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NIOSH Comments to DOL

COMMENTS OF THE NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH ON THE OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION PROPOSED RULE: OCCUPATIONAL EXPOSURE TO BENZENE

PART 1

29 CFR 1910
Docket No. 11-059C

J. Donald Millar, M.D.
Assistant Surgeon General
Director
National Institute for Occupational Safety and Health
March 1986

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16. Abstract (Limit: 200 words) This testimony concerned the proposed rule from OSHA regarding occupational exposure to benzene (71432). The possibility that the proposed 1 part per million (ppm) benzene standard did not substantially reduce significant risk and whether a different limit should be set were discussed. The possibility of using a 1ppm Permissible Exposure Limit (PEL) with a 40 hour time weighted average instead of the 8 hour Time Weighted Average (TWA) as proposed was evaluated. The risk of developing leukemia or any other adverse health effects from exposure to benzene at the current OSHA limit was compared to the risk from exposure to alternative limits of less than 10ppm. Engineering controls were considered to be the preferred method of reducing exposure to benzene. Types of respirators for use with benzene, and methods for testing respirators were discussed. NIOSH has indicated that inclusion of a short term exposure limit must be based on whether adverse health effects have been associated with peak exposures and whether or not such exposure can be controlled. Information was provided on the level of benzene contamination in commonly used solvents. Methods for determining compliance with a benzene exposure limit of less that 10ppm were mentioned. Provisions for medical examinations and other worker related safety practices were discussed.

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NIOSH Comments on the Occupational Safety and Health Administration
Proposed Rule: Occupational Exposure to Benzene
Docket No. 11-059C

The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Occupational Safety and Health Administration's Proposed Rule: Occupational Exposure to Benzene [50 FR 50512], and we offer the following comments in response to the specific issues raised in this proposal.

1. Does OSHA's proposed 1 ppm benzene standard substantially reduce significant risk and is it feasible and appropriate? Should a different exposure limit be set, and what are the reasons?

NIOSH believes that a reduction of the existing OSHA Permissible Exposure Limit (PEL) of 10 parts per million (ppm) to a PEL of 1 ppm will reduce the risk of developing leukemia. However, NIOSH also believes that a PEL of 1 ppm as an 8-hour time-weighted average (TWA) in the absence of a limit on short-term exposures will not provide the level of protection sought by the proposed rule.

NIOSH made a recommendation to OSHA for a benzene standard in July 1977. At that time, Edward J. Baier, Deputy Director of NIOSH stated:

> "We recommend that occupational exposure be controlled so that no worker will be exposed to benzene in excess of a ceiling concentration of 1 part per million parts of air (ppm) (3.2 milligrams per cubic meter of air). Current sampling technology dictates that samples be collected by charcoal tube at 1 liter per minute for one hour. This one hour sampling time is one-half that which was proposed by NIOSH in its update recommendations of 1976."

Since 1977, NIOSH has provided additional data to OSHA that indicate a further reduction in the PEL may be necessary to adequately protect workers from developing leukemia as a result of benzene exposure. At OSHA's request, NIOSH conducted a study (Susten et al., 1985) to determine the extent of dermal absorption of benzene. In addition, NIOSH has also made estimates of the risk of developing leukemia as a result of benzene exposure (Rinsky et al., 1985) using the epidemiologic data obtained from a cohort of rubber hydrochloride workers.

In support of NIOSH's position, data are described on pharmacokinetics, evidence of cytotoxicity, results from long-term exposures, results from short-term exposures, and the role of skin absorption to the overall exposure to benzene.

Parke and Williams (1953) reported that two days after gastric intubation of C^{14} labelled benzene to rabbits that 80% of the radioactivity could be accounted for in expired air or as urinary metabolites; thus as much as 20% of the initial dose may have remained in the body either as benzene or its metabolites.

Berlin (1985) has also presented data that demonstrate the slow removal of benzene from the body in which he described the results of an experimental study of human volunteers experimentally exposed to benzene by inhalation. The subjects were exposed at 4 ppm or 8 ppm for 6 hours a day for 5 days. In order to determine the kinetics of removal of benzene, Berlin determined the concentration of benzene in expired air. Berlin concluded that the kinetics of benzene removal appear to involve distribution and removal from at least two body compartments. Removal from the first compartment was relatively rapid, having a half time of about 2.5 hours; however, removal from the second compartment was much slower, having a half time of about 24 hours.

The implication of these two sets of data is clear; benzene or some of its metabolites persist in the body following inhalation exposure. Over a workweek, a worker exposed to benzene may not be able to eliminate all of the benzene absorbed during the workshift. Thus, NIOSH concludes that once benzene enters the body, it is removed slowly and may persist either unchanged or as metabolites and that, therefore, cumulative dose is a major consideration in arriving at a recommended exposure limit.

In June of 1985 the Chemical Industry Institute of Toxicology (CIIT) provided a copy of a manuscript to OSHA that described the cytogenetic effects of benzene exposure on rats and mice. In their study, CIIT investigators exposed groups of DBA/2 mice (5 mice per group) to benzene by inhalation at concentrations of 10 ppm, 100 ppm, or 1,000 ppm for 6 hours. Groups of 5 Sprague Dawley rats were also exposed for 6 hours to benzene at 0.1 ppm, 0.3 ppm, 1 ppm, 3 ppm, 10 ppm, or 30 ppm. Lymphocytes were cultured for sister chromatid exchange (SCE) analysis as well as for the determination of micronuclei; slides of bone marrow were also prepared.

Results obtained from the mouse studies revealed exposure-related increases in the frequency of SCE's and micronuclei at all exposure concentrations. In rats exposed

to benzene at 3 ppm, 10 ppm, and 30 ppm, the frequency of SCE's was also exposure related and statistically significant when compared to controls. The results obtained from rats exposed at 1 ppm were described by the investigators as having borderline significance since they were statistically significant as determined by the Student's t-test but not statistically significant as determined by the Mann-Whitney U test.

The CIIT results are significant from several points of view. First, they demonstrate the cytotoxicity of benzene, an event that may be associated with the induction of cancer. Second, the results obtained at 3 ppm are well below the existing OSHA standard. Third, the effect was observed after only a single exposure to benzene in air, as compared to the day-in and day-out exposure for workers.

In pointing out that these results need confirmation by results obtained from humans, they CIIT investigators state:

> "The present study accurately defines the shape of the dose response curves for these cytogenetic endpoints and indicates that a 6-hour exposure to concentrations of approximately 1 ppm BZ (benzene) and above can induce measurable cytogenetic effects in rodents."

NIOSH has recently received a final report on NIOSH Grant 5R03OH01713-02 (Attachment 5). The results described in this report have bearing on the issue of a PEL for benzene since the effects described below were observed following exposure to benzene concentrations at and below the current OSHA PEL of 10 ppm. In that study, mice were exposed in utero to benzene at 5 ppm, 10 ppm, and 20 ppm for 6 hours/day for 10 consecutive days on days 6 through 18 of gestation. In summary, the investigators reported no evidence of maternal toxicity as a result of benzene exposure, but several indicators of hematopoietic toxicity were observed among fetal animals exposed at 5 ppm, 10 ppm, and 20 ppm. In addition, some of the indicators of toxicity persisted in 2-day old neonates. Furthermore, in adult male mice re-exposed to benzene at 10 ppm, 10 weeks after birth, a significant depression of bone marrow Colony Forming Unit-Erythroid was observed.

As stated previously, NIOSH has updated its study of rubber hydrochloride workers exposed to benzene. This paper was provided by NIOSH to OSHA at OSHA's request in August of 1985. The results of that paper demonstrated that for the model used by Rinsky et al. (1985) cumulative dose provides a better fit to the data obtained from the cohort of rubber hydrochloride workers than any other model.

The results of the modeling conducted by Rinsky et al. (1985), "indicate that an exponential decrease in risk of death from leukemia would be achieved by a lowering of occupational exposure to benzene. Thus, according to the model derived in the present study, a worker exposed to benzene at an average exposure of 10 ppm daily at work for 40 years would have an increased risk of dying from leukemia of 221.4 (C.I. 4.8 to 9897). If the average daily exposure were lowered to 1 ppm, the risk would decrease to 1.7 (C.I. 1.2 to 2.5). At 0.1 ppm, the risk would be nearly indistinguishable from background (OR = 1.06, C.I. 1.02 to 1.10)."

Using the Crump and Allen (1985) risk assessment which examined not only the Rinsky cohort but also the cohorts of Askoy and Dow, OSHA has determined that at 1 ppm as an 8-hour TWA there will be 5-16 excess deaths from leukemia due to exposure to benzene per 1,000 exposed workers. The Crump and Allen estimates are derived from a linear extrapolation in the low dose range; therefore, to arrive at 1 excess death per 1,000 workers exposed to benzene, an exposure of 0.0625 ppm to 0.2 ppm as an 8-hour TWA would be required. This estimate compares favorably with that of Rinsky et al. (1985).

NIOSH recognizes that there are a number of assumptions and caveats inherent in the modeling performed by Rinsky et al. (1985). Among these are the fact that the environmental data used is incomplete, and therefore where gaps in measurement existed, estimates were constructed. Furthermore, the data that did exist probably did not account for exposures caused by any spills or leaks that may have occurred. It is also important that the potential for skin absorption was not examined. It is also possible that the workers in the pliofilm department were exposed to benzene in other departments where they may have worked.

Acknowledging these caveats: (1) there is a positive exposure-related increase in leukemia among the workers described in this study; and (2) the linear extrapolation described by this model indicates that even at a benzene exposure of less than 1 ppm for 40 years, there is a risk of developing leukemia.

The historical prospective study by Wong (1983) reviewed by OSHA in the proposed rule is also important in deriving an exposure limit for benzene. In his study, Wong (1983) found that chemical plant workers intermittently exposed to peak benzene concentrations of less than 25 ppm had a relative risk of about 3.4 for death from lymphatic and hematopoietic cancer. This study is also limited by the lack of detailed

historical exposure data, but as Wong (1983) describes this problem was partially dealt with by classifying benzene-exposed workers into groups having uniform tasks for which current benzene exposures could be determined.

There are several other aspects of the Wong (1983) study that are notable. A statistically significant dose-response relationship between leukemia as well as all lymphopoietic cancer and cumulative exposure in ppm · months was found. Secondly, the job of each member of the exposed cohort in this study was characterized by an 8-hour TWA as well as a peak benzene exposure.

Recognizing that the workers examined in this study may have had exposures to other chemicals in addition to benzene, Wong (1983) compared the results of the benzene-exposed workers to those obtained from workers in other areas of the plant where benzene was not present. Such an approach should in the opinion of NIOSH reduce the potential for confounding of results.

In summary, the pharmacokinetic data, the evidence of cytotoxicity, and the results of recent epidemiologic studies of workers exposed to benzene by inhalation provide a consistent basis upon which to predicate a recommendation for a new PEL for benzene.

While the OSHA proposed standard of 1 ppm does in fact "substantially reduce the risk of leukemia," NIOSH believes that the 5-16 deaths per 1,000 workers that would be expected based on the OSHA estimate, is far greater than warranted. Therefore NIOSH recommends that the PEL for benzene be reduced to 0.1 ppm as an 8-hour TWA and that there be a limit on short-term exposures of 1.0 ppm as determined in any 15-minute sampling period.

It is important to understand that the basis for the recommendation of 0.1 ppm is founded upon the data described above. The single exposures described in the CIIT (1985) study plays a significant role. The findings obtained from these more traditional studies are supported by the results of the modeling conducted by Rinsky et al. (1985) and Crump and Allen (1985).

The pharmacokinetic data, the data reported by CIIT and the data reported by Wong (1983) provide a basis for the recommendation for a limit on short-term exposures. The pharmacokinetic data demonstrate the persistence of benzene in the body following its inhalation. The CIIT animal data demonstrates the ability of single benzene exposures of 3 ppm

to induce cytotoxicity and the study by Wong (1983) demonstrates the ability of intermittent exposures to peak benzene concentrations of 25 ppm and less to cause leukemia.

The recommendation presented by NIOSH and the proposed OSHA standard are designed to protect against the effects of inhaled benzene, they do not account for the possibility of skin absorption.

As OSHA has recounted in the preamble to the proposed rule, the data of Susten et al. (1985) clearly demonstrate that significant benzene absorption can occur among workers who use solvents that contain about 0.5% benzene. As OSHA stated in the preamble:

> "NIOSH calculated that a worker building 150 tires per day could absorb approximately 6 mg of benzene daily through intact skin . . . . The 6 mg of benzene absorbed through the skin may be compared to an estimated 14 mg of benzene that would result from inhalation of 1 ppm over an 8 hour day."

Thus, under these conditions, a worker may absorb about 20 mg of benzene over an 8-hour shift. It should be noted that this study was conducted using a petroleum distillate that contained 0.5% benzene. If a worker is exposed to solvents containing a greater percentage of benzene, then the total amount of benzene absorbed would be greater than the 6 mg reported by Susten et al. (1985). Therefore, it is possible that any benefit derived from an airborne exposure limit such as that described by either NIOSH or OSHA will not provide full protection if workers are not protected from potential skin absorption. NIOSH concludes that when there is the potential for skin absorption, personal protective equipment and clothing that is impermeable to benzene must be provided to ensure the adequacy of the standard.

Rinsky, R.A., Smith, A.B., Hornung, R., Filloon, T.G., Young, R.J., Okeen, A.H. & Landrigan, P.J. (1985) Benzene and Leukemia: An Epidemiologic Risk Assessment. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health.

Susten, A.S., Dames, B.L., Burg, J.R., & Neimeier, R.W. (1985) Percutaneous Penetration of Benzene in Hairless Mice: An Estimate of Dermal Absorption During Tire-Building Operations. Amer. J. Ind. Med. 7:323-335.

Parke D.V. & Williams (1953) Studies in Detoxification 49. The Metabolism of Benzene Containing [^{14}C] Benzene. Biochem J., 54:231-238.

Berlin, M. (1985) Low Level Benzene Exposure in Sweden: Effect on Blood Elements and Body Burden of Benzene. Amer. J. Ind. Med., 7:365-373.

Exerson, G.L., Wilmer, J.L., Steinhagen, W.H., & Kligerman, A.D. (1985) Induction of Cytogenetic Damage in Rodents After Short-term Inhalation of Benzene: Manuscript submitted for publication and provided to OSHA June 7, 1985.

Snyder, C.A. (1985) Final Report NIOSH Grant 5R03OH01713-02.

2. Should OSHA adopt a 1 ppm PEL with a 40-hour time-weighted average instead of the 8-hour TWA proposed herein? If so, on what basis?

NIOSH does not believe that a 40-hour averaging period is supported by the health effects data.

The health effects data described in answer to question 1 clearly demonstrate that the exposure of workers to benzene must be carefully controlled so that the total dose available to workers is minimized. If a 40-hour averaging period is used, it would allow a 15-minute exposure of greater than 150 ppm. Even for an 8-hour averaging period, it is reasonable to foresee a 15-minute average exposure to benzene of about 32 ppm. Such an exposure is also similar to those reported by Wong (1983) to be associated with disease. Such an exposure, if averaged over 8-hours, would yield a TWA of 1 ppm, thereby masking the peak exposures that may have occurred.

3. What is the risk of developing cancer (leukemia) or any other adverse health effects that might arise from exposure to benzene at OSHA's current limits and from exposure to alternative limits of less than 10 ppm?

Because of the uncertainties surrounding the precise determination of workplace exposures, the time between exposure and onset of disease, the contribution of skin absorption, and the precise mechanism of the disease process, it is not possible to determine the true risk of developing leukemia as the result of exposure to benzene. Nevertheless, the Crump and Allen estimates and the estimates of Rinsky et al., discussed in answer to question 1, seem reasonable and appear to be in general agreement with each other. In addition, Wong (1983) found that chemical plant workers intermittently exposed to peak benzene concentrations of less than 25 ppm had an elevated relative risk of death from lymphatic and hematopoietic cancer.

NIOSH has reviewed OSHA's risk calculations and agrees with OSHA that a reduction in exposure from 10 ppm benzene to 1 ppm reduces the risk of mortality from leukemia. As noted in response to question 1, Rinsky et al. (1985) have calculated that an average exposure of 10 ppm for 40 years yields an odds rate (OR) of 221; at 5 ppm for 40 years, the OR is 14.8; at 1 ppm for 40 years, the OR is 1.7; and at 0.1 ppm for 40 years, the OR is 1.06. However, we believe that the question posed here by OSHA oversimplifies some aspects of the risk calculation. First, the calculation does not consider the contribution of skin absorption to the overall dose received by a worker exposed to benzene. Second, the Rinsky et al. (1985) risk estimates transmitted to OSHA in August 1985 indicate that ppm.years provides a more accurate fit to the documented mortality experience of benzene-exposed cohorts, the contribution of skin absorption was not examined. While this may not have been a problem at the higher exposures reported by the authors, it would be a factor at the exposures at the lower end of the curve. Third, neither the OSHA or the NIOSH estimates consider the contribution of peak exposures to a worker's total body burden; such consideration is suggested by the data of Wong (1983) as well as the pharmacokinetic data described by Parke and Williams, and Berlin and the data provided by CIIT.

4. What are the numbers of workers exposed to benzene; their current exposure levels; the methods of monitoring; duration and frequency of exposure; the jobs being performed; and the Standard Industrial Classification (SIC) codes for industries and processes using benzene?

In April of 1983, NIOSH provided OSHA with a number of field study reports that contained data on workplace benzene exposures. The majority of those reports were based on evaluations of the printing, refining, and chemical manufacturing industries; others described benzene exposures in hospital and university laboratories. Included in that transmittal was a report by Richard Hartle of NIOSH entitled "Occupational Exposure to Benzene at Automotive Service Stations." A copy of the letter transmitting these reports, as well as a summary of the data contained in the reports is attached (Attachment 1).

5. Which of the following control methods are available to reduce exposures to benzene to alternative 8-hour TWA's of 5, 1, 0.5, and 0.1 ppm? a. Engineering; b. Work practices, housekeeping, and administrative controls.

OSHA has asked for detailed information concerning the costs for these options and the time necessary for their implementation. While cost estimation is an area in which

NIOSH has little expertise, we feel it is important to reiterate our long standing commitment to the application of engineering controls as the preferential method for reducing exposures, regardless of the exposure limit being considered. In the case of benzene, however, it is also important to reduce or eliminate skin absorption since it may contribute to the total body burden. In some instances, this can account for an amount of benzene in the body equal to 50% of that absorbed through an 8-hour inhalation at 1 ppm (Susten et al., 1985).

6. What is the lowest feasible level of benzene exposure achievable by engineering controls and work practices? For example, can benzene exposures be reduced by present technologies to 5 ppm, 1 ppm, 0.5 ppm, or 0.1 ppm?

Attachment 1 provides data in response to this question. Once again, however, we reiterate our concern for the contribution of skin absorption to the total body burden of benzene.

7. What are the capital and operating costs to achieve those lower exposure levels? Are those costs economically feasible for the affected industries? How would the time allowed to install these engineering controls affect these costs?

NIOSH has looked at specific engineering controls, and their approximate costs have been identified in several NIOSH Control Technology Assessments. Copies of these reports are provided for the purpose of identifying feasible engineering controls.

8. What is the appropriate compliance strategy utilizing engineering controls, work practices, and respirators for reducing exposure to benzene?

In response to this question, NIOSH is providing OSHA with a copy of our comments submitted to OSHA in June 1983 for Docket H-160, Health Standards: Methods of Compliance (Attachment 2).

9. Are there conditions under which respirator use should be permitted in addition to those proposed?

We believe that OSHA should clarify the intent of (g)(1)(iv) which states that respirators can be used "in work situations where the employer can document that benzene is present in a work area less than 30 days a year."

In Table 1, Respiratory Protection for Benzene, OSHA will require the use of a half-mask chemical cartridge respirator with an organic vapor cartridge for exposures to benzene of

less than or equal to 10 ppm. Should OSHA choose to retain Table 1 in the final rule and accept the use of respirators other than those recommended by NIOSH, we would have additional concerns regarding the respirator portions of the standard.

Because benzene is a carcinogen, NIOSH recommends the use of only the most protective respirator. Therefore, NIOSH recommends that either a self-contained breathing apparatus with a full facepiece operated in the pressure-demand mode or a Type C supplied-air respirator with a full facepiece operated in the pressure-demand mode, in combination with an auxiliary self-contained breathing apparatus operated in the pressure-demand mode, be used.

Should OSHA choose to retain Table 1 in the final rule, we have other concerns. OSHA proposed to allow powered air-purifying respirators (PAPR's) with full facepieces in concentrations up to 100 times the standard. Results of NIOSH and other's research suggest that a workplace protection factor of this order is inappropriate and excessive.

Only PAPR's with full facepieces are allowed in this draft standard. Why then is there a need to specify airflow rates for PAPR's with loose fitting hoods or helmets? Since PAPR's have minimum airflows of 115 Lpm (tight fitting) and 170 Lpm (loose fitting), cartridge/canister tests must be run at the actual airflow of the device. A challenge concentration of 150 ppm at 64 Lpm and a service life of 4 hours may not ensure that a PAPR running at its normal airflow rate and used for protection at 100 ppm will last one full shift. This is particularly true since the initial operating airflow rate of the PAPR may be over 400 Lpm. Since benzene is not considered to have adequate warning properties, test protocols must be severe enough to thoroughly ensure the safety of the PAPR.

A worker's environment may contain solvent vapors other than benzene. Thus, the canister's sorbent will adsorb these vapors as well and shorten the life of the canister. Therefore, changing cartridges or canisters on a daily basis does not assure protection from overexposure.

The inclusion of qualitative and quantitative fit test methods as examples of test protocols that OSHA will accept is preferable to limiting acceptance to only those tests listed in the regulation. The way the regulation is written now, improved test methods developed in the future cannot be accepted.

In paragraph (h), OSHA requires that protective clothing and equipment be provided by the employer. NIOSH recommends that OSHA modify the first sentence to read: "Personal protective clothing and equipment which has been selected based on data obtained from tests of the material against benzene or any benzene-containing solvent in use in the workplace shall be worn where appropriate and provided by the employer."

10. Are there any unique conditions in work settings where benzene is produced or used where feasible engineering controls are not available?

NIOSH has no comment.

11. Have there been technological improvements or changes in the production or use of benzene for the purpose of improving productivity or product quality which have also resulted in reductions in benzene exposures?

NIOSH has no comment.

12. What are the appropriate scientific and industrial hygiene principles to determine whether a short-term exposure limit should be incorporated into a standard? Does the evidence available indicate that a STEL should be included in this benzene standard? If so, what should that short-term limit be?

As OSHA pointed out on page 50554 of the preamble to the proposed rule, NIOSH has previously provided OSHA with our opinion on the issue of short-term exposure limits. In summary, inclusion of such a limit must be based on whether adverse health effects have been associated with peak exposures and whether or not such peak exposures can be controlled. NIOSH believes that the health effects data recounted by OSHA clearly demonstrate the need for a limit on short-term exposures. As stated, in response to question 1, NIOSH recommends that short-term exposures to benzene not exceed 1 ppm as determined in any 15-minute sampling period.

The NIOSH responses to questions 1, 2, and 3 above are also germane to this issue.

13. What is the level of benzene contamination in petroleum naptha, toluene, xylene, and other solvents currently in use?

Data contained in the Industrial Solvents Handbook indicate that the benzene content of various solvents range from 0.01%

to 0.6%. Recent field data collected by NIOSH indicate that benzene content in unleaded gasoline varies between 0.3% and 1.4% with a mean of 1.0%. This indicates that benzene content in gasoline appears to be decreasing compared to data obtained in 1978 and provided to OSHA in 1983 (Attachment 1). The 1978 data demonstrate a range of 0.5-2.3% with a mean of 1.3%.

14. What processes are available to reduce benzene contamination in solvents? To what levels can benzene contamination be reduced in solvents, and what are the economics of those processes after reaching large scale production?

NIOSH has no comment.

15. What measurement and analytical methods are available for use in determining compliance with a benzene exposure limit of less than 10 ppm?

NIOSH analytical methods 1500 and 1501 are attached (Attachment 3). Method 1500 has been validated by NIOSH for use in determining 8-hour TWA exposures over the range of about 5 ppm to about 20 ppm. Method 1501 is preferred for determination of peak, ceiling, and TWA determinations and has been validated by NIOSH over the same range as method 1500.

Although the current NIOSH method has not been officially validated at levels below 5, it is our opinion that the method can be used at concentrations as low as 0.5 ppm. The Health and Safety Executive (HSE) of the United Kingdom has recently published "DHS 50; Benzene in Air" (Attachment 4). This method is described as being useful over the range of less than 0.1 ppm to about 100 ppm for 8-hour TWA determinations as well as 10-minute determinations.

According to the HSE, the method is ". . . suitable for the measurement of airborne benzene vapour in the concentration range of 3 to 300 mg/m^{-3} (about 1 to 100 ppm, V/V) for exposure times between 10 min. and 8 h. This range may be extended to 0.3 mg/m^3 or lower for 8-h sampling periods."

16. Is it necessary to establish provisions for medical examinations, respirators, personal protective clothing and equipment, hygiene facilities and practices, regulated areas, maintenance of records, housekeeping employee information and training, and labels and signs? What form should such provisions take in the final standard? To what extent are these provisions currently being employed by industry and what are their costs?

NIOSH has reviewed some of the existing literature concerning the efficacy of medically screening workers exposed to benzene

as an aid in prevention of disease. Goldstein (Assessment of Toxic Agents at the Workplace) recommends a preexposure hematologic assessment, with quarterly examinations of the complete blood count thereafter, paying particular attention to increases in the mean corpuscular volume and decreases in the lymphocyte count. Goldstein discounts the value of routine monitoring of the urine of workers for phenol, a metabolite of benzene, but monitoring for urinary phenol is only a minor subject in his presentation. Goldstein does not propose a modification of his recommendations dependent on the level of exposure of the workers.

Lauwerys has described monitoring urinary phenol as an indicator of benzene exposure but only cursorily discusses the value of hematologic monitoring (Human Biological Monitoring of Industrial Chemicals Series, CED). Lauwerys suggests that peripheral blood analysis of workers exposed to benzene is not useful as a measure of exposure but can be used to detect those who might be particularly susceptible to the myelotoxic action of benzene. Lauwerys believes that while two tests, urinary monitoring for phenol and measurement of benzene concentration in exhaled air, may be valuable for evaluating current exposure, benzene is not the sole source of phenol and that at very low exposures "(cumulative total less than 1 ppm, i.e., 0.15 ppm for 8-hrs), this technique is not sensitive enough for confirming exposure. For integrated exposure exceeding 10 ppm x h (cumulative total) the correlation between phenol excretion and benzene exposure is only valid on a group basis."

The position of NIOSH on a recommendation for biological monitoring would be more easily understood by putting it in the context of a "continuum of prevention" (Halperin) of benzene toxicity. The first and by far the best means of preventing benzene toxicity is to adequately control exposure and insure that the controls are effective by environmental monitoring. In NIOSH's view, the current OSHA proposal fails to satisfy this requirement because of the lack of a limit on short-term exposures and the possibility of cutaneous exposure.

If controls are ineffective or there is significant skin absorption, biological monitoring of the worker to determine the presence and amount of benzene or its metabolites in an exposed worker's body may have benefit. Although there is data that demonstrate the value of urinary phenol in such a situation, the literature also indicates that, as expected, as exposure concentration decreases the correlation between urinary phenol and benzene exposure concentrations also decreases. If environmental benzene exposures are controlled to at least 1 ppm with an appropriate limit on short-term exposures and if cutaneous exposure is controlled, then

urinary phenol monitoring would not have predictive value. Urinary monitoring for determination of phenol would be valuable for detection of an unacceptable exposure. Therefore, under a circumstance of suspected airborne exposure of at least 10 ppm or when skin absorption is suspected to have occurred, OSHA should require monitoring for urinary phenol and specify remedial actions, such as removal from exposure, and determination of the source exposure.

Next in the continuum of prevention is medical screening, also called medical surveillance or periodic testing. The purpose of medical screening is to identify early signs and symptoms of disease in a worker. When medical screening is conducted as part of the preexposure examination, it can help detect individuals with an increased susceptibility to adverse health effects as a result of exposure.

In summary, Goldstein and Lauwerys agree that hematologic screening may be a valuable tool for the identification of those individuals who will demonstrate marrow toxicity. Neither proposes that hematologic testing will prevent leukemia or aplastic anemia. It is implicit in their discussions, however, that suppression of hematologic function is an adverse effect to be prevented in itself. This is particularly true if the natural history of some cases of leukemia and aplastic anemia indicates that these diseases have occurred among workers who have demonstrable depression of marrow function. The relevant question then in deciding whether to conduct hematologic testing is the level of exposure in the population to be screened and the probable incidence of hematologic abnormality from the literature that can be expected to occur as a result of that exposure. Although not discussed by either Goldstein or Lauwerys, because monitoring is conducted on the assumption that some workers exposed at even so-called "acceptable levels" may exhibit an adverse biologic response, NIOSH believes that all monitoring data should be made available for epidemiologic analysis so that OSHA can use this data to target inspections and compliance activities to those companies, industries, or occupations with the worst health experience.

While the literature on the relationship of hematologic abnormalities and benzene is extensive, only two articles allowed us to calculate the effectiveness of these tests in detecting the adverse effects of benzene. In both of these studies, workers were exposed at benzene concentrations that are unacceptable. In the Askoy report, workers were exposed at 30-210 ppm for 3-17 years. In the report by Goldwater, workers were exposed at 11-1060 ppm for 6 months to 3 years. There have been several articles examining longitudinal screening data of workers exposed at lower benzene

concentrations (Townsend et al., 1978 and Hancock, 1984). Unfortunately, these investigators examined either average or more recent hematologic values rather than making a determination of the actual values existing at the time benzene exposure occurred.

From the Goldwater and Askoy reports, we calculated sensitivity as the prevalence of an abnormal test in those exposed, specificity as the prevalence of a normal test in the nonexposed, and predictive value as the probability that an abnormal positive test is from an exposed rather than unexposed individual. In the Goldwater report, 14% of the exposed had a white blood cell count (wbc) of less than 5,000 as compared to 0% in the nonexposed. Depending on certain assumptions, the predictive value of wbc's was between 85% and 99%. Similarly, for erythrocyte counts the sensitivity was 48%, specificity 97%, and predictive value between 95% and 97.4%. For platelet count, the sensitivity was 62%, specificity 82%, and predictive value between 77% and 98%. Thus, based on analysis of Goldwater's data, common hematologic tests are sensitive specific and predictive following exposures in the range of 11-1060 ppm. Askoy did not report the distribution of results derived from control subjects, and therefore specificity was not calculable. Nevertheless, based on his finding that 9.7% of the exposed workers had a wbc count of less than 4,000, the sensitivity of the wbc is calculated to be approximately 10% and predictive value is 80% (assuming 2.5% of controls with wbc less than 4,000 and equal population size). For platelets, the sensitivity is 2% and predictive value is 42% (assumptions noted above). There are no data on red blood cells, and again it must be remembered that the workers described by Askoy were exposed at 30-210 ppm.

Therefore, NIOSH concludes that at the exposure concentrations described by Askoy and Goldwater, the ability of hematologic screening tests to discern those workers with adverse effects due to exposure from those with random positive results is quite good. Unfortunately, because of the constant background of false positives in the general population, the predictive value of these tests worsens as exposure concentration decreases. Therefore, because of the lack of information on how these hematologic parameters are affected at exposure concentrations below 10 ppm, we are unable to accurately predict their usefulness. However, since the proposed standard does not include provisions for a limit on short-term exposures and because we are concerned about percutaneous absorption, NIOSH believes that the determination of formed elements of the blood contributes to the prevention of benzene-induced disease.

Askoy et al. Hematological effects of Chronic Benzene Poisoning in 217 Workers. Brit J. Industrial Med. 1971 28:296-302.

Goldwater et al. Disturbances in the Blood Following Exposure to Benzol. J. of Lab and Clin Med. 26:957-964, 1941.

Hancock DG and Moffitt AE. Hematological Findings Among Workers Exposed to Benzene at a Coke Oven By-product Recovery Facility. Arch. Environmental Health 39:414-418, 1984.

Townsend et al. Health Exam Findings Among Individuals Occupationally Exposed to Benzene. J. Occup. Med. 20:543-548, 1978.

17. In order to perform an economic feasibility analysis, it is helpful to have a financial and economic profile of the industries producing and using benzene. The following information is requested to aid in the preparation of that profile. Data should be provided for the last five years. Data already submitted to OSHA or JRB need not be resubmitted.

NIOSH has no comment.

18. OSHA and JRB have performed detailed feasibility analyses for the industry sectors where impacts would be significant and OSHA believes that impacts in other segments would not be substantial. Comments are requested from any other industry segments on additional impacts which should be considered prior to issuing a final standard.

NIOSH has no comment.

19. The benzene record includes copies of the Regulatory Impact Analysis and the JRB report, and this document presents OSHA's feasibility analysis. Comments are requested on those analyses, the feasibility and the cost-effectiveness of the proposed standard and alternatives.

NIOSH has no comment.

20. The Agency has prepared a draft Regulatory Flexibility Analysis analyzing the impacts of the proposed standard on the small businesses which OSHA believes may be affected and adapting the proposed standard to take into account the circumstances of small business where appropriate. The following information is requested for small businesses in addition to the information OSHA has gathered.

NIOSH has no comment.

21. The National Environmental Policy Act (NEPA) of 1969 (42 U.S.C. 4321 et seq.) requires that each Federal agency consider the environmental impact of major actions significantly affecting the quality of the human environment. Any person having information, data, or comments pertaining to possible environmental impacts is invited to submit them and accompanying documentation to OSHA.

NIOSH has no comment.

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