American Journal of Industrial Medicine 27:661–676 (1995)

Benzene Exposure Assessment in Rubber Hydrochloride Workers: A Critical Evaluation of Previous Estimates

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Many risk assessments for leukemia associated with benzene exposure have been based on the mortality experience of the rubber hydrochloride worker cohort. Although there have been several different historical exposure assessments proposed for this cohort, Paustenbach et al. [1992, J Tox Environ Health], recently published a new historical characterization of benzene exposures based on data previously developed by Rinsky et al. [1981, Am J Ind Med] and further modified by Crump and Allen [1984: OSHA]. Adjustments by Paustenbach et al. in the Rinsky et al. data result in retrospective benzene exposure estimates far greater than those previously reported, by an order of magnitude in many cases. Judgments made on the significance of dermal contact and interpretation of historical measurement data led Paustenbach et al. to arrive at exposure estimates for this cohort that are in conflict with what is known about the adverse effects of benzene exposure. More reasonable estimates for dermal absorption are included in this report that do not substantially affect total estimates of benzene exposure for the cohort. The exposure estimates originally presented in the Rinsky et al. article appear in concordance with data not previously reported in any analyses. © 1995 Wiley-Liss, Inc.*

Key words: benzene, leukemia, rubber hydrochloride, retrospective exposure assessment, risk assessment

INTRODUCTION

Observed excess leukemia cases in several epidemiologic studies [Aksoy et al., 1974; Vigliani, 1976; Infante et al., 1977; Rinsky, et al., 1981; Ott et al., 1987; Yin et al., 1987] have resulted in the classification of benzene as a human carcinogen. Since its appearance in the *American Journal of Industrial Medicine* in 1981, the cohort of rubber hydrochloride (RH) workers has been at the center of risk assessment conducted to evaluate the role of benzene exposure in the development of leukemia. A number of subsequent analyses have examined the results of both the original and

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Accepted for publication July 12, 1994.

the updated RH worker cohort studies in an attempt to establish an acceptable level of occupational and environmental exposure to benzene.

For the most part, the subsequent research accepted the retrospective exposure performed by NIOSH or put forth an alternative historical exposure scheme based on simpler assumptions. After 1992, however, several analyses of this cohort were based on a retrospective exposure assessment performed by Paustenbach et al. [1992], which claimed to be a more exhaustive and accurate characterization of the benzene exposures experienced by members of the cohort. The exposure reconstruction by Paustenbach et al. [1992] was substantively different from those previously suggested by NIOSH and others, in that rubber hydrochloride workers were assigned much higher personal exposures, sometimes more than an order of magnitude higher.

It is generally believed that no better cohort of benzene workers exists in the United States on which to base an assessment of risk. Therefore, historical exposure estimates for this cohort are of paramount importance in calculating risk of leukemia following benzene exposure. If the reanlaysis by Paustenbach et al. [1992] does indeed represent a more accurate reconstruction of historical exposures for these workers, then the calculated estimate of risk per unit dose of benzene will be substantially lower than previously estimated.

In fact, such new analyses were presented at the ACGIH TLV Committee meeting in 1994 where a proposed reduction to the benzene TLV was being considered. Crump [1992], Paxton et al. [1994], and Spirtas [1993] all developed risk estimates based on the Paustenbach et al. [1992] dose reconstruction that were less than those based on the Rinsky et al. [1981] and Crump and Allen [1984] retrospective exposure estimates. Similar reanalyses appeared at a meeting of the International Program on Chemical Safety in Hannover, Germany, at the time the IPCS Benzene Environmental Health Criteria Document was being drafted [WHO, 1993]. Other researchers have accepted the claim of Paustenbach et al. [1992] that theirs was indeed an improved dose reconstruction [API, 1993; Beatty, 1993; Paxton, et al., 1994a,b].

CRITIQUE OF PREMISES

This report critically examines the premises set forth by Paustenbach et al. [1992]. As with all retrospective exposure assessments where actual monitoring data are incomplete, Paustenbach et al. were required to make assumptions about work practices, engineering controls, and numerous other factors that affect derived benzene exposure estimates. They use several lines of reasoning for increasing the benzene exposure estimates previously reported by Rinsky et al. [1981] and Crump and Allen [1984]. These upward adjustments are justified on the basis of: (1) inaccuracy of benzene analytical methods employed for historical measurements, (2) estimated length of the work week at two of the three plants where RH film was manufactured, (3) installation and use of exhaust ventilation controls, (4) benzene absorption through the skin of workers in the cohort, (5) selection and use of respirators by the workers, and (6) evidence of overexposure in available medical information for the plants. Paustenbach et al. [1992] also indicate that shortages of rubber during World War II would have led to decreased RH film production at one of the plants so that they decreased previously estimated benzene exposure concentrations at this plant for a 4-year period.

Paustenbach et al. [1992] state that their estimates are "better" and "more plausible" than those derived by Rinsky et al. [1981] and by Crump and Allen [1984]. However, a careful examination of their report clearly shows *annual average* benzene exposure concentrations in excess of 250 parts per million (ppm) for one job title and ~150 ppm for several others. Many of these estimated exposures reportedly lasted for years. The predicted benzene exposures for the two most highly exposed job categories extended over a decade.

Sustained exposure to benzene at the levels derived by Paustenbach et al. have been known for almost a century to cause severe blood dyscrasia, including pancytopenia and aplastic anemia [LeNoir, 1897; Snyder et al., 1993]. The benzene exposure concentrations predicted by Paustenbach et al. would likely have caused an epidemic of fatal nonmalignant blood disorders in this cohort of workers [WHO, 1993]. Yet none was observed [Infante et al., 1977; Rinsky et al., 1987]. In the cohort, only one worker died of aplastic anemia and that was in 1966. This 64-year-old man had worked in the rubber hydrochloride department from 1943 to 1965.

Paustenbach et al. [1992] supported their claim of elevated benzene exposures among the RH cohort in the early 1940s based on the study of the 1,104 benzene-exposed workers in the rubber industry published by Wilson [1942] and discussed in the proceedings for a Department of Labor conference on hazards in the rubber industry in 1942. According to the conference proceedings, the 1,104 employees were exposed to "more than 100 ppm of benzol over 'any considerable period of time.'" Paustenbach et al. conclude from this statement, however, that the benzene exposure concentrations were 150 ppm or greater for "some members of the Pliofilm work force."

NIOSH records indicate that through the end of 1942, the year of the Department of Labor conference, a total of only 164 workers had been employed in the RH plant. Therefore, the entire RH population would constitute only a fraction of the 1,104 workers described in the conference proceedings. The number of RH workers among the 1,104 employees and their overall health experience remains uncertain, although one of the three fatalities from aplastic anemia among the 1,104 rubber workers was reportedly from the RH plant.

More recently assembled information [WHO, 1993] makes it seem implausible that annual average benzene exposures in excess of 100 ppm were commonplace across the 1,104 workers in the study or in the rubber hydrochloride plants. According to the WHO document, that level of benzene exposure would result in a case incidence rate for aplastic anemia of ~10%. Less than 2.3% of the 1,104 workers in this study had developed aplastic anemia. If annual average benzene exposure concentrations of 150 ppm or greater were routine as purported by Paustenbach et al., a case incidence rate for aplastic anemia much greater than 10% would be anticipated.

Within the confines of this report, it is not possible to address all of the issues raised by the Paustenbach et al. [1992] retrospective exposure assessment. For the sake of brevity, only five lines of reasoning that are problematic are critically reviewed here. These include their: (1) review of the use of engineering controls in rubber hydrochloride plants, (2) assertion that dermal exposures to benzene substantially added to the total body burden, so that estimates of exposure should be adjusted upward, (3) series of arguments that actual measurement data reflect "background" concentrations instead of peak exposures, (4) contention that the methods used to estimate exposure concentrations in the early years were biased low, and (5) their application of a method developed by Crump and Allen to make TLV-based adjustments to more recent exposure measurements in order to estimate early exposure concentrations.

Evidence of Engineering Controls

The Department of Labor conference proceedings [1942] are quite informative about the use of local exhaust ventilation in the rubber hydrochloride plants. Just two paragraphs after the discussion of health effects in the 1,104 employees exposed to benzene, the plant physician states, ''At present benzol is used in the manufacture of pliofilm but in an enclosed system. Hooded ventilation with negative pressure is installed over all spreaders.'' Control of benzene emissions from the spreaders was provided by ''hooded ventilation with suction above and forced general draft ventilation in the room.'' Concentrations of benzene in the vicinity of the RH spreader units was stated in the proceedings to be controlled to a level ''in the neighborhood of 20 to 60 parts per million.'' The proceedings further mention ''earlier unsuccessful attempts to remove benzol fumes with downdraft ventilation only.''

Remarkably, the benzene concentration range and the ventilation controls are never mentioned in the Paustenbach et al. article, even though the concentration range is the only report of airborne benzene concentrations associated with the rubber hydrochloride industry prior to 1946. (The proceedings of this conference were not cited in the previous exposure assessments by Rinsky et al., 1981, and Crump and Allen, 1984.) Further, the explicit mention of two successive ventilation systems in the rubber hydrochloride plants in the conference proceedings conflicts with several Paustenbach et al. statements, such as ''only general division ventilation was provided'' and ''the general (dilution) ventilation system that was designed into the St. Marys process'' in 1946 ''was the first engineering control measure installed at a Pliofilm facility.''

Paustenbach et al. also state: ''In November 1946, following cases of benzene toxicity observed at St. Marys, management apparently embarked on a major program to reduce airborne concentrations of benzene.'' The source of this information is attributed to Fluker [1946]. The Industrial Commission of Ohio report by Fluker actually states that ''extensive exhaust equipment has recently been installed for the elimination of benzol vapors generated by presses'' and that ''tests were made with benzol detectors and the results indicate that concentrations have been reduced to a safe level and in most instances range from zero to 10 or 15 parts per million.'' There is no mention of the ''major program to reduce airborne concentrations of benzene'' that Paustenbach et al. claim to have occurred in 1946. Such an effort apparently occurred prior to 1942 according to the Department of Labor conference proceedings.

Paustenbach et al. also state in reference to the 1946 testing of the ventilation system that ''only a single air sample was collected at the filters before engineering controls were installed, and the concentration was 250 ppm. Samples collected several years later after engineering controls showed levels of 19–50 ppm (Rinsky et al., 1981). The state of Ohio concluded that the filter-press ventilation system was sufficient to maintain benzene concentrations below 100 ppm and typically below 35 ppm (Fluker, 1946).''

We have been unable to locate any measurement near 250 ppm in the reports associated with the rubber hydrochloride industry prior to 1949 except one detector tube measurement in a storage room dated October 11, 1946 [Rinsky et al., 1981].

The storage room, however, was not the location of the filters in question. Paustenbach et al. do not document any additional monitoring data beyond those previously cited in the literature [Rinsky et al., 1981].

Most importantly, however, the Fluker report states "concentrations have been reduced to a safe level and in most instances range from zero to 10 or 15 parts per million." There is no mention in the Fluker report of "benzene concentrations below 100 ppm and typically below 35 ppm" attributed to the Fluker report by Paustenbach et al. The benzene concentrations of 10–15 ppm related to this process in 1946 reported by the state of Ohio appear relatively consistent with measurements of 6–10 ppm at this location in 1974 and 1975 as indicated in the previous NIOSH exposure reconstruction.

Paustenbach et al. [1992] have apparently overlooked important information in the literature related to the use and testing of control ventilation in the rubber hydrochloride plants even though they extensively cite other information from the very same page of that source. The oversight results in broad claims of knowledge on the part of Paustenbach et al. over when control ventilation systems were installed in these plants during the 1940s that directly conflict with these same sources. The benzene concentrations in the rubber hydrochloride plants reported by the state of Ohio in 1946 and by the employer representative at the 1942 Department of Labor conference are very similar to the benzene exposure concentrations determined by Rinsky et al. [1987] for this period of time. Rinsky et al. developed these concentrations based on interviews with management and workers in the rubber hydrochloride plants and without the benefit of the 1942 Department of Labor report.

Dermal Absorption

Paustenbach et al. developed a model to calculate the amount of benzene absorbed through the skin of exposed RH film workers. Their model is:

$$M = X \times N \times A \times t \times R$$

where M is the total mass absorbed and is the product of the molar concentration of benzene (X), number of contacts per day (N), surface area of skin contact (A), duration of the contact (t), and rate of absorption of benzene per unit skin area per unit time (R). The estimated mass absorbed through the skin is converted to an estimate of the equivalent airborne concentration of benzene by:

$$C = M / (K \times R \times B)$$

where C is the estimated airborne concentration in ppm and is equal to the mass absorbed dermally (M) divided by the product of respiration rate (R), which is set at 9.6 cubic meters per day, the inhalatory retention of benzene (B), which is estimated at 50%, and a constant (K), 3.2 mg/m^3/ppm, to convert from mass per volume to ppm. According to Paustenbach et al., equivalent airborne concentration calculations allow the dermal exposure estimates to be added to the respiratory exposure estimates. However, several problems exist in the application of this model.

Paustenbach et al. state: "Based on worker interviews and other records, we have been able to identify several points in the RH process that required employees to have significant dermal contact with benzene." (The authors never specify what other records were used.) They further state: ''Hanke et al. (1961) showed that liquid benzene passed through the arms of human volunteers at a rate of 0.4 mg/cm^2/h. Research in animals has reached similar conclusions (Franz, 1984; Maibach and Anjo, 1981). The work of Hanke et al. (1961) is believed to be the best one to use to estimate doses received from dermal exposure since the rate was determined in workers' forearms over a period of 1.5–2 h.'' An evaluation of the literature cited by Paustenbach et al. may lead to an alternative and perhaps more reasonable conclusion.

Hanke et al. [1961] actually report two estimates for the absorption of benzene through the skin of humans, 0.24 and 0.4 mg/cm^2/h. The first was based on urinary excretion of phenol, a metabolite of benzene. The second estimate was determined by measurement of residual benzene that was applied to the surface of the skin but not absorbed. Hanke et al. [1961] very clearly state in their original work: ''It should be noted that the results given here concerning the absorption rate of liquid benzene by the skin refer to an extreme case, where the skin of the exposed subject is totally saturated with benzene at the contact site; therefore, they are maximal values.''

In the Maibach and Anjo [1981] work cited by Paustenbach et al. [1992], the same conclusion was reached regarding the work by Hanke [1961]. Maibach and Anjo state: ''Hanke et al. employed analytical methods sufficiently sensitive to detect benzene absorption, although not sufficiently precise to accurately quantitate that absorption.'' ''The results indicate that urinary phenol was elevated in individuals dermally exposed to benzene (maximum value of 1.58–28.3 mg/L as compared to a maximum of 16.0 mg/L in nonexposed individuals). Large variations in experimental values occurred among individuals.''

Maibach and Anjo [1981] further state: ''In spite of deficiencies cited and the limited precision, the similarity of results obtained by the two independent methods used by Hanke et al. is at least indicative of an absorption rate upper limit of less than 0.24 to 0.4 mg/cm^2/hr for the severe conditions of exposure employed. These conditions involved continuous exposure by direct contact with 100% benzene and surface occlusion for 1.25 to 2 hr. Respecting the occlusion, the occlusive effect employed by Hanke et al. may have had the effect of increasing the reported absorption rate more than 10-fold.''

Despite these warnings by Hanke et al. [1961] and by subsequent researchers, Paustenbach et al. [1992] chose to use the maximum value, 0.4 mg/cm^2/h, which had been characterized as ''an extreme case'' [Hanke et al., 1961] and ''likely to be substantially overestimated'' and the results of ''severe conditions'' [Maibach and Anjo, 1981]. Franz [1984], in a work also cited by Paustenbach et al., estimated values of benzene absorption through human skin substantially below the rate selected by Paustenbach et al. The 0.4 mg/cm^2/hr rate selected for use in the dermal absorption calculations by Paustenbach et al. that they describe as ''the best one'' is also apparently the highest estimate that appears in the published literature.

Paustenbach et al. also appear to overestimate the potential for dermal absorption of benzene in other aspects of their model. They state that the surface contact area was 1,980 cm^2 for all dermally exposed workers, molar concentration of benzene was estimated at 0.95, the number of skin contacts per day had a range of 0.17–1, and the duration of the contact had a range of 0.2–1.5 hr. The selection of these values appears to reflect maximum possible values. More realistic estimates may also be derived.

TABLE I. Comparison of Equivalent Airborne Concentration of Benzene for Dermally Absorbed Fraction With Estimates From Paustenbach et al. [1992]

		Utterback and Rinsky				Paustenbach et al.			
Exposure category	Contacts per day	Surface area, cm^2	Duration hr/d	Uptake rate mg/cm^2/hr	Amount absorbed mg/d	Surface area, cm^2	Duration hr/d	Uptake rate mg/cm^2/hr	Amount absorbed mg/d
W'side fltr press	1	600	0.5	0.05	12.9	1980	0.5	0.4	376
D'side fltr press	1	600	0.2	0.05	5.2	1980	0.2	0.4	150
Quencher	1	600	1.5	0.05	38.7	1980	1.5	0.4	1129
Cleaning neutralizer	0.17	600	1.0	0.05	4.4	1980	1.0	0.4	128

First, Paustenbach et al. used 1,980 cm^2 for the skin contact surface area, which appears to be a substantial overestimation. With the typical 70 kg male they used, this skin contact area would include both hands and both arms from fingertips to elbows. Second, the rubber hydrochloride solution was not a 95% benzene but was diluted by rubber hydrochloride. The estimated concentration of rubber hydrochloride in benzene for job titles that Paustenbach et al. identified as having potential for dermal contact was at least 10%. If completely depolymerized, the RH would reduce the estimate of benzene concentration to a maximum of 86 mole %. At the filter press, the only job that consistently required periodic contact, the mixture was a thick slurry made mostly of solids of the rubber and soda ash. The benzene concentration here may have been even lower.

More reasonable estimates of the effect of dermal exposure on the equivalent air concentration are shown in Table I. These estimates are based on maximum likely values for the skin contact area of 600 cm^2 (equivalent to both hands), 86 mole % benzene in solution, and a dermal benzene uptake rate of 0.05 mg/cm^2/hr [Maibach and Anjo, 1981; Franz, 1984]. The contact times and frequencies of contact given by Paustenbach et al. are used for our calculations, although these again seem overestimated.

The data in Table I clearly show the effect of the more reasonable estimates for skin contact area, solution strength, and uptake rate. Differences between our estimates and those from Paustenbach et al. are due almost entirely to differences in skin contact area and uptake rates. The resulting equivalent airborne concentrations of benzene for the wetside filter press, dryside filter press, quencher, and cleaning neutralizer are 0.83 ppm, 0.34 ppm, 2.52 ppm, and 0.29 ppm, respectively. These estimates are ~3% of the values given by Paustenbach et al. of 24 ppm, 8 ppm, 73 ppm, and 8 ppm, respectively, for these same job classifications.

It is also noteworthy that the rubber hydrochloride component of the benzene solution would form a film on the surface of the skin with the evaporation of the benzene. Daily or even weekly deposition of this film on the skin of both hands and arms as suggested by Paustenbach et al. is likely to cause significant irritation. Removal of this film from the skin would probably have required either benzene or a similar solvent or very aggressive mechanical means. Wilson [1942] stated: "If there is any skin absorption, a macular dermatitis will appear at the site of exposure."

In any case, substantial changes in skin structure and irritational response would almost certainly have occurred, which would, over a short period of time, force workers to avoid skin contact with the benzene solution of rubber hydrochloride altogether. There are no reports of such irritation. It is for this reason that the frequency and duration of contact selected by Paustenbach et al. also appear overestimated.

As a result of elevated values selected for variables in the model for dermal uptake of benzene by workers in the RH cohort, the model consistently predicts elevated estimates of equivalent benzene concentration in air. Therefore, Paustenbach et al. substantially overestimate the potential for benzene dermal uptake by workers.

Representativeness of Benzene Samples

Paustenbach et al. [1992] contend that historical benzene concentrations that were measured with detector tubes and combustible gas indicators (CGI) are representative of "background" or average concentrations in the RH plants areas. This assertion is inadequately supported with citation of information from the scientific literature.

To begin with, Paustenbach et al. state that Rinsky et al. [1986] believed "grab samples were representative of the peak concentrations and these measurements were collected selectively in those areas where benzene exposure was highest." The Rinsky et al. report [1986] actually states: "Episodes of high exposure due to such temporary circumstances as spills and process upsets were probably overlooked by the industrial hygiene surveys and are not reflected in our calculations of exposure." They further state: "If the environmental data are in error, we believe they likely err by overestimating actual average concentrations." These statements are made by Rinsky et al. [1986] in regard to all industrial hygiene samples in the RH plants, not just the grab samples as purported by Paustenbach et al. There is no claim or implication by Rinsky et al. that the industrial hygiene measurements reflect peak or maximum concentrations, only that they overestimated the average concentrations. This conclusion is consistent with general industrial hygiene practice where plant industrial hygienists collect most of their samples for compliance and hazard recognition, i.e., worst-case scenarios [Checkoway et al., 1987; Harris, 1991]. These sampling strategies result in measurements that are usually greater than average exposure concentrations.

Paustenbach et al. display some appreciation for this issue when they state: "For the results of surveys using these tubes to accurately reflect the 8-h TWA workplace concentrations, a careful sampling program based on time-weighted worker activity patterns would have been necessary. While it is acknowledged that the St. Marys industrial hygiene program probably focused on those activities that were likely to produce the highest concentration of benzene, it is not clear that the samples were taken at times when benzene exposure would have been at its highest." However, just two paragraphs later, they state: "We believe there is sufficient evidence that grab (detector tube and CGI) samples are representative of the general background levels of benzene in the building and usually do not reflect short-term peak concentrations." In the intervening two paragraphs data used by Paustenbach et al. are not the actual data available for the RH plants.

In these two paragraphs, Paustenbach et al. compare measurements of benzene in the RH plants made with charcoal tubes and detector tubes. The apparent purpose

TABLE II. Personal Charcoal Tube Sample Results in ppm for Benzene in the Neutralizer Area of the St. Marys Rubber Hydrochloride Film Manufacturing Process

	Platform				Scrap area			
Date	A	B	C	D	A	B	C	D
1973								
8/30						7.9		
10/29		9.98	5.10	9.58		10.95	3.98	12.55
1974								
1/4								14.20
2/25		1.53		6.50				
4/11							7.05	
5/3		13.6	3.86	8.44				
5/20			6.92					
6/17	7.15		4.90	11.00	5.24			
9/25						36.00		
10/17		0.53						
11/27			5.87	4.52			5.13	
			6.72				1.59	
Ave.	7.15	6.41	5.56	8.01	5.24	9.43	10.75	13.38
Overall Ave.	6.64				10.46			

of the comparison is to show that detector tube readings of benzene have historically underestimated benzene concentrations in RH plants. These two methods were used to measure benzene in RH plants only in 1973 and 1974 at the St. Marys location [Rinsky et al., 1981; Paustenbach et al. 1992].

Paustenbach et al. selected the neutralizer area of the RH plant for comparison of the two methods. They claim that the actual charcoal tube data in the neutralizer area of the RH plants during 1973 and 1974 "suggest 25 ppm." However, the average benzene measurement results were 6.6 ppm on the platform, 10.5 ppm in the scrap area, and 7.9 ppm overall (Table II). It simply does not follow that these data "suggest" 25 ppm. Paustenbach et al., however, use the "suggested 25 ppm" charcoal tube results as the standard to compare with the detector tube measurements. Many of these detector tube results were at concentrations below the limit of detection (5 ppm) for the tubes reportedly used at that time [Rinsky et al., 1981]. The overall average of the detector tube readings in this area was ~3 ppm, again well below the limit of detection. Any readings below the limit of detection are, by definition, extremely unreliable, as would be any average of measurements that included these values. Therefore, the particular detector tube data that Paustenbach used to compare against their apparently erroneous estimate of 25 ppm TWA are highly unreliable.

Paustenbach et al. [1992] then adjust the detector tube and CGI samples upward to reflect "peak" exposure concentrations. These adjustments are not trivial, with concentrations as high as 750 ppm and time periods of up to 4 hr in seven of the eight job categories at both St. Marys and Akron. These adjustments are in addition to all others that are noted in this report.

Paustenbach et al. partially justify use of upwardly adjusted grab samples as average concentrations by stating, "during the hearing on the revised benzene standard, RH workers testified that they were instructed not to enter areas where respirators were required when wearing sampling devices." However, they fail to note that this restriction would only affect results of personal sampling devices. The only personal sampling in the RH plants used charcoal tubes. Paustenbach et al. fail to recommend any adjustments in the charcoal tube data based on this argument. The argument has no basis for adjustments in the detector tube and CGI measurements since these methods were not compatible with personal monitoring.

Further, since data are not available for peak exposure estimates, Paustenbach et al. use data from supposedly similar operations in other industries. The speculative nature of this practice aside, none of the data that appears in Table 9 of the Paustenbach et al. [1992] article has been published in the open literature. All references are to internal reports from private industry. Apparently, these reports have not endured scientific peer review.

Finally, Paustenbach et al. cite an article by Cook [1945] as evidence that benzene exposures in the RH plants during the early 1940s were elevated. They state: "It should be remembered that benzene workplace concentrations of 100–150 ppm were not uncommon in numerous industries during these decades (Cook, 1945)." In fact, there is no mention in the Cook article of any benzene exposure concentrations in excess of 100 ppm. Interestingly, Cook [1945] argues that there is sufficient evidence that the 100 ppm maximum allowable concentration in force at the time was not protective and he recommended that 50 ppm be adopted as the maximum allowable concentration. Cook [1945] supports his position by citing a report of two apparent benzene poisonings that occurred where the benzene concentration was estimated at <75 ppm.

Detector Tube Accuracy

A basis of one of the more global adjustments in the environmental data from the rubber hydrochloride film plants used by Paustenbach et al. is that detector tubes and combustible gas meters underestimate the actual concentrations of benzene in air at the time of measurement. Several articles from the industrial hygiene literature are cited in support of their position. The two articles that are relied upon most heavily are by Hay [1961] and by Pagnotto et al [1961]. However, significant uncertainties are stated in the conclusions presented in both these articles.

Hay evaluated the response of three detector tube systems, Kits A, B, and C, for aromatic hydrocarbons under laboratory and field conditions. Hay found in his laboratory that: "At 25 ppm, the (then) TLV of benzene, Kit B indicated an average value of 40 ppm, an inaccuracy of 60% above the true concentration, while Kits A and C were both 40% low giving readings averaging around 15 ppm. At ten times the TLV (250 ppm), Kits B and C gave values 14% and 50%, respectively, below true concentration. Kit A, having an upper limit of 100 ppm, read 40% below the true concentration at 100 ppm and increasingly worse at higher concentrations."

Kit A was apparently identical to the tubes used for benzene monitoring at the RH film plants at least during the period prior to 1964 when a new detector tube system was first marketed. The Hay study does show that, in the laboratory, bias of the different detector tube systems he tested could be positive or negative in comparison with the reference method. Kit A, however, was consistently low. The reference method for benzene used by Hay was absorption into isopropyl alcohol and analysis by uv spectrophotometry. No information is given by Hay on the number of comparisons that were made nor is any statistical evaluation of the accuracy and precision of the reference method given.

At the same time, laboratory evaluations were made on the detector tubes, Hay also evaluated a silica gel sampling method for benzene. The benzene captured on the silica gel was analyzed by water elution and gas chromatography. Hay subsequently used this method as a reference method for comparison with the detector tubes under field conditions. No evaluative information is given in the article for the reference method under lab conditions except that collection efficiency of the silica gel was 93% over the range of the tests.

Hay [1961] reports that during field testing at a coke oven plant, Kit A and Kit B detector tubes overestimated the concentration of benzene in air in comparison with the silica gel method. Kit C detector tubes failed to respond in many cases. At the TLV, which was 25 ppm at the time of Hay's work, the Kit A detector tube response was on average 70 ppm benzene. Hay attributes the inconsistency between the laboratory, where Kit A underestimated the benzene exposure, and the field results, where it overestimated the benzene concentration, to the presence of interfering contaminants in the plant atmosphere. Kit B detector tubes tested at the same time also read correspondingly high at 80 ppm, which was a much closer agreement between Kits A and B than was seen in the laboratory results. Hay also points to the difficulty in reading the stain length in detector tubes as another source of uncertainty for the comparisons.

The essential problem with Hay's work [1961] is that sufficient data are not given to fully evaluate the benzene analytical methods used for comparison with the detector tube methods. None of the reference methods for benzene used by Hay for comparison with the detector tubes in both laboratory and field conditions has been widely used for benzene in air. The isopropyl alcohol trapping of benzene is not sufficiently explained or described in the Hay article to determine accuracy and precision of the method.

Other researchers have reported on the inaccuracy of silica gel as a collection medium, particularly for nonpolar organic compounds such as benzene [Van Mourik, 1965]. Silica gel capacity for some organic compounds is substantially reduced by water vapor. In humid atmospheres, silica gel sampling methods frequently result in underestimation of actual concentrations of organics in air. Since Hay does not discuss this phenomenon as a source of potential bias in his field exercises, perhaps he was unaware of the possible effect of humidity on the silica gel benzene sampling method he used.

Most importantly, however, Hay concludes that "the results of this study show all of these (detector tube) kits to be unsatisfactory in terms of the quantitative results obtained. Their value seems to be limited to semiquantitative indications of benzene concentrations in environments to which the tubes have been calibrated." By his own admission, Hay's results are inconsistent and unreliable and, therefore do not support the adjustments by Paustenbach et al. [1992] in the detector tube values used for estimation of the rubber hydrochloride worker benzene exposures.

Combustible Gas Indicator Accuracy

In the early years of RH production, benzene concentrations were also estimated with combustible gas indicators (CGI). Paustenbach et al. cite an article published by Pagnotto et al. [1961] to indicate that the CGI underresponds by ~50% to concentrations of benzene in air. The article by Pagnotto et al., however, used an unsophisticated and inaccurate method of estimating the benzene in air concentration in vapors emitted from a naphtha mixture. A later article in the same title series and by the same authors, Elkins et al. [1963], explains the error of estimation in their first article. Paustenbach et al. fail to mention this second article in their analysis of CGI accuracy.

Essentially, Pagnotto et al. [1961] postulated that the concentration of benzene vapors emitted from bulk naphtha sources could be estimated by the product of the total CGI response and the percent of benzene in the liquid naphtha. They assumed that the proportion of benzene in the naphtha vapors was the same as that of benzene in the naphtha liquid. This assumption would be true only if the naphtha were completely evaporated, which was apparently not the case where their measurements were taken. As a minor component at <10% of the solvent mass and one of the more volatile hydrocarbons in the naphtha, benzene evaporates from the solution at a higher rate than the other more predominant components of the naphtha mixture. As a result, the method used by Pagnotto et al. [1961] substantially underestimated the actual concentration of benzene in the vaporous emissions from naphtha, leading Paustenbach et al. [1992] to erroneously conclude that CGI inaccurately responds to benzene in air. The later study by Elkins et al. [1963] appropriately attributes the cause of the benzene vapor enrichment to Raoult's Law.

Paustenbach et al. further criticize the accuracy of the CGI by reporting that interviews with workers at the rubber hydrochloride film plants revealed "field calibration of the CGI used in the (RH film) operations was often rudimentary during the 1940s—for example, employees frequently used a Zippo lighter to determine whether the instrument was operating." In fact, use of the cigarette lighter has nothing to do with the instrument calibration. The cigarette lighter is a convenient and very transportable hydrocarbon emission source. After routine calibration of the instrument in the laboratory, the CGI may be checked for operational status in the field by testing its response to hydrocarbons from the lighter, a practice that remains commonplace even today.

Paustenbach et al. also claim that the CGI may underrespond to benzene in air as a result of changes in the instrument sensitivity between calibration and field usage. This claim, as it applies to the rubber hydrochloride plants, is not supported with any factual information in their article. If the instrument was recently calibrated, instrument response should closely estimate the concentration of benzene in air. NIOSH [1974] evaluated the response of a large group of combustible gas meters. The CGIs closely approximated concentrations of benzene in air as low as 420 ppm (3% of the lower flammable limit of benzene), the lowest concentration evaluated by NIOSH.

The CGI used to estimate benzene concentrations in the RH film plants by the Ohio Health Department staff were apparently manufactured by MSA [Seferin, 1977]. These meters, like essentially all CGI, have a range of 0–100% of the lower flammable limit (LFL) of organic compounds. Most of the MSA meters have span adjustments that allow the response at 100% LFL to be adjusted for different organic compounds. Also, most of the MSA meters have more sensitive reading scales, usually at 10% LFL. McInerney [1977] states that such a meter was used by company personnel to assess exposures in the rubber hydrochloride film plants.

Cook [1947] clearly explains the sensitivity of this type of instrumentation. On the 0–100% LFL scale, the first graduation would correspond with 1% or 2% of the LFL, depending on the instrument. If the instrument was calibrated for benzene, these graduations would correspond to either 140 or 280 ppm. If this same instrument was operated on the 0–10% LFL scale, these graduations would correspond to 14 ppm or

28 ppm. This explanation of instrument sensitivity is greatly different from the testimony of McInerney [1977] at the 1977 OSHA benzene hearings. McInerney makes a substantial error in explaining the dual range capability of the MSA CGI when he states that "the other lower scale, which has a 10 to 1 dilution factor, reads from 0 to 10% of the lower explosive limit." A 10–1 dilution of the gas stream will result in lower instrument sensitivity, not the increased sensitivity that McInerney indicates.

Also, McInerney [1977] erred in his description of the accuracy of CGI readings when he states "the first mark on the scale would be one-half of 1% or roughly 90 ppm in air." If the more sensitive 0–10% LFL scale were used, the first mark on the scale would correspond with ~15 ppm as explained by Cook [1947]. The readings reported by the Ohio Industrial Hygiene Engineer [Seferin, 1956] imply that such a sensitive scale was used for the CGI readings used in the Rinsky, et al. [1981] exposure assessments. For example, the estimates of benzene concentration reported for the storage room by the state of Ohio were 0–15 ppm.

TLV Ratio Method

Crump and Allen [1984] had previously made upward adjustments in the NIOSH benzene exposure estimates for the RH worker cohort. Their method of adjustment assumes that as the TLVs became more restrictive, benzene exposures in industries were lowered, presumably through work practice and engineering control measures. Therefore, Crump and Allen contend that exposures for historical periods may be reasonably estimated based on proportionate changes in the TLVs for benzene.

Crump and Allen [1984] increased recent benzene exposure estimates for specific job titles by the ratio of the historical TLV to the TLV at the time of the measurements. Similar adjustments in the historical estimates of solvent exposures have been suggested elsewhere [Harris, 1991]. When Paustenbach et al. [1992] applied this method to the RH cohort, the Crump and Allen estimates for many job titles exceed 250 ppm annual average exposure concentration for many consecutive years. These estimates seem unrealistically high in light of the recently assembled data by WHO [1993].

Paustenbach et al. employ the TLV ratio method in addition to their many other adjustments to estimate benzene exposure. However, their overall estimates for the Akron facility include *annual average* benzene exposure concentrations greater than the TLV 8-hr TWA for workers in seven out of eight job titles for the period of 1958–1965, and for six out of eight job titles for the period of 1949–1957. It is illogical, on one hand, to argue that the industry was sensitive to the TLVs and would lower their exposure concentrations accordingly, while, on the other hand, showing the same industry in gross violation of those limits for the majority of the workers. These facilities were repeatedly visited by industrial hygiene inspectors from the state of Ohio to evaluate potential benzene exposures. Moreover, these were unionized plants whose employees had access to occupational health professionals. Therefore, it seems unreasonable to assume persistent exposures to benzene grossly over the recommended level.

There are other contradictions in the results obtained by Paustenbach et al. using the Crump and Allen method of adjusting exposure estimates. For instance, they argue, on one hand, that the construction of the Akron II facility, which replaced the

Akron I facility, incorporated all of the engineering controls that had previously been installed at the St. Marys plant. They then derive estimates of exposure for the Akron II plant greater than the estimates for the Akron I plant in its final 2 years of operation and also greater than concentrations at the St. Marys plant for some job titles. In addition, the change in plants coincides with the lowering of the TLV for benzene in 1948 from 100 ppm to 50 ppm 8 hr TWA and the further lowering in 1949 to 35 ppm 8 hr TWA. It is inconsistent to suggest when a more advanced plant is constructed at the same time the TLV is reduced by 65% that the benzene exposures would increase, particularly when the premise for selection of the dose estimation paradigm is that exposure concentrations in these plants are responsive to changes in the TLV.

CONCLUSIONS

In summary, Paustenbach et al. [1992] use selected information, sometimes improperly cited, to adjust previously reported benzene exposure estimates for the RH worker cohort. The previous estimates by Rinsky et al. [1981] and Crump and Allen [1984] were largely based on short-term and probably inaccurate sampling results collected as early as 1946. The Paustenbach et al. method involved multiple adjustments of these early monitoring results by a number of factors that are apparently based on worse-case assumptions. Their factors are determined through extrapolation of data collected under substantially different and frequently unknown conditions. As a result, Paustenbach et al. estimate annual average exposures to benzene that are in some cases almost an order of magnitude greater than the actual measurements.

The Paustenbach et al. reconstruction has many cohort members exposed to prolonged levels of benzene in excess of 100, 150, and even 200 ppm. Some of the highest benzene exposures supposedly lasted as long as a decade. One would assume that such extreme exposures would produce an epidemic of serious benzene poisonings among the cohort with resulting death from hematopoietic disorders such as aplastic anemia. But no such epidemic occurred.

The RH process that existed in 1975 when the process was terminated was fundamentally the same as it was shortly after it began in the early 1940s. Benzene exposures were monitored during the 1970s by a number of industrial hygienists using currently accepted methods [UNC, 1983; Rinsky et al., 1986]. There have been no reports of substantial engineering improvements after 1942 to limit benzene exposures to a large number of cohort members over the decades of operation at St. Marys and Akron. Rather, as initially reported by Rinsky et al. [1981] there had been some traditional engineering controls, such as a few hoods installed, and perhaps some work practices had been improved. The Paustenbach et al. approach falls short of their claim of providing more "plausible" exposure estimates for the cohort than those previously derived by Rinsky et al. [1986]. The NIOSH benzene exposure estimates for the RH cohort [Rinsky et al., 1981] remain the most consistent with all available information about the conditions that prevailed in RH manufacturing—even with information that has been discovered [U.S. Department of Labor, 1942] after the estimates were first derived.

REFERENCES

Aksoy M, Erdem S, SinCol G (1974): Leukemia in Shoe-workers Exposed Chronically to Benzene. Blood 4:837–841.

American Petroleum Institute (API) (1993): Summary of API presentation to the Chemical Substances TLV Committee of the ACGIH, Bethesda, MD, September 13.

Beatty PW (1993): American Petroleum Institute and Western States Petroleum Association Benzene Task Forces Presentation to ACGIH, Bethesda, MD, September 13.

Checkoway H, Dement JM, Fowler DP, Harris RL, Lamm SH, Smith TJ (1987): Industrial hygiene involvement in occupational epidemiology. Am Ind Hyg Assn J 48:515–523.

Cook WA (1945): Maximum allowable concentrations of industrial contaminants. Ind Med 14:936–946.

Cook WA (1947): Review of automatic indicating and recording instruments for determination of industrial atmospheric contaminants. Ind Hyg Quart 8:42–48.

Crump K (1992): Exposure response analyses of pliofilm cohort, Clement International Corporation Report, December.

Crump K, Allen B (1984): Quantitative Estimates of Risk of Leukemia from Occupational Exposure to Benzene. Exhibit 152 (Appendix B), Docket H-059b, Benzene. Washington, DC: Occupational Safety and Health Administration.

Elkins HB, Comproni EM, Pagnotto LD (1963): Industrial benzene exposure from petroleum naphtha. Am Ind Hyg Assn J 24:99–102.

Franz TJ (1984): Percutaneous absorption of benzene. Holdsworth CE, MacGregor JA, Call RW, Lane ML (eds): "Applied Toxicology of Petroleum Hydrocarbons." In MacFarland HN, Princeton, NJ: Princeton Scientific, pp 61–70.

Hanke J, Kutkiewicz T, Petrowski J (1961): The absorption of benzene through the skin in man. Med Pract 12:413–426.

Harris RL (1991): Measures to facilitate future epidemiologic studies. Appl Occup Environ Hyg 555–559.

Hay EB (1961): Exposure to aromatic hydrocarbons in a coke oven by-product plant. Am Ind Hyg Assn J 21:386–391.

Infante PK, Rinsky RA, Wagoner JK, Young RJ (1977): Leukemia in benzene workers. Lancet 2:76–78.

Lenoir C (1997): Bull Mem Soc Med Hop Paris 3:1251.

Maibach HI, Anjo DM (1981): Percutaneous penetration of benzene and benzene contained in solvents used in the rubber industry. Arch Environ Health 36:256–260.

McInerney HM (1977): Exhibit 121, Docket H-059, Benzene. Washington, DC: Occupational Safety and Health Administration.

National Institute for Occupational Safety and Health (NIOSH) (1974): Evaluation of portable direct reading combustible gas meters, No. 74-107, Cincinnati, OH.

Ott GM, Touwnsend JC, Fishbeck WA, Langner RA (1978): Mortality among individuals occupationally exposed to benzene. Arch Environ Health 33:3–10.

Pagnotto LD, Elkins HB, Brugsch MD, Walkey JE (1961): Industrial benzene exposure from petroleum naphtha: I. Rubber coating industry. Am Ind Hyg Assn J 22:417–421.

Paustenbach DJ, Price PS, Ollison W, Blank C, Jernigan JD, Bass RD, Peterson HD (1992): Reevaluation of benzene exposure for the Pliofilm (rubberworker) Cohort, (1936–1976). J Tox Environ Health 36:177–231.

Paxton MB, Chinchilli VM, Brett SM, Rodricks JV (1994a): Leukemia risk associated with benzene exposure in the pliofilm cohort: I. Mortality update and exposure distribution, risk analysis 14: 147–154.

Paxton MB, Chinchilli VM, Brett SM, Rodricks JV (1994b): Leukemia risk associated with benzene exposure in the pliofilm cohort: II. Risk estimates, risk analysis 14:155–161.

Rinsky RA, Young RJ, Smith AB (1981): Leukemia in benzene workers. Am J Ind Med 2:217–245.

Rinsky RA, Smith AB, Hornung R, Fillon TG, Young RJ, Okun AH, Landrigan PJ (1986): Benzene and leukemia: An epidemiologic risk assessment. Cincinnati: National Institute for Occupational Safety and Health.

Rinsky RA, Smith AB, Hornung R, Fillon TG, Young RJ, Okun AH, Landrigan PJ (1987): Benzene and leukemia: An epidemiologic risk assessment. NEJM 316:1044–1050.

Seferin S (1977): Letter to Ivan Hall: Goodyear Tire and Rubber Co., February 13, 1956, Exhibit 84.B.22, Docket H-059, Benzene. Washington, DC: Occupational Safety and Health Administration.

Snyder R, Witz G, Goldstein BD (1993): The toxicology of benzene. Env Health Persp 100:293–306.

Spirtas R (1993): Comments to the Chemical Substances TLV Committee of the ACGIH, Bethesda, MD, September 13.

University of North Carolina (1977): Preliminary Environmental Survey Report, St. Marys, OH, November 11, Exhibit 187.B.6, Docket H-059, Benzene. Washington, DC: Occupational Safety and Health Administration.

Van Mourik (1965): Experiences with silica gel as adsorbent. Am Ind Hyg Assn J 26:498–508.

Vigliani EC (1976): Leukemia associated with benzene exposure. NY Acad Sci 271:143–151.

Wilson R (1942): Benzene poisoning in industry. J Lab Clin Med 27:1517–1521.

World Health Organization (WHO) (1993): International Programme on Chemical Safety, Environmental Health Criteria 150, Benzene, Geneva.

Yin SN, Li Q, Tain F, et al. (1987): Leukemia in benzene workers: A retrospective cohort study. Br J Ind Med 44:124–128.