvania; and Dow at Midland, Michigan (both of which are styrene units which use ethylbenzene as a feedstock.)

than one. The net effect of these changes is a decrease of six ethylbenzene/styrene units from the number assumed by JRB.

3. Nitrobenzene/Aniline -- Three of the nitrobenzene/aniline units reflected in JRB's Table 3-3 have been shut down.225/ A fourth, U.S. Steel at Haverhill, Ohio, uses phenol rather than nitrobenzene. A fifth, the second Mobay unit at New Martinsville, West Virginia, produces aniline as a by-product in the production of iron oxide. No benzene is present at that unit. This results in a net reduction of five units industry-wide.

4. Cyclohexane -- Three of the cyclohexane units included in JRB's calculation (American Petrofina at Big Spring, Texas; CORCO at Ponce, Puerto Rico; and Exxon at Baytown, Texas) have been shut down.

5. Monochlorobenzene -- One of the monochlorobenzene units assumed by JRB (Dow at Midland, Michigan) has been shut down.

6. Cumene/Phenol -- Benzene is present in cumene units, where benzene and propylene are combined to make cumene. No benzene is present in phenol units, where cumene is reacted to

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225/ These are American Cyanamid at Willow Island, West Virginia; DuPont at Gibbstown, New Jersey; and one of the Mobay units at New Martinsville, West Virginia. The DuPont unit may restart some time in the future.

make phenol. Three of the cumene facilities included in JRB Table 3-3 have been shut down.226/ In addition, eleven of the facilities included in JRB's cumene/phenol listing are phenol plants that use cumene as a raw material. No benzene is present in these plants.227/

7. Other -- In addition to the feedstock categories listed by JRB, two other plants use benzene and have been added to the CMA total.228/

B. Employee Exposure Profile

1. Number of Employees Exposed to Benzene (and Person-Years of Benzene Exposure) in the Petrochemical Industry

JRB estimates that 12,242 employees are exposed to benzene in the petrochemical industry.229/ This estimate

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226/ These are Monsanto at Chocolate Bayou, Texas; Chevron at El Segundo California; and Union Carbide at Penuelas, Puerto Rico.

227/ These are Allied Chemical at Frankfort, Pennsylvania; Diamond Shamrock at Tuscaloosa, Alabama; Dow (Oyster Creek Division) at Freeport, Texas; Ferro Corporation at Sante Fe Springs, California; General Electric at Mt. Vernon, Indiana; Georgia Pacific at Plaquemine, Louisiana and Bound Brook, New Jersey; Koppers at Follansbee, West Virginia; Merichem Company at Houston, Texas; U.S. Steel at Haverhill, Ohio; and Stimson Lumber at Anacortes, Washington.

228/ These are Koppers at Petrolia, Pennsylvania (resorcinol) and Monsanto at Anniston, Alabama (biphenyl).

229/ See JRB Report at 3-16.

(assumed to represent person-years of benzene exposure) is used by JRB to calculate the alleged benefits (in terms of reduced leukemia mortality) that might be expected from establishing alternative PELs. JRB's estimates of risk reduction benefits are seriously flawed for a variety of reasons discussed in these Comments. For the moment, we wish to focus only on one very simple but fundamental reason -- i.e., JRB has vastly overestimated the person-years of benzene exposure of employees in the petrochemical industry.

It is not unreasonable to estimate that 12,242 petrochemical workers are assigned for at least some portion of the year to positions in which there is exposure to benzene. The basic flaw in JRB's analysis (as it applies to the calculation of risk reduction benefits) is the implicit assumption that each of these 12,242 employees is assigned to a post where there is exposure to benzene throughout the year. This assumption is incorrect.

The most logical way to estimate worker exposure to benzene in the petrochemical industry is to:

(1) identify the types of benzene-exposed job assignments that are found at various types of petrochemical units and the number of employees performing that job assignment in the plant on any one shift;

(2) where applicable, multiply the value developed in step (1) times the number of shifts needed to provide round-the-clock (plus vacation) coverage of the job assignment;

(3) sum the totals derived in step (2) for each job assignment at the particular type of petrochemical plant;

(4) multiply the plantwide value developed in step (3) by the number of plants of that type in the industry;

(5) sum the plant category totals to develop a total for the petrochemical industry as a whole;

(6) add the number of benzene-exposed workers in any special job category (i.e., on-site distribution) not included in the foregoing total.

This calculation is presented in Table I below.

As can be seen from Table I, approximately 4,400 employees would be required to provide full-time coverage for the various benzene-exposed work assignments in the petrochemical industry on any given day.230/ Consequently, there are approximately 4,400 annual aggregate person-years of benzene exposure (at varying concentrations) among employees in the petrochemical

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230/ Indeed, this probably is an overestimate, since it treats vacation time as though it adds an additional shift.

Table I

Estimate of Number of Employees Potentially Exposed to Benzene in the Petrochemical Industry (Assuming the Employees Are Assigned To the Benzene-Exposed Positions Throughout the Year)

Type of Unit	Number of Process Positions	Number of Employees Assigned to Process Position*/	Number of Support **/ Employees	Total Benzene-Exposed Employees Per Unit (Process Plus Support)	Number of Plants	Total Benzene-Exposed Employees
Ethylene Units	1	5	15	20	~~38~~	~~760~~
Benzene Derivative Plants	2	10	15	25	~~48~~ 44	~~1,200~~ 1,100
Hydro-dealkylation Units	2	10	15	25	16	400
Pygas (Hydrofining) Units	2	10	15	25	13	325
B/T/X (Extraction) Units	6	30	15	45	35	1,575
TOTAL (Where Applicable)					~~150~~ 145	~~4,725~~ 4,705
Additional Employees Assigned to Distribution***/						~~400~~
GRAND TOTAL						~~5,125~~ 4,398

*/ This assumes that 5 employees are needed to provide round-the-clock coverage on each process position plus vacations.

**/ The breakdown of support employees is assumed to be as follows:

Laboratory	= 3
Wastewater Treatment	= 4
Maintenance	= 8
Total Support	= 15

***/ The distribution estimate is limited to employees working in the plant to hook up barges, rail tank cars, and tank trucks. The estimate assumes two distribution workers for each ~~petrochemical~~ benzene derivative unit -- i.e., 2x(35+48) = ~~166~~. The distribution estimate does not include workers employed on outside terminals or barges, which would add approximately 270 employees to the total.

industry. This figure, 4,400 person-years of exposure (rather than the 12,242 person-years of exposure assumed by JRB), would be the approriate value to use in any computation of potential risk reduction benefits resulting from application of alternative PELs to the petrochemical industry. Since JRB utilizes the figure of 12,242 in its calculation of risk reduction benefits,231/ its estimate of benefits is high by a factor of three for that reason alone.

For purposes of computing costs, however, the figure of 12,242 employees is appropriate. Although there are approximately 4,400 benzene-exposed job assignments to be staffed on a full-time basis throughout the year, many companies make a practice of rotating employees into and out of these benzene-exposed positions for portions of the year. (This contributes to job satisfaction and creates a pool of employees with a broad base of knowledge and experience who can be called upon to cover a variety of job assignments when employees regularly assigned to particular positions are absent from work.) As a result, 12,242 is a reasonable estimate of the total number of employees who have benzene-exposed job assignments for some non-trivial period (e.g., more than 30 days) during the course of a year.

231/ See JRB Report, Tables 3-20 through 3-23.

Although these 12,242 employees would accumulate no more aggregate person-years of exposure than 4,400 employees assigned to these positions throughout the year, the cost of implementing the standard for 12,242 employees is much greater than the cost of implementing the standard for 4,400 employees. Thus, engineering controls at these plants will cost the same regardless of whether one employee is assigned to the benzene-exposed position throughout the year or three employees rotate through that position during the course of the year. At the same time, since each of these employees would have to be provided with medical surveillance and training under the standard, many of the annual costs of the standard will triple when applied to 12,242 rather than 4,400 employees.

In short, 4,400 is the proper figure to use when computing potential benefits of the standard, while 12,242 is an appropriate figure to use when computing costs.

2. Current Exposure Levels of Petrochemical Employees

Based on information provided by the American Petroleum Institute ("API"), JRB has calculated the number of petrochemical workers who allegedly are exposed to various 8-hour TWA benzene concentrations in six exposure intervals ranging from 0-.01 ppm at one extreme to 10+ ppm at the other extreme.232/ JRB's

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232/ See JRB Report, Table 3-8.

estimate shows 5,460 petrochemical workers exposed between 0 and .1 ppm; 4,064 workers exposed between .11 and .5 ppm; 1,224 workers exposed between .51 and 1 ppm; 1,212 workers exposed between 1.1 and 5 ppm; 159 workers exposed between 5.1 and 10 ppm; and 122 workers exposed at or above 10 ppm.233/ Several points must be made regarding JRB's estimate.

First, as discussed at pages ___-___ above, the total number of employees exposed at the various concentration levels is greatly overstated if it is interpreted to s employees are exposed to benzene at these levels throughout the year. Rather, it reflects employees exposed to benzene for at least some portion of the year, possibly a matter of just a few months.

Second, the percentage distribution of benzene exposure levels utilized by JRB is derived from information provided by API rather than from information provided by CMA. This difference is significant, since the information provided by CMA shows that the percentage of chemical industry workers exposed to an 8-hour TWA greater than 1 ppm is more than twice as high as the comparable percentage provided by API.234/

Third, the exposure information collected from CMA (and, presumably, the exposure information collected from API as

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233/ Id.

234/ See JRB Report, Table 3-7.

well) cannot be relied upon to establish fine distinctions among exposure levels below 1 ppm. The current OSHA Benzene Standard establishes a PEL of 10 ppm. Exposure measurements taken to ensure compliance with a PEL of 10 ppm need not be calibrated for a high degree of accuracy at an exposure level of 1 ppm or below. And, in fact, the experience of many CMA companies indicates that benzene monitoring methods (designed to ensure compliance with a PEL of 10 ppm) have not historically been calibrated to record accurately and reproducibly benzene concentrations of less than 1 ppm in the workplace. Accordingly, we are extremely skeptical about supposed distinctions reported in exposure levels below 1 ppm.

Fourth, JRB's exposure profiles are based on information that was solicited from various associations and individual companies. Our understanding is that the data provided to OSHA and JRB reflect the prevailing or average 8-hour TWAs for the various operations as to which information was reported.235/ These average or prevailing exposure levels indicate only that benzene exposures in the identified operations fall, on average, within the exposure range reported to OSHA or JRB.236/ This does not mean that the average 8-hour TWA is never exceeded, or even

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235/ See, e.g., Declarations of _____, _____, _____, and _____, submitted herewith as Appendices __-__.

236/ See id.

that such exceedances occur only infrequently. Rather, it means that some exposure measurements will exceed this value while others will fall below it, with the various measurements averaging out to the reported level. Thus, a report that the prevailing 8-hour TWA for 70 percent of a company's benzene-exposed workers is less than 1 ppm should not be interpreted to mean that the company is presently complying with the equivalent of a 1 ppm PEL for those employees.237/ While their average 8-hour TWA exposure may be less than 1 ppm, occasions on which the 8-hour TWA exceeds 1 ppm may not be infrequent.

In short, achieving a prevailing or average 8-hour TWA of 1 ppm is very different from complying with a mandatory PEL of 1 ppm, since the latter implies that on whatever day an OSHA inspector may choose to take measurements, the 8-hour TWA would be found not to exceed 1 ppm. To ensure that exposures are below a specified PEL 95 percent of the time, a company probably would have to reduce average benzene exposure levels to less than one-half of the PEL, a point that OSHA itself appears to recognize.238/ Consequently, it is a grave misconception to assume,

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237/ See id.

238/ See 50 Fed. Reg. at 50552, col. 3 ("where exposure measurements are above one-half of the permissible exposure limit, . . . the employer cannot be reasonably confident that the employee may not be overexposed"). Examples of 8-hour TWA data sets averaging approximately 0.5 ppm which, under a statistical sampling program developed by Du Pont, would not meet a PEL of 1 ppm 95 percent of the time are provided in Appendix ___, along with a paper describing the Du Pont statistical procedure.

as JRB does, that an employer whose workers are exposed to benzene concentrations of 1 ppm or below on average would not have to implement any additional controls in order to comply with a PEL of 1 ppm. What average benzene measurements below 1 ppm can be taken to imply in many cases is that the employer has a 95 percent assurance that a PEL of 2 ppm is not being exceeded.239/

Because of this misconception regarding the meaning of exposure information collected by JRB, statements in the JRB Report to the effect that 85 percent of petrochemical units have already achieved 1 ppm as an 8-hour TWA exposure level240/ or that only 63 percent would incur additional compliance costs to achieve a PEL of 0.5 ppm241/ simply are not reliable or credible.

239/ See NIOSH comments on a possible short-term exposure limit for ethylene oxide, 50 Fed. Reg. 64, 70 (January 2, 1985) ("As a practical matter, an employer would have to maintain concentrations in the vicinity of 0.5 ppm in order to ensure that an 'exceedance [of 1 ppm] due to random variation' had not occurred."). See also Liedel, et al. (NIOSH), Exposure Measurement, Action Level and Occupational Environmental Variability (1975). Cf. EPA Guideline Series, Control of Volatile Organic Compound Leaks from Synthetic Organic Chemical and Polymer Manufacturing Equipment (EPA-450/3-83-006, March 1984) at 3-12 ("if a random annual inspection indicated that no more than two percent of valves are leaking, the probability is greater than ninety-five percent that an average of one percent of valves leaking is actually being achieved in practice"). Depending on the nature of the work operation and the number and distribution of measurement data points, long-term average exposures may have to be maintained at a level considerably below one-half of the PEL in order to provide 95 percent assurance that the PEL will not be exceeded on a random inspection basis.

240/ See JRB Report at 4-20.

241/ See JRB Report at 5-32.

They result in a gross underestimate of the number of petrochemical facilities that would have to implement additional engineering and work practice controls in an effort to comply with a PEL of 1 ppm or below. Moreover, this misconception has led JRB to reach facile conclusions regarding the feasibility of a 1 ppm standard that the exposure information, when properly understood, does not warrant.

C. Inventory of Benzene Emission Sources at Petrochemical Facilities and Identification of Job Assignments Where Use of Respirators May Be Needed To Comply with the Proposed Standard

JRB identifies four principal sources of benzene exposure at petrochemical facilities:

- Equipment leaks
- Process sampling
- Wastewater collection systems
- Loading of railcars, tank trucks, and barges.242/

In evaluating the feasibility of alternative PELs, JRB identifies what it believes to be appropriate controls for these benzene emission sources and calculates compliance costs based on the assumption that these are the only controls necessary to achieve

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242/ See JRB Report at 4-20.

the respective PELs. On the basis of this analysis, JRB concludes that a PEL of 1 ppm can feasibly be achieved through the use of engineering and work practice controls in the petrochemical industry, except for those employees exposed during barge loading or in maintenance operations. In both of these latter cases, JRB concludes that "respirators are required to achieve the 5.0 and 1.0 ppm alternative PEL's . . . ."243/

While it is correct that respirators would be required to achieve a PEL of 1 ppm in barge loading and maintenance operations, JRB fails to identify several other important benzene emission sources or tasks which, either regularly or from time-to-time, would require the use of respirators to achieve a PEL of 1 ppm or a short-term exposure limit ("STEL") of 5 ppm averaged over 15 minutes.244/ Moreover, efforts to reduce benzene emissions from these additional sources through the use of engineering and work practice controls would significantly increase the costs of complying with the standard beyond the amounts estimated by JRB. These additional benzene emission sources are as follows:

243/ See JRB Report at 4-2.

244/ The need to utilize respirators might not be limited to the workers directly performing the specific activity but might encompass other employees who are present in the vicinity of the activity as well.

1. Instrument Maintenance and/or Calibration -- Process instrument maintenance and/or calibration is perhaps the most difficult operation in which to control benzene exposures; at the same time, it is an operation which is critical to the proper functioning of the plant. Although JRB does not identify instrument maintenance and/or calibration as an important source of benzene exposure, the fact is that in most facilities this activity may potentially create the highest benzene exposures in the plant. And the activity will affect not only the instrument technician, but other employees who have to be present in the area as well. Moreover, in contrast to equipment maintenance operations, instrument maintenance must take place while the process continues to run; consequently, clearing the benzene out of the equipment prior to opening for maintenance or calibration of the instrument (e.g., pH probe replacement) is not possible.

In some cases, use of pump-loops from reactors to instruments will allow isolation and clean-out prior to calibration or maintenance, but this approach is not always possible. Where pump-loops and other specialized systems can be utilized, use of respirators may not be necessary; however, JRB did not evaluate or include costs for these specialized systems in its feasibility analysis. In those cases where such specialized systems cannot be used, respiratory protection probably would be required to comply with a PEL of 1 ppm or a STEL of 5 ppm, just as it is in regular maintenance and loading

operations.245/ Moreover, since instrument maintenance and calibration is an intermittant task which should not require hard physical labor, it is an assignment in which respirators can be used effectively and in which engineering controls generally would not achieve a significant reduction in overall employee exposure despite large implementation costs.246/

2. Intraplant Transfer of Benzene -- Although JRB recognizes the need for respirator protection during interplant transfers of benzene in barge loading, the Report fails to recognize the exposures associated with intraplant transfers of benzene -- such as the filling of day tanks, the "pigging" of common transfer lines, and other intraplant distribution operations which create fugitive and secondary emissions. Respirators may well have to be worn if benzene exposures of distribution operators and other employees involved in these intraplant transfer operations are expected to be kept below 1 ppm as an 8-hour TWA and 5 ppm as a 15-minute STEL. Benzene emissions in these intraplant transfers can be controlled through the use of dedicated piping. However, this would be very expensive, and the costs have not been taken into account in the JRB Report.

245/ At a PEL of 1 ppm, instrument technicians (and probably operating personnel in the immediate vicinity as well) might have to wear respirators to comply with the 8-hour TWA or with a 5 ppm STEL. At a higher PEL and STEL, respiratory protection probably would be required only for the instrument technician.

246/ Cf. 50 Fed. Reg. at 50512, 50558, col. 3.

3. Dewatering of Benzene Storage Tanks -- Drawing water from benzene storage tanks is a routine operation that potentially can result in significant fugitive and secondary emissions. Depending on the location of the tank, these emissions can affect benzene exposures of operating personnel as well as of workers actually performing the operation. Process requirements or environmental concerns require that the water, which is saturated with benzene, be removed from the tanks. Draining a saturated solution of benzene in water will result in emissions equivalent to those that arise when pure benzene is drained. To eliminate these emissions and the resulting exposures, interface controls and closed piping would be needed for each and every tank. Again, JRB has not factored this into its estimate of compliance costs.

4. Gauging of Tanks -- Another source of benzene emissions overlooked by JRB is the gauging of tanks, an operation that is necessary in order to document raw material usage and production quantities. The gauging is accomplished by inserting a calibrated measuring device into the tank through an open hatch, an operation which occurs approximately monthly in most facilities and creates exposures that might well exceed a 5 ppm STEL in the absence of respiratory protection. In many cases, there are no automatic guaging devices that can be depended on to provide reliable measurements. Even where such devices do exist, it would be very cost-ineffective to install them to control

exposures that occur only once a month, a point that OSHA itself has recognized.247/

5. Process Upsets, Spills and Vent Failures -- The spills and emissions that occur during process upsets and vent failures give rise to benzene emissions which are unplanned and initially uncontrolled. While these events are nonroutine in nature, the fact is that they do occur from time to time, and respirators are likely to be required when they do occur. We understand subsections (b) and (g)(1)(v) of the proposed standard to treat these events as "emergencies" under which use of respiratory protection to comply with the PEL is permitted. Such an emergency respirator use provision is critical and should clearly be included in the final standard regardless of what decision is made with respect to the PEL.

6. Process Venting -- Various process vessels and storage tanks at petrochemical plants must be vented from time to time. Process venting of a vessel or tank in which benzene is present contributes to benzene concentrations in the ambient air. Depending upon where the vessel is located, process venting may contribute to occupational exposure to benzene. JRB appears to have completely ignored such process emissions as sources of

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247/ See 50 Fed. Reg. 50512, 50558, col. 3, 50560, col. 3. In any event, JRB has not taken the costs of automatic guaging devices into account in computing the costs of the standard.

benzene within petrochemical facilities. The JRB Report does not evaluate whether these process vents would have to be controlled in order to comply with a 1 ppm standard and, if so, what the cost of such controls would be.

7. Regular Maintenance -- JRB acknowledges the difficulty of controlling exposure to benzene by maintenance workers and concludes that respirators will be required to maintain benzene exposures of maintenance workers below a PEL of 1 ppm. However, JRB fails to recognize that, during some maintenance operations, operating personnel also may have to be provided with respirators to comply with a 1 ppm standard. While major maintenance typically is performed on a campaign basis when the unit is shut down, routine maintenance occurs on an on-going basis and is performed while the unit is running. This routine maintenance will increase background concentrations of benzene and may require respirator use by the operating personnel as well as by the maintenance workers themselves. For example, the repacking or repair of spare equipment often involves both maintenance and operating personnel in the same location. OSHA should make clear that respirators may be used as a means of compliance for operators (as well as maintenance personnel) when the operator is exposed in a maintenance situation.

In sum, JRB has failed to address all of the benzene emission sources at petrochemical plants. Occupational exposures

associated with some of these sources clearly are significant. The significance of exposures associated with others has yet to be determined. The consequences of JRB's failure to address all these sources are twofold:

First, it means that JRB has not identified all of the controls that would be required to achieve the emission reductions contemplated by the Report and, derivatively, by the proposed standard. Since the feasibility and cost of these additional controls have not been evaluated, JRB's conclusions regarding technological and economic feasibility are suspect.

Second, JRB has failed to identify all of the work assignments and activities in which a PEL of 1 ppm and a 15-minute STEL of 5 ppm could not be achieved through the use of engineering and work practice controls. For these activities -- most of which occur only intermittently -- respirators would be required to ensure that employees are not exposed above 1 ppm as an 8-hour TWA (and/or above 5 ppm as a 15-minute STEL); alternatively, a PEL in excess of 1 ppm would be appropriate.

D. JRB Has Overestimated the Emission Reductions That Would Result from the Controls Identified in the Report.

1. Baseline Case Assumptions

JRB makes the following assumptions regarding baseline controls at petrochemical facilities where benzene exposures

exceed 1 ppm as an 8-hour TWA. According to JRB, the baseline controls and practices at such plants are as follows:

- Uncontrolled process sampling points.
- No pretreatment of benzene-containing wastewater.
- Absence of double mechanical seals on all pumps and compressors.
- Open hatch top-loading of pure benzene from BTX units into railcars and tank trucks.248/

JRB's assumption regarding baseline controls in the petrochemical industry must be corrected in three principal respects.

First, JRB mistakenly assumes that open-hatch top-loading of benzene into railcars and tank trucks is a standard industry practice. In fact, standard industry practice involves bottom loading and/or closed-loading systems with the use of dry disconnect. This is basically the same approach to controlling benzene emissions during railcar and tank truck loading that JRB recommends as a means of reducing benzene exposures during those operations.249/ Since they already are standard practice in the industry, it is unrealistic to assume that a further reduction in benzene exposures will result from implementing these controls.

248/ See JRB Report at 4-21.

249/ See JRB Report at 4-28.

Second, JRB is wrong in assuming that baseline practices have not included leak detection programs. In fact, while formal leak detection programs as contemplated by JRB250/ may not have been standard in the industry in past years, less formal leak detection activities were widespread. In some cases, formal leak detection programs were implemented in order to comply with EPA's new source performance standards for volatile organic compounds or as part of the control technique guidelines followed under State Implementation Plans in order to attain or maintain the ambient air quality standard for ozone. In other cases, less formal leak detection activities were carried on as part of preventative maintenance programs. In short, formal or informal leak detection procedures have been in place for some time at most petrochemical plants. Moreover, EPA's new benzene fugitive emissions standard, adopted under Section 112 of the Clean Air Act, formalizes leak detection requirements throughout the petrochemical industry.251/ Consequently, implementation of a leak detection program as contemplated by JRB cannot be expected to result in a significant reduction in benzene emissions.

Third, contrary to JRB's assumption, process sampling is widely controlled in the petrochemical industry today. JRB

250/ See JRB Report at 4-10.

251/ National Emission Standard for Equipment Leaks of Benzene in the Petrochemical and Petroleum Refining Industries, 49 Fed. Reg. 23498 (June 6, 1984).

proposes the use of ventilated enclosures to minimize benzene emissions during process sampling. In fact, most petrochemical companies already employ closed-system, minimum emissions sampling devices, which provide more effective control than the sampling approach proposed by JRB. Accordingly, there is no reason to believe that any further significant reduction in benzene emissions would be realized from further controls on process sampling.

2. Control of Wastewater Emissions

JRB suggests that a significant reduction in emissions from benzene-containing wastewater at petrochemical plants can be achieved by installing an oil/water separator.252/ In fact, while installation of an oil/water separator is a relatively inexpensive undertaking, it is not likely to result in significant emission reductions from benzene-containing wastewater at the process unit itself.

The example cited by JRB apparently involved the use of an oil/water separator at the wastewater treatment site prior to bio-oxidation of the wastewater. Use of an end-of-pipe oil/water separator just prior to introducing the wastewater into the treatment plant is an appropriate and effective device to reduce

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252/ See JRB Report at 4-22.

the insoluble benzene and oil phase prior to biological oxidation of the wastewater. And, in fact, most industrial waste treatment facilities already utilize oil/water separation prior to bio-oxidation. But addition of an oil/water separator back at the process operating unit would be redundant and, in any event, would have relatively little impact in reducing benzene emissions in the area of the operating unit. Indeed, it may actually increase exposures at the operating unit by adding a new source of benzene emissions in an area where employees are present.

The real solution to the problem of emissions from benzene-containing wastewater collected at the process unit would be either (i) to steam strip the benzene in a closed system at the operating unit or (ii) to install a closed piping system to transfer the wastewater from the process unit to the treatment plant. In the absence of steam stripping or a closed pipe system, the potential for benzene concentrations to exceed 1 ppm near wastewater collection sites at the process unit is substantial. While steam stripping or a closed piping system can effectively reduce these emissions from benzene-containing wastewater, either of these approaches is very expensive. JRB has not taken the costs of these expensive control techniques into account in its feasibility analysis.

E. Control of Fugitive Emissions

JRB assumes that baseline control practices at petrochemical plants which are not currently achieving a PEL of 1 ppm do not include the use of double mechanical seals for pumps and compressors or the implementation of a leak detection program. In JRB's view, use of double mechanical seals on pumps and compressors and adoption of a monthly leak detection program would result in a substantial reduction in benzene fugitive emissions, making achievement of 1 ppm as a PEL feasible.

JRB's optimistic projection of the emission reductions achieveable through the use of double mechanical seals and monthly monitoring in the petrochemical industry is unfounded. In the first place, as JRB recognizes, the only equipment with a significant percentage of leaks at petrochemical plants are pump and compressor seals.253/ This contrasts markedly with the situation at petroleum refineries, where a wider range of equipment displays a significant leak percentage.254/ Moreover, even in the case of pump and compressor seals, the leak percentage at petrochemical plants is much lower than the comparable leak percentages at petroleum refineries.255/ This reflects the good maintenance practices that are followed at petrochemical plants.

253/ See JRB Report at 4-24 and Table 4-2.

254/ See JRB Report at Table 4-1.

255/ Compare JRB Report, Table 4-1, with id., Table 4-2.

The use of double mechanical seals on pumps and compressors in petrochemical plants is not likely to achieve a substantial reduction in emissions even on those pumps and compressors that do leak. In the first place, there are very few compressors handling gases with significant benzene concentrations in the petrochemical industry. A typical ethylene plant will have a single compressor. The same is true of toluene dealkylation and pyrolysis gasoline hydrogenation units. Other types of petrochemical plants typically have no compressors. Consequently, further control of compressor seals is unlikely to result in significant reductions in benzene emissions at petrochemical plants.

As discussed above, the percentage of leaking pumps and compressors at petrochemical plants is relatively low, and very few compressors in benzene service are found in the petrochemical industry. For those reasons alone, the potential to reduce benzene fugitive emissions through the use of double mechanical seals on pumps and compressors is quite limited. It also is limited by the fact that emission rates from pumps and compressors in the petrochemical industry are relatively low under existing practices.

JRB does not present data on emission rates from pump and compressor seals at petrochemical plants, although the Report presumably relies on data derived from tests sponsored by

EPA.256/ Additional information available from the general literature also has been compiled by EPA.257/ An examination of these sources suggests that the use of double mechanical seals is not likely to result in as great an emission reduction as JRB apparently assumes.

The available information indicates that, where good maintenance practices are followed, emission rates from leaking pumps and compressors in the petrochemical industry are low even when double mechanical seals are not used. Thus, use of a single mechanical seal in light liquid service is estimated to result in volatile organic compound leakage at a rate of only 6 grams per hour when good maintenance practices are followed and process fluid is used to flush the seal.258/ Where a water flush is used, the emission rate from a single mechanical seal is estimated to be only 0.02 grams per hour.259/ Similarly, when

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256/ See Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, "Fugitive Emission Sources of Organic Compounds -- Additional Information on Emissions, Emission Reductions, and Costs," Document No. EPA-450/3-82-010 (April 1982).

257/ See Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, "Guideline Series -- Control of Volatile Organic Compound Leaks from Synthetic Organic Chemical and Polymer Manufacturing Equipment," Document No. EPA-450/3-83-006 (March 1984).

258/ J. Schroy, "Prediction of Workplace Contaminant Levels," in NIOSH Symposium Proceedings, Control Technology in the Plastics and Resins Industry, U.S. Department of Health and Human Services (NIOSH) Publication No. 81107 (January 1981), pp. 190-206.

259/ Id.

rod packed reciprocating seals are used on gas compessors and good maintenance practices are followed, volatile organic compound emission rates are estimated to be 16 grams per hour in the case of single rod packed seals and 13 grams per hour in the case of double rod packed seals.260/

As indicated by the low leak percentage rates for pumps, compressors and related equipment in the petrochemical industry, petrochemical plants do follow good maintenance practices with respect to these potential sources of fugitive emissions. Accordingly, the low emission rates associated with the use of good maintenance practices are what one would expect to find in the petrochemical industry. For that reason, installation of double mechanical seals would not be expected to result in any significant reduction in benzene fugitive emissions at petrochemical plants.

The reduction in benzene emissions resulting from a monthly leak detection program also is likely to be much smaller than JRB assumes. For one thing, as indicated above, fugitive emissions from pumps and compressors in the petrochemical industry are much lower than JRB assumes. If double mechanical seals were installed as JRB suggests, the volume of fugitive emissions presumably would decline somewhat further. In either case, the

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260/ Id.

volume of fugitive emissions that could potentially be reduced as a result of monthly inspections would not be substantial.

Second, JRB's assumption that a monthly leak detection program would reduce "leakage from valves and pumps in light liquid service by 77 and 80 percent, respectively" is based on test data for petroleum refineries. The percentage reduction at petrochemical plants is likely to be much smaller. This is particularly true, since the percentage of leaking valves and pumps in light liquid service at organic chemical plants is much lower than the comparable percentages at petroleum refineries.261/ Thus, even if the reduction percentages were the same, the absolute emission reduction would be smaller.

Finally, as indicated above, leak detection activities (of a greater or lesser degree of formality) have been standard practice for some time in the petrochemical industry and are now formalized under EPA's National Emissions Standard for Equipment Leaks of Benzene.262/ The leak detection program proposed by JRB would represent little or no improvement over current practice and is very unlikely to result in a significant reduction in benzene exposures at the plants.

261/ Compare JRB Report, Table 4-1, with id., Table 4-2.

262/ See pp. __-__, supra.

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In short, because of (i) a misunderstanding of baseline controls and practices and (ii) unrealistic assumptions regarding current emission levels and the effectiveness of controls, JRB has greatly overestimated the potential for achieving further reductions in benzene emissions and exposure levels in the petrochemical industry. For this reason alone, the feasibility of achieving 1 ppm as a PEL at petrochemical plants is much more problematical than JRB suggests.

F. JRB's Conclusion That a 1 ppm PEL Is Technologically Feasible in the Petrochemical Industry Is Unjustified.

As indicated above, JRB concludes that, with the exception of barge loading and maintenance operations (where use of respirators would be required), a PEL of 1 ppm as an 8-hour TWA and a 15-minute STEL of 5 ppm would be technologically feasible in the petrochemical industry. In the preceding sections of these Comments, we showed that this conclusion is unsupported for several reasons, including the following:

1. JRB's assumption regarding the extent to which petrochemical operations are presently meeting a PEL of 1 ppm reflects a misunderstanding of the measurement data provided by members of the industry.263/

263/ See pp. __ - __, supra.

2. JRB has failed to identify several important sources of benzene in the petrochemical industry, including a variety of activities in which engineering controls are not feasible and others in which engineering controls have not been identified or costed by JRB.264/ A variety of task-related exposures other than just barge loading and maintenance operations would require the use of respirators to ensure that a PEL of 1 ppm or a STEL of 5 ppm is not exceeded.

3. JRB has vastly overstated the extent to which benzene emissions can be reduced through the implementation of designated engineering controls and work practices in the case of railcar and tank truck loading, process sampling, wastewater collection, and fugitive emissions.265/ At the same time, JRB has failed to take account of the very large expenses that would have to be incurred in reducing benzene emissions from wastewater collection through the use of steam stripping or closed pipe systems.

In short, current benzene exposures in the petrochemical industry are higher than JRB appears to assume, while the potential for reducing these exposures is much smaller than JRB assumes. The fact is that, even if all of the

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264/ See pp. __ - __, supra.

265/ See pp. __ - __, supra.

engineering controls and work practices identified by JRB were implemented, it is unlikely that most petrochemical plants would be able to assure compliance (at a 95 percent level of confidence) with a PEL of 1 ppm and a 15-minute STEL of 5 ppm without using respirators on a variety of job assignments that extend beyond barge loading and maintenance.266/

G. JRB Has Greatly Underestimated the Costs of Complying Wtih a Standard Having a PEL of 1 ppm as an 8-Hour TWA.

JRB's approach to estimating compliance costs with alternative PELs is basically as follows:

(1) A baseline of current industry practice was established on the basis of exposure data for 27 petrochemical process units, representing approximately 15 percent of total process units in the industry.

(2) On the basis of exposure data collected from these 27 units, JRB projected that only 22.2 percent of petrochemical

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266/ In this connection, we would note that in setting a 40-hour time-weighted average benzene exposure limit of 5 ppm (with a goal of 1 ppm), the Ontario Ministry of Labour concluded that reducing the 40-hour time-weighted average benzene exposure of workers below 1 ppm "would be exceedingly difficult for the coke oven by-products plants and petrochemical companies." Ontario Ministry of Labour, Summary of Information and Data Gathered by the Ministry of Labour After the October 11, 1983 Public Meeting on the Proposed Benzene Regulation (October 1984) at 28. A copy of the Summary is submitted herewith as Appendix _ .

facilities would "incur compliance costs to achieve the 1 ppm 8-hour TWA exposure level."267/ The value of 22.2 percent was then multiplied by the number of petrochemical units of each production type to derive an estimate of the number of units of each type that would incur compliance costs to achieve a PEL of 1 ppm.

(3) The various kinds of petrochemical plants were grouped into three Model categories representing large, medium and small production units.268/

(4) The values derived in steps (2)and (3) were then combined to predict how many process units in each Model category would require engineering and work practice controls (and thus incur compliance costs) to achieve a PEL of 1 ppm.269/

(5) Costs to achieve a PEL of 1 ppm at each Model unit were then developed and multiplied times the number of units affected in each Model category.

(6) The aggregate costs for each of the three Model categories were then summed to produce an estimate of aggregate industry-wide compliance costs.

267/ JRB Report at 5-33.

268/ See JRB Report at 15-33.

269/ See JRB Report at 5-35 and 5-36.

In performing the foregoing calculations, JRB assumed that no engineering controls would be used to reduce exposures in barge loading.270/ Similarly, no cost estimates were developed for reducing exposures at railcar loading facilities, because JRB was unable to estimate the number of railcar loading facilities at BTX units.271/

For a variety of reasons, JRB's estimate of compliance costs in the petrochemical industry is unfounded and vastly understates the true costs that would be involved in attempting to comply with a PEL of 1 ppm.

For one thing, JRB's assumption that only 22.2 percent of petrochemical plants would incur any compliance costs to achieve a PEL of 1 ppm is unrealistic. It is based on a sampling of only 15 percent of the industry, a sampling which may very well not be representative of the industry as a whole.272/ Moreover, two of the plants included in the survey are aniline units at which almost no benzene is present,273/ and there are only

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270/ See JRB Report at 5-39.

271/ See id.

272/ In addition, there is no indication of how the particular plants were selected. We do not know what percentage of all questionnaires sent out by JRB was returned. Moreover, it may be that plants which returned questionnaires are more likely to have lower benzene exposure levels than plants which did not respond.

273/ The only benzene to be found at an aniline unit occurs in a small stream that is approximately 5 percent benzene.

three operating aniline units in the petrochemical industry.274/ At the same time, JRB's sample included only two ethylene units, even though it estimates that there are 46 ethylene units industry-wide.275/ This does not appear to be an appropriate mix of units upon which to base industry-wide exposure level estimates.

Quite apart from the question of the representativeness of the sample is the question of how to interpret the exposure data provided to JRB. As indicated at pp. __ - __ above, what JRB received was information regarding the prevailing or average 8-hour TWA benzene exposures in the job assignments or operations for which monitoring results were reported. The fact that the 8-hour TWA at a particular operation is slightly below 1 ppm on the average is very different from establishing that the operation already is in compliance with a PEL of 1 ppm which cannot be exceeded on a random inspection basis. Furthermore, as discussed at page __ above, historical measurements of benzene exposures at or below 1 ppm are of questionable precision and accuracy. Therefore, JRB's exposure profile at concentration levels below 1 ppm is not reliable.

274/ See p. _ _ supra.

275/ JRB Report, Table 5-8.

In addition to underestimating the number of petrochemical facilities that would incur compliance costs to achieve a PEL of 1 ppm, JRB, as discussed above, did not identify all of the benzene emission sources in the plants that would have to be controlled; nor did JRB identify all of the necessary controls for the sources listed in the Report. For example, contrary to JRB's assumption, installation of an oil/water separator is not likely to be effective in reducing benzene exposures from wastewater collection streams at the process units.276/ Instead, expensive steam stripping or closed pipe systems would have to be installed; yet JRB makes no allowance for these costs in its analysis. Nor has JRB estimated any costs for automatic guaging devices, or for interface controls and closed piping in the dewatering of benzene storage tanks, or for dedicated piping in intraplant transfers of benzene. Yet, unless respirators are to be permitted in these tasks, these expensive engineering controls may be required.

For the foregoing reasons, the JRB Report cannot be taken as presenting a realistic and supportable analysis of the costs of complying with a 1 ppm 8-hour TWA standard having a 15-minute STEL of 5 ppm. Needless to say, JRB's estimate of the cost of complying with a 0.5 ppm standard is even less credible.277/

276/ See pp. __ - __, supra.

277/ We would note that in an Addendum to the JRB Report, Meridian Research, Inc., developed a reduced cost estimate for

[Footnote continued next page]

G. Feasibility Considerations Dictate Setting the PEL Above 1 ppm, or at a Minimum, Establishing Compliance Criteria Which Account for Exposure Variability.

In the preceding sections, we have shown that the feasibility of achieving a 1 ppm 8-hour exposure limit and a 5 ppm STEL on a never-to-be-exceeded basis in the petrochemical industry is highly questionable and ~~that the problem is compounded further by~~ variability in measurements of exposure. We also have shown that the health risk, if any, at exposure levels in the neighborhood of 1 ppm is nonexistent or negligible.278/ In these circumstances, the best available evidence does not support establishment of a 1 ppm standard which would be deemed violated whenever the PEL is exceeded.

[Footnote continued from preceding page]

complying with a 1 ppm benzene standard in the petrochemical industry, based upon the assumption that the industry will incur some of the costs estimated by JRB in order to comply with EPA's National Emission Standard for Equipment Leaks of Benzene in the Petrochemical and Petroleum Refining Industries. 49 Fed. Reg. 23498 (June 6, 1984). See Meridian Research, Inc., "Addendum to Technological Feasibility and Economic Impact Study of Alternative Standards for Benzene," July 16, 1984. As noted above, the JRB Report did not provide a realistic and supportable estimate of the costs of complying with a 1 ppm benzene standard; accordingly, the revised estimate prepared by Meridian Research, which takes the JRB estimate as a starting point, is subject to the same criticisms as the JRB Report. Moreover, in evaluating the economic feasibility of an OSHA standard, it is not appropriate to ignore the cumulative impact of the costs of complying with standards issued by other agencies as well as by OSHA itself. Cf. ASARCO, Inc. v. OSHA, ____ F.2d ___, ___ (9th Cir. 1984).

278/ See pp. ___ - ___. supra.

One way of dealing with this situation would be to establish a higher PEL than OSHA has proposed -- e.g., a PEL of 2 ppm. Such a standard would respond to the difficulties of reducing benzene exposures below 1 ppm through the use of engineering and work practice controls for all job assignments in the petrochemical industry and would take account of the inherent variability of exposures. In these respects, it would be consistent with the action taken by the Ontario Ministry of Labour, which recently established a 5 ppm 40-hour time-weighted average exposure limit for benzene.279/ Moreover, as discussed above,280/ to comply with a 2 ppm standard, employers would have to maintain average exposures below 1 ppm, thus providing all of the health protective benefits that OSHA has calculated for a 1 ppm standard.

At the very least, OSHA should recognize the inherent variability in measurements of benzene exposures281/ by providing some means for averaging benzene exposure measurements in order to determine whether a violation of the standard exists. OSHA has suggested that this might be accomplished by allowing an employer to rebut a presumptive exceedence of the PEL by showing that an average of at least five 8-hour time-weighted

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279/ See p. ___ - ___, supra.

280/ See p. ___, supra.

281/ See pp. ___ - ___ & n.__, supra.

measurements taken in the same area (or for the same job assignment) within a "reasonable time" of the apparent exceedence is below the PEL. If the employer presents such information, a citation for violating the standard would not be issued unless remonitoring by the OSHA inspector confirms the initial measurement in excess of the PEL.282/

CMA strongly endorses this averaging approach to determining compliance or non-compliance and suggests that one year [18 months?] would be a "reasonable time" within which the rebutting measurements should have to have been taken.

IV. There Is No Basis for Adopting a Short-Term Exposure Limit in the Benzene Standard.

The proposed standard does not contain a short-term exposure limit ("STEL"). However, the rulemaking notice refers to a possible STEL of 5 ppm averaged over a 15-minute period283/ and requests comment on whether a STEL is needed for benzene.284/ For the reasons discussed below, we believe a STEL is not needed and should not be included in the Benzene Standard.

282/ See 50 Fed. Reg. 50512, 50515, cols. 1-2.

283/ See, e.g., id. at 50555, col. 3.

284/ See id. at 50554, col. 1.

A. Principles To Be Used in Determining Whether a STEL Is Needed

Requirements in an occupational health standard must be "reasonably necessary or appropriate to provide safe or healthful employment and places of employment."285/ This is as true for a STEL as for the 8-hour PEL itself. Thus, as a matter of law, a STEL may not be adopted unless it will serve a demonstrated health-protective function.

As a matter of science and public health policy, a STEL is justified to supplement an 8-hour time weighted average PEL in only two sets of circumstances --

(1) Where there are recognized acute health effects associated with short-term exposures of the type that might be expected to occur even if compliance with the 8-hour PEL is achieved;286/

(2) Where there is a demonstrated "dose-rate effect" for the chronic health effect of concern -- i.e., where short-term exposures to the substance present a chronic health risk above and beyond their contribution to cumulative exposures. As explained by the Environmental Mutagen Society, a STEL is appropriate where there is "a greater yield of damage (effect) from an acute treatment as compared to a chronic or fractionated treatment for the same total dose."287/

285/ Section 3(8) of the Occupational Safety and Health Act of 1970, 29 U.S.C. § 652(8). See also Industrial Union Department, AFL-CIO v. American Petroleum Institute, 448 U.S. 607, 639-646 (1980).

286/ [Cite to ACGIH Booklet.]

287/ Statement of the Environmental Mutagen Society, quoted in 50 Fed. Reg. 64, 66, col. 3 (January 2, 1985) (emphasis in original).

OSHA itself has clearly recognized and endorsed these principles, stating that a demonstrated dose-rate effect is a "critical" finding "to justify the adoption of . . . [a] STEL . . . ."288/ In this regard, OSHA has explained that "it is necessary to have data that compares the biological outcomes that result from . . . two exposure scenarios before a conclusion can be reached that a dose-rate effect exists."289/ Under the two exposure scenarios,

> health effects observed in a test group receiving a given total dose over a continuous period of time must be compared with the health effects observed in a separate test group receiving the same total dose over a shorter period.290/

No such set of exposure scenarios exists in the case of benzene. Nor, as discussed below, does the evidence which exists under other exposure scenarios justify the finding of a dose-rate effect for benzene.

B. The Best Available Evidence Does Not Support a Finding That Short-Term Benzene Exposures Consistent With the Proposed 8-Hour PEL Will Present a Significant Risk of Material Health Impairment.

288/ Id. at 73, col 3. See also id. at 73, col. 3 (an observed dose-rate effect over a certain dose range would have to be demonstrated "[b]efore a STEL can be justified based on health effects from short-term exposures").

289/ Id. at 75, col. 1.

290/ Id. at 74, col. 1.

1. Non-Malignant Health Effects.

As discussed at pages ___ - ___ above, the non-malignant health effects of benzene appear to have a chronic exposure threshold of approximately 40-50 ppm. Exposure levels would have to be considerably higher than that in order for non-malignant effects to result from short-term exposure. Since the proposed 8-hour PEL effectively precludes short-term exposures in excess of the threshold for non-malignant health effects,291/ a STEL cannot be justified as necessary to protect against risks of acute benzene toxicity.

2. A Dose-Rate Effect for Benzene-Related Leukemia Has Not Been Demonstrated.

As indicated above, none of the existing data sets even approach the two exposure scenarios that OSHA has described as necessary in order to reach a conclusion that a dose-rate effect exists for benzene-related leukemia.292/ Even apart from the absence of the required exposure scenarios, the fact is that the epidemiological and animal data that do exist, as well as the available biological and pharmacokinetic information, do not provide a basis for concluding that benzene-related leukemia is dose-rate dependent.

291/ See pp. __-__, infra.

292/ See pp. __-__, supra.

For the most part, the human epidemiological studies do not provide sufficient information to develop short-term exposure profiles, separate and apart from cumulative exposure estimates, for members of the cohorts that were studied. Thus, the risk assessments that have been performed all relate increased risk to total cumulative exposure (or average exposure for a specified period).

The limited information that is available regarding the effect of intermittent, short-term exposures is either inconclusive or inconsistent with a postulated dose-rate effect. Thus, in the Rinsky Study, no statistically significant excess of leukemia cases was found among numbers of the cohort who had less than five years of employment with benzene exposure.293/ As Drs. Crump and Allen observed after analyzing the Rinsky data for workers having varying degrees of cumulative and peak exposures:

> This analysis does not support the hypothesis that peak exposure has any [impact] upon risk over that which can be explained by the contribution of these exposures to cumulative dose. If anything, it suggests that high exposures are less effective per ppm-year in producing leukemia than lower exposures.294/

293/ See 50 Fed. Reg. 50512, 50519, col. 1

294/ Crump Report at 21.

To the extent it indicates anything about the relationship between benzene and leukemia, the Wong Study supports a similar conclusion. Thus, as stated by Dr. Wong: "The findings in this study suggested that cumulative exposure (ppm-months), and not peak exposure, was the major parameter in quantifying mortality risk from lymphopoietic cancer."295/ OSHA has interpreted the Wong Study in the same way, stating:

> No significant peak exposure response relationship was observed. These findings suggest that a cumulative dose concept may be better than a maximum peak exposure concept when trying to determine dose-response relationships.296/

Thus, the epidemiological data do not show a dose-rate effect for benzene. Nor do the data from animal studies. OSHA points to a study by Irons (Ex. 159-41A) as suggesting that intermittent exposures may be more potent in producing certain bone marrow effects than continuous exposure.297/ But, apart from the fact that these bone marrow effects are different from leukemia, the fact is that the intermittent exposures in the Irons study were at the identical level of benzene as the continuous exposures.298/ Thus, Irons' study does not

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295/ Wong Study at 61.

296/ 50 Fed. Reg. 50512, 50523, col. 2.

297/ Id. at 50554, cols. 1-2.

298/ See Preliminary Regulatory Impact and Regulatory Flexibility Analysis for the Benzene Standard, December 1985 (Ex. ___) at III-15.

demonstrate a dose-rate effect in which higher short-term exposures have a greater health effect impact than lower long-term exposures amounting to the same cumulative dose.299/

The studies of cytogenetic effects in animals to which OSHA refers300/ also fail to demonstrate a dose-rate effect for benzene-related leukemia. The cytogenetic effects involved in those tests have no known clinical significance or demonstrated causal relation to benzene-related leukemia.301/ Furthermore, there is no basis for concluding that the observed effects relate to short-term peaks rather than to overall cumulative exposure. Since the dose was administered at a constant rate, the latter hypothesis is at least as likely as the former.

In sum, neither the epidemiological data nor the animal studies demonstrate a dose-rate effect for benzene-related leukemia. Nor does the biological or pharmacokinetic information provide a basis for presuming that a dose-rate effect exists, for, as OSHA acknowledges: "The basic mechanism by which benzene affects bone marrow precursor cells is still unclear."302/ Thus,

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299/ What the Irons data might suggest is that exposing workers to benzene continuously is more protective than exposing them to the same level of benzene from time to time.

300/ See 50 Fed. Reg. 50512, 50554, col. 3.

301/ See pp. __-__, supra.

302/ 50 Fed. Reg. 50512, 50516, col. 3.

there is no basis for finding dose-rate dependency in the case of benzene-related leukemia or for adopting a STEL to protect against dose-rate effects.

C. The Proposed Standard Would Protect Against High Short-Term Exposures Even Without the Adoption of a STEL.

Even without a STEL, the proposed standard would protect against high short-term benzene exposures in a variety of ways.

First, and most fundamentally, the proposed 8-hour PEL of 1 ppm, as OSHA recognizes, automatically establishes a maximum 15-minute exposure limit of 32 ppm even if no other benzene exposure occurs during the course of the day.303/ In practice, the proposed 8-hour PEL would establish a much lower 15-minute limit, since workers would be exposed to background levels of benzene during all or substantial periods of the workday. For example, if exposure for the rest of the shift is at the action level of 0.5 ppm, the maximum 15-minute exposure would be 16 ppm.

Furthermore, where several short-term exposure excursions occur during the day, additional limits automatically are placed on the maximum level of each excursion. Thus, as OSHA points out, where an employee is exposed to three 15-minute

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303/ See 50 Fed. Reg. 64, 76, col. 3.

4007 excursions per day, the maximum exposure at each excursion could
4008 be no more than approximately 10 ppm in order to comply with an
4009 8-hour PEL of 1 ppm.304/ Since background levels of benzene will
4010 exist in combination with multiple short-term excursions in most
4012 cases, the maximum 15-minute exposure level generally would have
4013 to be kept in the range of 5-10 ppm in order to assure compliance
4014 with an 8-hour PEL of 1 ppm.

4016
4017 Finally, it is important to bear in mind that employers
4017 would have to maintain average 8-hour exposures at or below 0.5
4018 ppm in order to have a high degree of assurance that the PEL of
4019 1 ppm is not exceeded.305/ Accordingly, 15-minute exposures
4021 would have to be held to even lower levels than the foregoing
4022 discussion would suggest. In all of the respects discussed
4023 above, the 8-hour PEL, as OSHA has pointed out elsewhere, places
4024 "internal limitations on the levels and durations of short-term
4025 exposures" and acts "as a check on the number and extent of
4026 short-term exposures during the day."306/

4028
4029 In addition to the inherent mathematical constraints
4029 imposed by the 8-hour PEL, OSHA and its contractor, JRB Associ-
4032 ates, have preliminarily concluded that the same engineering

4034 _____
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4010 304/ See id.

4020 305/ See pp. __-__ & n.__ supra.

4027 306/ See 50 Fed. Reg. 64, 73, col. 2, 76, col. 3.

4033 controls and work practices that will be used to achieve the
4034 8-hour PEL of 1 ppm would reduce 15-minute short-term exposures
4035 as well.307/ Moreover, short-term exposure excursions are most
4039 likely to occur in those activities -- such as maintenance and
4040 repair, vessel cleaning, and other operations in which benzene
4041 exposures are intermittent in nature and limited in duration --
4042 where respirators would be used to comply with the 8-hour PEL in
4043 any event. As discussed above, it is precisely in these situa-
4045 tions that the feasibility of complying with a 5 ppm STEL would
4046 be most questionable.308/ Thus, in combination, the engineering
4047 and work practice controls and respirator requirements of the
4048 standard will effectively establish an informal STEL under the
4049 Benzene Standard.

4050
4051 The proposed standard also establishes requirements for
4052 training and providing information to employees regarding health
4053 risks of benzene and methods of protecting against those risks.
4054 This training, combined with the sign and labeling requirements
4055 and the regulated area provisions of the standard, will further
4056 minimize the risk that employees may be exposed to unacceptably
4058 high short-term concentrations of benzene without wearing appro-
4060 priate respiratory protection.

4061 _____
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4035 307/ See Preliminary Regulatory Impact and Regulatory
4036 Flexibility Analysis for the Benzene Standard, December 1985 (Ex.
4037 __) at IV-7; 50 Fed. Reg. 50512, 50543, col. 1.

4046 308/ See pp. __-__, supra.

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In short, the internal limitations imposed by the 8-hour PEL itself, along with a variety of requirements for methods of compliance, respirator usage and employee training, will assure that 15-minute benzene exposures will be limited to levels that do not pose any significant risk of material health impairment to workers.

* * * * *

In announcing the proposed Benzene Standard, Acting Assistant Secretary of Labor, Patrick R. Tyson, stated that "right now, we don't have the scientific evidence before us to justify a STEL" for benzene.309/ Similarly, the American Conference of Governmental Industrial Hygienists ("ACGIH") recently proposed to remove the STEL for benzene on the ground that . . . . . .310/ We concur with the judgment that a STEL for benzene is not warranted. Under the principles that should govern in this area, there simply is no justification for adopting a 15-minute STEL for benzene.

309/ The Washington Post, December 4, 1985 at __.

310/ [Cite to ACGIH Booklet.] OSHA has described ACGIH's Threshold Limit Value Committee as "a respected group . . . [consisting] of professional industrial hygienists (and toxicologists) in the employ of various governmental bodies." 50 Fed. Reg. 64, 71, col. 3.

V. Medical Surveillance

Section 1910.1028(i) of the proposed standard provides for the medical surveillance of benzene-exposed workers. CMA supports the inclusion of appropriate medical surveillance requirements in the Benzene Standard. While the proposed medical surveillance provisions are well conceived overall, we believe they should be revised in a number of respects discussed below.

A. Employee Coverage

The proposed standard requires that each covered employer institute a medical surveillance program for all employees (1) who are exposed at or above the action level for 30 or more days per year; or (2) who are exposed to benzene above the PEL for 10 or more days per year; or (3) who have been exposed to more than 10 ppm of benzene for 30 or more days in a past year while employed by their current employer.311/ We support providing medical surveillance to employees who are exposed to benzene at or above the action level for 30 or more days per year, or above the PEL for 10 or more days per year. However, we question the medical necessity and administrative feasibility of providing medical surveillance to employees who are not currently

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311/ See proposed Section 1910.1028(i)(1)(i). In addition, medical examinations are to be provided for employees exposed in an emergency situation. See proposed Section 1910.1028(i)(4). This provision is discussed at p.__ infra.

exposed to benzene simply because they were exposed to more than 10 ppm benzene for more than 30 days in a prior year.

According to OSHA, the aims of medical surveillance are as follows:

> 1. Early detection and reversal of cytopenias and aplasias.
>
> 2. The prevention of some leukemias by reducing dose to the more susceptible workers.
>
> 3. Early recognition and treatment of those cases of leukemia which might occur and improvement in remission rate and duration.
>
> 4. Better evidence of the effectiveness of the proposed standard.312/

Providing medical surveillance to formerly exposed workers is not likely to advance these objectives.

Since these workers would not currently be exposed to benzene above the action level, they clearly would not be at risk of developing cytopenias and aplasias as a result of current exposure. Furthermore, since a 10 ppm standard has been in effect for the past 15 years, any cytopenias or aplasias that might have been associated with high benzene exposures in the past would have been detected or have run their course long ago. Thus, with respect to these formerly exposed employees, medical

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312/ 50 Fed. Reg. 50512, 50563, col. 2.

surveillance would not play any role in detecting and reversing cytopenias and aplasias.

Nor would medical surveillance play any role in preventing leukemias in these workers by reducing their benzene exposures. Under the proposed standard, any employee who is still subject to even a minor benzene exposure of 0.5 ppm for 30 days per year or 1 ppm for 10 days per year would be subject to medical surveillance. A worker whose benzene exposure is below even these low thresholds (of approximately 0.03 ppm-year) can hardly be said to be receiving a dose that would have to be reduced in order to prevent a significant risk of leukemia.

Providing medical surveillance for employees who were exposed to more than 10 ppm benzene in the past, but who are not currently exposed above the action level, will not provide any useful evidence regarding the effectiveness of the proposed standard. Nor would it provide useful evidence of a comparative nature, since these employees would have had past exposures in excess of the current 10 ppm standard.

The only rationale for including these workers in the medical surveillance program that has even the semblence of plausibility is early recognition and treatment of leukemia cases which may be attributable to high exposures in past years. However, since a 10 ppm standard has been in effect since 1971 (with a 10 ppm ANSI recommendation in effect since 1969), it is

unlikely that very many current employees (who are not now exposed above the action level) would fit the medical surveillance criterion. Moreover, if past exposures in excess of 10 ppm did create a risk of leukemia for these workers, the latency period (which OSHA estimates as 11 years313/) would have run some time ago, so that the leukemias should already have become apparent. Thus, medical surveillance of these employees is very unlikely to result in the early recognition and treatment of benzene-related leukemias attributable to past exposures in excess of 10 ppm. Moreover, there is likely to be very little improvement in remission rate or duration of any leukemias that are identified through medical surveillance.

In sum, there is little if any medical justification for requiring medical surveillance of workers who would not otherwise be covered as a result of their current exposures. Yet the task of identifying workers who were exposed to more than 10 ppm benzene in a past year could be enormously difficult and burdensome -- so much so, that the slight possibility of some marginal health benefit is far outweighed by the administrative burdens.

As noted above, a 10 ppm standard has been in effect since 1971. Accordingly, very few current employees are likely

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313/ See id. at 50524, col. 3.

to have been exposed to more than 10 ppm benzene without respiratory protection during the past 15 years. Thus, identification of employees who fit the medical surveillance criterion based only on past exposures above 10 ppm would have to focus on employment and exposure records from the 1950's and 1960's. Exposure data for those years are likely to be sparse, much less reliable than recent exposure data, and difficult to tie to particular current employees. These difficulties would be compounded by the fact that workers frequently are transferred between work sites on a temporary or more-or-less permanent basis. Further complications would arise in the case of employers which have closed some of their plants or have gained new employees through acquisitions of other companies or industrial units. In either event, there is a good chance that records for the past few decades may have been lost or simply not transferred.

In short, the task of identifying formerly exposed employees for purposes of medical surveillance would be formidable to say the least, even when the search is limited to workers whose exposures occurred while employed by their current employer. If benzene exposures that may have occurred while the worker was employed by a previous employer had to be identified, the task simply would become impossible.

Because of the enormous administrative burdens involved and the extreme unlikelihood that any significant health benefit would be realized, the requirement that medical surveillance be provided for formerly exposed employees should be deleted from the standard. If it remains, however, it must, at the very least, be clarified in several respects.

For one thing, as in the case of currently exposed employees, the test should be stated in terms of 8-hour time-weighted average exposure. Thus, coverage should apply only to employees who had more than an 8-hour time-waited average benzene exposure of 10 ppm for 30 or more days in a year prior to the effective date of the standard. Second, OSHA should attempt to mitigate the administrative burden by stating explicitly in the preamble to the standard that the employer need only make a "reasonable effort" to identify formerly exposed employees who meet the foregoing criterion. One approach that might be considered is requiring the employer to investigate past benzene exposures only in the case of those employees who identify themselves to the employer as likely to have had 8-hour average exposures of more than 10 ppm. In that way, the scope of the search could at least be focused on areas where the likelihood of a positive identification is highest.

B. Frequency of Periodic Examinations

Section 1910.1028(i)(3) provides that periodic medical examinations shall be provided at least semi-annually. While semi-annual examinations might be appropriate if workers were exposed to benzene levels of 10 ppm or above, we believe that annual medical surveillance will be sufficient if the PEL is reduced to the level OSHA has proposed.

OSHA's rationale for semi-annual examinations consists of the following two elements:

> 1. Early detection of marrow suppression before the cell counts are low enough to be life threatening, followed by removal should, in affected persons, prevent significant morbidity including hemorrhage or infection or mortality . . . .
>
> 2. Employee questioning and counseling during the periodic examination to determine possible exposure to other bone marrow toxins . . . and other chemicals at work, in hobbies and in the home may enable the physician to counsel the employee as to reducing risks.314/

The second prong of OSHA's rationale is entirely unpersuasive. There is no reason why counseling employees about the risks of other bone marrow toxins cannot be done effectively on an annual basis.315/ The first prong of the rational (early

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314/ 50 Fed. Reg. 50512, 50565, col. 1.

315/ In addition, one may question whether OSHA should be concerned about counseling for non-occupational health risks related to personal habits and hobbies.

detection of marrow suppression) also fails to justify a semi-annual frequency for periodic examination. As discussed at pages __-__ above, marrow suppression unrelated to leukemia should not be associated with benzene exposures at the levels that are of concern in this proceeding. And, if benzene exposures at levels in the neighborhood of 1 ppm create any risk of leukemia at all, the risk will be very low. Thus, medical surveillance, whether provided annually or semi-annually, is not likely to result in the early detection of leukemia. Moreover, since the most likely form of leukemia to be found is acute myelogenous leukemia, the disease is likely to progress too rapidly once detected for medical surveillance to be of significant benefit.

OSHA correctly points out that various formed elements of the blood have relatively brief life spans, measured in days in some cases.316/ If medical surveillance is to be provided at an interval corresponding to the life span of these blood elements, it would have to be given on a weekly or monthly basis to ensure that the examination falls within the brief period in which the abnormality is first observable. Semi-annual examinations offer relatively little advantage over annual examinations in this respect.

316/ See id at 50565, col. 1-2.

C. Required Elements of Medical Examinations

For the most part, we believe that OSHA has identified the appropriate types of laboratory tests for inclusion in medical examinations of benzene-exposed workers. We would, however, comment on two specific points.

1. Chest X-Rays

Proposed Sections 1910.1028(i)(2) and (3) state that workers required to wear respirators for at least 30 days a year must be provided with a pulmonary function test and a chest X-ray at the initial examination and at subsequent 3-year (pulmonary function test) and 5-year intervals (chest X-ray). The objective of these tests is to assure that workers wearing respirators "will not be compromised by a pulmonary defect not detected by regular clinical examinations ."317/ According to OSHA, the pulmonary function test "will pick up obstructive and restrictive pulmonary disease while the x-ray is designed to pick up lesions which may be clinically silent."318/

CMA supports the concept of medically screening employees required to wear respirators in order to determine their pulmonry fitness. We also agree that the pulmonary

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317/ Id. at 50564, col. 3.

318/ Id.

function test is an appropriate procedure to employ for this purpose, and the 3-year repeat frequency seems appropriate. However, we do not believe there is justification for requiring chest X-rays as a matter of course in order to determine pulmonary fitness. Instead, the question of whether a chest X-ray is provided should be left to the discretion of the examining physician. We reach this conclusion for two reasons.

First, in contrast to a pulmonary function test, a chest X-ray is likely to provide little, if any, information about the employee's current pulmonary function or capacity. A chest X-ray also is likely to be of little use in predicting future diminished pulmonary capacity, given the multitude of factors that may be influential in this connection.

Second, and of fundamental importance, chest X-rays create an increased cancer risk that should be avoided whenever the chest X-ray is not really needed. For this reason, both the Food and Drug Administration ("FDA") and the American College of Radiology have strongly recommended against mandatory employment pre-placement chest X-rays of workers who have not been selected on the basis of individual history or examinations. FDA's National Center for Devices and Radiological Health has recommended:

> All mandated routine screening examinations of unselected populations should be discontinued, unless a significant yield can be shown.319/

319/ FDA The Selection of Patients For X-Ray Examinations: Chest X-Ray Screening Examinations (September 1, 1983), as summarized in 13 FDA Drug Booklet 13 (August 1983).

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The American College of Radiology has made similar recommendations in a formal Policy Statement concerning chest X-ray examination in occupational medicine. The Policy Statement, in relevent part, reads as follows:

> Preemployment/Preplacement Examinations for Appropriate Job Placement:
>
> Preplacement chest X-ray examinations should be done selectively based on pertinent factors in the (1) occupational and medical hi tory, (2) clinical examination, and (3) proposed work assignment.
>
> Exposure Surveillance
>
> Chest X-ray surveillance of persons who work with or may be exposed to substances that adversely affect pulmonary function or cause pulmonary disease should be based on a periodicity consistent with the current understanding of the disease process.320/

Neither benzene exposure nor respirator use are suspected of adversely affecting pulmonary function or causing pulmonary disease. Accordingly, in light of the marginal contribution that chest X-rays may make to evaluating pulmonary function and the radiation risks associated with chest X-rays, OSHA should not establish a mandatory requirement for periodic chest X-rays in the Benzene Standard. Instead, the question whether a chest

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320/ American College of Radiologly Policy Statement, Referral Criteria For Chest X-Ray Examinations (September 22, 1982).

X-ray is to be provided should be left to the discretion of the examining physician, at least after the initial baseline examination.

2. Emergency Examinations

Section 1910.1028(i)(4) of the proposed standard requires that a urinary phenol test be performed in the case of employees who are exposed to benzene in an emergency situation. OSHA has asked whether the provision of a urinary phenol test is appropriate and whether measurement of blood or breath benzene also should be required.

At the outset, we would urge OSHA to clarify the emergency exposure provisions of the standard, so that they more accurately reflect the exposure scenario that is of concern. Section 1910.1028(b) of the proposed standard defines "emergency" to mean any occurrence "which may or does result in an unexpected significant release of benzene." Since the principal function of the term "emergency" is to trigger special medical examinations, the last clause of the definition should be revised to read as follows: "which results in an unexpected significant release of benzene." The fact that an occurrence "may . . . result in an unexpected significant release of benzene" would not justify an emergency medical examination if the release does not actually occur.

A corresponding revision should be made in Section 1910.1028(i)(1)(i) of the proposed standard, which currrently requires medical surveillance, inter alia, "for employees who have been exposed to an emergency situation." We believe that this clause could be clarified by providing that medical surveillance is required for "employees who have been exposed to an unexpected significant release of benzene in an emergency situation." A corresponding change should be made in Section 1910.1028(i)(4)(i), so that emergency examinations would be required: "If the employee is exposed to an unexpected significant release of benzene in an emergency situation . . . ."

Once the foregoing clarifications are made, we support the provision of a urinary phenol test to employees who have been exposed to unexpected significant releases of benzene. However, OSHA should not mandate that the tests be given "at the end of the employee's shift." The level of phenol in the urine is likely to reach its peak three to four hours after the emergency exposure. If the urinary phenol test must invariably be given at the end of the shift, this peak would be missed in those instances in which the emergency occurs either early or late in the shift. Proposed Section 1910.1028(i)(4)(i) should, therefore, be revised to provide that the urinary phenol test be given "at the appropriate interval following exposure" rather than "at the end of the employee's shift."

While we support the provision of a urinary phenol test in emergency exposure situations, we do not believe that measurement of blood or breath benzene should be required. The urinary phenol test will identify all cases in which follow-up blood tests are appropriate. (Indeed, if anything, the urinary phenol test is likely to produce false positives, since phenol levels may be elevated for reasons other than exposure to benzene.) There simply is no need for blood or breath tests, particularly since the timing of such tests would be critical in light of the rapid metabolization of benzene.321/

D. Criteria for Referral to a Hematologist or Internist

Section 1910.1028(i)(5) of the proposed standard establishes "normal" parameters for hemoglobin level, thrombocyte count, and leukocyte count, and provides that where blood count results fall outside of these parameters, the blood count must be repeated within two weeks. If the "abnormality" persists, the employee must be referred to a hematologist or internist for further evaluation "unless the [examining] physician has good reason to believe such referral is unnecessary."

CMA supports the concept of referring employees with "abnormal" blood count results to a hematologist or internist for

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321/ See 50 Fed. Reg. 50512, 50566, col. 2.

further evaluation in appropriate cases. However, in light of the uncertainty as to whether particular blood count results are "normal" or "abnormal" in the case of a particular individual, we believe tht medical judgment and physician discretion should play a large role in determining whether referral is indicated in individual cases. There is no question that variations from hypothetically "normal" blood count limits may be related to such factors as sex, age, race, smoking, exercise, and geography.322/ As OSHA recognizes, "all these factors need to be cosidered when defining acceptable levels of formed blood elements for preemployment assessment as part of routine medical surveillance and for decisions to refer benzene workers to a hemotologist."323/

With the foregoing points in mind, we would urge that the medical referral provisions of the standard be revised to provide a clearer emphasis upon the role of medical judgment and physician discretion in this area. This could be accomplished by: (1) deleting the requirement that the blood count be repeated within two weeks,324/ and (2) removing the specific

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322/ See id. at 50565, col. 3 - 50566, col. 1. For example, blacks have been reported to have lower white cell counts than whites. See _____. In addition, the question of what limits are "normal" may vary from one laboratory to another.

323/ 50 Fed. Reg. 50512, col. 3.

324/ The appropriate interval for repeating a blood count may be greater than two weeks in some cases. This would be true,

[Footnote continued next page]

triggering values from the standard itself and including them, instead, as recommended guidelines in an appendix to the standard.

E. Medical Removal and Wage Rate Retention.

Section 1910.1028(i)(8) of the proposed standard provides that an employee who is referred to a hematologist/internist for further evaluation must be temporarily removed from benzene exposure and that a decision on whether the removal should continue is to be made by the examining physician after consulting with the hematologist/internist. We believe that these provisions for medical removal are appropriate.

In this regard, we would emphasize the particular importance of having the examining physician, rather than the hematologist/internist, make the decision as to whether the removal should continue. While the advice of the hematologist/internist will be an important element in the ultimate decision, the examining physician will be much more familiar than the outside hematologist/internist with the occupational environment and the nature of benzene exposures. He will, therefore, be in the best position to evaluate the need for contining medical removal.

[Footnote continued from preceding page]

for example, when the physician suspects that the "abnormal" count is the result of a virus of greater than two-weeks' expected duration.

As proposed, the standard does not contain a wage rate retention provision. That is, employers are not required to provide an alternative job at the same rate of pay to employees who are subject to medical removal. The decision not to include a rate retention provision in the proposed standard was correct, since such a provision is neither legally supportable nor necessary in practice.

On the legal side, two considerations are relevant. First, we believe there is a substantial question as to whether OSHA has authority to require wage rate retention under any set of circumstances. A rate retention provison would appear to conflict with Section 4(b)(4) of the Occupational Safety and Health Act of 1970, 29 U.S.C. § 653(b)(4), since it can be said to

> affect any workmen's compensation law or to enlarge or diminish or affect in any other manner the common law or statutory rights, duties, or liabilities of employers and employees under any law with respect to injuries, diseases, or death of employees arising out of, or in the course of, employment.

Moreover, the inference that Congress did not intend to authorize wage rate retention under the Occupational Safety and Health Act is strongly suggested by the fact that Congress passed the Act without expressly providing for rate retention only one year after considering and expressly including a rate retention provision in the Federal Coal Mine Health And Safety Act of 1969,

30 U.S.C., §§ 811(d), 843(b)(2)(3). For these reasons, despite the holding of the court in United Steelworkers of America AFL-CIO v. Marshall, 647 F.2d 1189 (D.C. Cir. 1980), cert. denied, 453 U.S. 913 (1981), a substantial question exists regarding OSHA's authority to include a wage rate retention provision in any occupational health standard.

But even if OSHA has authority to impose a rate retention requirement in some cases, it is clear, under American Textile Manufacturers Institute, Inc. v. Donovan, 452 U.S. 490, 538 (1981), that a rate retention provision, if authorized at all, "must be justified on the basis of [its] relation to safety and health." As the Supreme Court emphasized in that case, OSHA does not have a roving commission to establish wage rate retention requirements, since "the Act in no way authorizes OSHA to repair general unfairness to employees that is unrelated to achievement of health and safety goals . . . ." Id. at 540.

In the case of benzene, a rate retention provision could not be justified on the basis of a relation to safety or health. In the United Steelworkers decision, there was concern that employees might take a chelating agent in order to reduce the levels of lead in their blood in order to avoid being transferred to a lower paying position. This, it was feared, might result in workers being exposed to concentrations of lead which, in light of their true blood lead levels, might be dangerous to

their health. This potential problem does not exist in the case of benzene, since employees have no way of making an abnormal blood count appear normal, and cannot manipulate the results of pulmonary function tests in order to make their pulmonary function appear better than it actually is. In short, there is no health justifiction for requiring rate retention under the Benzene Standard.

Nor does there appear to be any need for such a provision in practice. The fact is that very few employees will be removed from a benzene-exposed assignment because of adverse blood effects attributable to benzene exposure. Even under the current 10 ppm standard, the experience of the petrochemical industry indicates that virtually no removals attributable to benzene-related blood abnormalities have occured in recent years.325/ If anything, even fewer removals would be expected under the proposed standard, since it contemplates lower permissible levels of exposure than are presently permitted.

Moreover, rate retention is the subject of collective bargaining agreements and formal and informal personnel policies and practices in most affected industries. In the petrochemical industry, for example, ... [what can we say here?]. Thus, as OSHA observes "the details of [medical removal transfers] . . .

325/ [Cite to results of CMA Survey.]

are best left to collective bargaining and employer personnel policies."326/

In sum, a rate retention provision in the Benzene Standard would be improper as a matter of law, inappropriate as a matter of labor-management relations, and unnecessary in practice. Such a provision should not be included in the final standard.

F. Comments on Appendix C - Medical Surveillance Guidelines for Benzene

The medical surveillance guidelines of Appendix C require a few modifications in order to bring the information up to date, sharpen its accuracy, and avoid misleading implications that the described indicia are solely attributable to benzene etiology.

1. The General Provisions of Section V.A.

The first paragraph in section V.A. of Appendix C describes the principal relevant effects of benzene exposure as "alterations of the hematopoietic system as reflected by changes in the peripheral blood and leukemia." It also states that the purpose of the medical surveillance program is to observe early signs of "these effects." Alterations of the hematopoietic

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326/ 50 Fed. Reg. 50512, 50567, col. 1.

system, however, are not specific to benzene exposure but may arise from other causes of bone marrow depression or from idiopathic leukemia. This paragraph therefore should be modified as follows to avoid implying that any such observed effects necessarily would have occurred as the result of benzene exposure:

> The medical surveillance program is designed to observe indices for early signs of alterations of the hematopoietic system, as reflected by changes in the peripheral blood and leukemia. Alterations of the hematopoietic system are the principal effects of benzene exposure that form the basis for this regulation, but they are not specific to benzene etiology. The same effects may also arise as the result of idiopathic leukemia and other causes of bone marrow depression.

2. The Hematology Guidelines of Section V.B.

The hematology guidelines should be brought up to date by incorporating currently accepted practice. They should also avoid wrongly implicating benzene overexposure as the exclusive causal mechanism for the observed abnormalities.

a. The Hematology Guidelines Should Be Updated to Recognize the Use of Automated Blood Counters.

The opening paragraph of section V.B., which states that the guidelines are derived from the analysis of Dr. Jandl, should further indicate that the date of submission of that

information was 1977. It should also indicate that, in the intervening years, automated blood cell analyzers have come into common use in clinical laboratories and may properly be used to meet the requirements of Appendix C.

The requirement of section V.B.1. that blood counts be performed using an "automated (Coulter) counter" should be modified to delete the reference to "Coulter", a particular proprietary brand. That same section should also acknowledge that automated analyzers now provide an index of the distribution of red blood cell volume (RDW), which measures the heterogeneity of the red blood cell population. In fact, the RDW represents a coefficient of variation of red blood cell volume distribution. Section V.B.1. also should recognize that mean platelet volume (MPV) is a sensitive measure of platelets.

b. The Hematology Guidelines Should Be Modified To Avoid Inaccurately Attributing Certain Indicia to Benzene Exposure.

Section V.B.3. prescribes the minimum mandatory observations to be made from the peripheral blood smear and describes their significance. Subsections a through d are not particularly useful to the practitioner and do not represent universally accepted practice. They should be deleted from Appendix C. Subsection V.B.3.e., on the other hand, contains a comprehensive and generally helpful discussion of the observation of

hematologic abnormality and should be retained, with a few modifications.

The end of the first paragraph in subsection e notes that vacuolation in erythroblasts and myelocytes is a relevant phenomenon "induced by many toxins apart from benzene, including chloramphenicol and alcohol; and by infections."327/ This characterization of benzene as only one among several possible causes is correct. Statements to the contrary in the second and third sentences of the same paragraph should be made to conform by deleting inaccurate and misleading references to benzene as the cause of these general changes reflected in the peripheral blood.

The fourth sentence in the first paragraph of subsection V.B.3.e. states that "the findings of two or more cytopenias, or of pancytopenia, must be regarded as highly suspicious of more advanced although still reversible, benzene toxicity."328/ This effect is not specific to benzene exposure, but is true for all bone marrow depression etiology. Thus, the statement should be modified to delete "benzene toxicity" and replace it with "bone marrow depression."

The next sentence states that when pancytopenia develops and becomes associated with the appearance of immature

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327/ 50 Fed. Reg. 50512, 50580, col. 2.

328/ Id. col. 1.

cells, or with inappropriate elevations or monocytes, basophils, or eosinophils, "the findings must be regarded as evidence of benzene overexposure unless proved otherwise."329/ Although benzene exposure is one possible cause of such findings, it is not necessarily the most likely. The statement should be modified to provide that "the findings must be regarded as evidence of benzene overexposure if there are no other plausible or more reasonable explanations."

c. Various Other Statements in the Guidelines Should Be Altered in the Interest of Accuracy.

To avoid implying that a single observation is sufficient, the third sentence of subsection V.B.1. should specify that a "persistent decline from a normal to a subnormal" red cell count is indicative of potential toxicity. Also, the succeeding statements specifying normal values should be replaced with one that reminds the physician that a normal white count varies (1) among individuals, (2) in the same individual from day to day, and (3) from one laboratory to another. The determination of "abnormal" should be made case-by-case, based on these factors rather than through the application of absolute generic values.

If subsection d of section V.B.3. is retained, it should at least make clear whenever it cites an indicator as

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329/ Id.

evidence of benzene toxicity that the indicator is not pathognomonic. This fact is properly recognized in the second paragraph of subsection d, which provides that an increase in the proportion of band forms among the neutrophilic granulocytes "should be considered as an early warning of benzene toxicity in the absence of other causative factors (most commonly infection)."330/ Similarly, the first sentence in the third paragraph of subsection d should provide that an upward trend in the number of basophils is to be regarded as "possible evidence of benzene toxicity in the absence of other causative factors." And the last sentence of the fourth paragraph should contain the same phrase with regard to monocyte counts.

Finally, the fifth paragraph should make clear in its first sentence that acquired Pelger-Huet anomaly is an extremely uncommon indication of benzene produced injury. The subsequent sentences admit that the Pelger-Huet anomaly is sometimes hereditary and unrelated to leukemia, and that even when not hereditary, it is not invariably predictive of leukemia.331/ And OSHA acknowledges that only about two percent of leukemics exhibit the anomaly.332/ Proper emphasis would be placed on the predictive value of the Pelger-Huet anomaly if the paragraph were reworded in the following manner:

330/ Id. at 50579, col. 3 (emphasis added).

331/ Id. at 50579, col. 3 - 50580, col. 1.

332/ Id. at 50580, col. 1.

Approximately two percent of patients who ultimately develop acute myelogenous leukemia show the "pseudo" (acquired) Pelger-Huet anomaly. In this anomaly many, or sometimes the majority, of the neutrophilic granulocytes possess two round nuclear segments--less often one or three round segments--rather than three normally elongated segments. When this anomaly is not hereditary, it is often but not invariably predictive of subsequent leukemia. A finding in the peripheral blood of the acquired Pelger-Huet anomaly is therefore a serious indication of bone marrow injury that may result from benzene overexposure or other causes.