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Unprotected worker

Contents

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Commentary

Manipulated Data in Shell's Benzene Historical Exposure Study

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In 1983, in the face of mounting evidence of excess leukemia among workers at Shell Oil's Wood River (IL) and Deer Park (TX) petroleum refineries, Shell initiated the Benzene Historical Exposure Study (BHES). Shell's prior research had implicated occupational exposure to benzene as the source of the excess leukemia. The BHES report submission, which ultimately found no link between exposure and the excess morbidity, coincided with OSHA's planned hearings over a new regulatory standard for benzene. Over the next two decades, Shell published several papers based on or expanding the BHES data, all of which concluded that the excess of leukemia was unrelated to benzene. A review of the raw data on which Shell and its consultants relied reveals that Shell manipulated and omitted data in order to reach conclusions that exculpated it from liability and helped delay stricter benzene regulation. *Key words:* benzene, petroleum, occupational health, leukemia

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Scientists have raised concern about the toxic effects of benzene exposure since the early 1900s.[1,2] Workers are exposed to benzene through gasoline and various manufacturing processes. In 1948, the American Petroleum Institute (API) published a toxicological review for its members on benzene stating, "it is generally considered that the only absolutely safe concentration for benzene is zero."[3] The API did not require an epidemiologic study to establish a causal relationship between benzene and disease. This document was never made public, and the member companies never attempted to follow the recommendations in order to protect exposed workers and consumers. To forestall a Consumer Products Safety Commission ban of benzene use, petroleum companies promised to voluntarily remove it from consumer products in 1978. Yet today, it remains an additive in some consumer products, including dental adhesives and soft drinks.[4–8]

In 1977, Infante et al. published the first cohort study that quantitatively assessed the relationship between benzene exposure and leukemia.[9] The Infante study prompted the U.S. Occupational Safety and Health Administration (OSHA) to lower the permissible occupational exposure limit (PEL) for benzene from 10 ppm to 1 ppm in 1978.[10] Petroleum and allied industries challenged the limit, which was immediately stayed and eventually overturned by the U.S. Supreme Court in 1980. As a result, OSHA was required to gather additional proof of benzene's toxicity. In 1987, almost a decade after OSHA promulgated the 1978 standard, OSHA had developed sufficient evidence to predict the number of workers who would be protected by the original standard of 1 ppm, which was subsequently reenacted.[10] This regulatory delay resulted in 30 to 490 extra deaths from benzene-related leukemia and multiple myeloma that could have been prevented.[11] The debate over what constitutes sufficient proof of the adverse health effects of benzene makes the actions of petroleum industry agents during 1980–1987 particularly interesting in the history of benzene regulation.

In 1983, in anticipation of upcoming OSHA benzene regulatory hearings, Shell initiated the Benzene Historical Exposure Study (BHES) to explore the reported excess leukemia at two of their refineries. The BHES study report submitted to OSHA found no link between benzene exposure and the excess incidences of leukemia.[12] Over the next two decades, Shell published several papers based on or expanding the BHES data, all of which concluded that the excess risk of leukemia was unrelated to benzene exposure. We have been able to review the raw exposure data on which Shell and its consultants relied, as well as internal Shell communications during this time. Our review indicates that Shell manipulated and omitted BHES exposure data in order to reach these conclusions. If these conclusions had been accepted by OSHA, they would have greatly enhanced industry profits. Further, the manipulation of the BHES data was part of a larger pattern of

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TABLE 1 Data-manipulation Strategies Used in the BHES

Not separating out unexposed workers*
Misclassifying workers between exposure categories†
Comparing workers with the general population, allowing the healthy-worker effect (HWE) to bias the findings†
Splitting research into subsets to minimize ability to achieve statistical significance
Ignoring consultant recommendations on strategies to strengthen studies
Not blinding participant exposure category to interviewers
Differential treatment of positive and negative exposure data
Promoting only findings that benefit financial sponsor

*Gennaro and Tomatis common scenario 1.[13]
†Gennaro and Tomatis common scenario 2.[13]
‡Gennaro and Tomatis common scenario 3.[13]

corporate deception that helped delay stricter benzene regulation and exculpate the company from liability in tort litigation.

STRATEGIES FOR DATA MANIPULATION

In 2005, Gennaro and Tomatis published an article demonstrating how industry-funded epidemiologic studies can be intentionally designed to produce negative results.[13] They list three common scenarios in which study design flaws bias findings towards the null, cautioning, "When two of these errors occur at the same time, a "negative" result is practically certain."[13] The BHES report and derivative publications incorporate all three of these flaws as well as additional errors. Table 1 summarizes the data-manipulation strategies used.

INITIATION OF BENZENE HISTORIC EXPOSURE STUDY

Early Signs of Excess Cancer

Shell first became aware of an excess rate of leukemia at their refineries when a contract worker sued them in 1979, alleging that benzene exposure had caused his leukemia.[14] As a result of the suit, Shell compiled a list of leukemia cases in past employees.[14] Shell's Wood River, Illinois, Manufacturing Complex (WRMC) was the site of the largest number of leukemia deaths.[14] In 1980, Shell calculated a statistically significant proportionate mortality ratio (PMR) of 3.49 for leukemia at the WRMC. In 1983, Shell found a statistically significant leukemia PMR of 3.29 at another refinery, the Deer Park, Texas, Manufacturing Complex (DPMC).[14]

Shell Review Implicates Benzene in Leukemia Excess

In July 1983, Shell's consultant, Dr. Phillip Cole, of Epidemiological Resources, Inc., completed a second review of WRMC activities to explore the leuke excess. In his first review, he had concluded that "i likely that there was a real problem with leuken especially myelocytic leukemia at Wood River in years prior to 1980."[15] Further, one study aggregat data from other Shell sites indicated "if Shell has overall problem with Leukemia, it is not restricted Wood River."15 The second review used updated d for WRMC and clarified the number of cases of ac myelocytic leukemia (AML).[16] In consideration of 14 reported leukemia deaths, eight of which were fr AML, Dr. Cole found a statistically significant excess mortality from leukemia and a fourfold increase of r of death from AML among WRMC employees.[16] termed these data "highly statistically significant. T fact that virtually the entirety of the excess cases . . of the AML form is unequivocal evidence of a g uinely increased risk of death from this particular c dition."[16] Dr. Cole's summation was clear; "benzen an established cause of AML . . . there is no reasonal possibility that the data are the result of any error, r is it likely that these findings can be attributed to c founding by a non-occupational cause of AML . . . b zene is the most likely cause of the excesses seen."[16]

Impending Rule Making and the Strategic Response

On July 8, 1983, as part of their effort to gather t needed evidence to reinstate the benzene PEL, OSI requested that benzene manufacturers provide all av able data on occupational benzene exposures as well protocols of studies in progress.[14,17,18] OSHA indicat that they planned to establish a new PEL for benze by mid-1984. Manufacturers were expected to provi the requested data by August 1983. In addition, int ested parties were given an opportunity to submit su plemental information at hearings planned for Feb ary 1984.

By July 26, Shell's Vice President, Paul F. Deisler, had assembled "back up materials" for its President Shell's history with leukemia, including updated da from WRMC and DPMC, epidemiologic studies und way at other refineries, and an overview of OSHA's re ulatory activity.[14] The materials confirmed that WRM had a statistically significant SMR of 4.54 for AML. T parallel statistics for DPMC demonstrate the fi instance of obvious data manipulation. Mr. Deisl stated that the DPMC SMR of "~3.7" was "not quite 'st tistically' significant" at $p = 0.09$; however, this was f lowed by a footnote that read, "In addition, one ca with six mos. service but many years with another co pany is known to us."[14] There is no explanation or pr tocol justifying the exclusion of this case, its inclusi would have resulted in a statistically significant SMR.

Shell did not publish any of its internal SMR calc lations or either of Dr. Cole's reviews. Instead, da after the "background materials" were circulated to k

staff, Shell released an employee communication and press release that directly contradicted these secret results. On August 31, 1983, the Associated Press carried an article that led with, "Shell Oil Co. says it has found no link between benzene and a relatively high incidence of deaths from a certain type of leukemia in Texas and Illinois plants that handle the chemical." It concluded by quoting Shell's Corporate Medical Director, Dr. Joyner, "We have no reason to conclude that a leukemia risk currently exists at any of our refinery locations."[19]

Dr. Peter Infante, of OSHA, disagreed and responded,

> Regardless of the specific etiological factor(s) a highly significant increase of leukemia over the past ten years is clearly apparent at the Wood River facility. Some may consider this an epidemic. Yet your 'employee communication' resulting from this study . . . clearly contradicts the study results and the interpretation of those results by your consultant [Cole]. . . . I would like to suggest you consider issuing a revised 'employee communication' in light of the above comments.[18]

However, Shell never issued a revised communication; it had other priorities. According to Shell Vice President Deisler, "It is of utmost importance . . . to continue our studies to assess early exposures and mitigation rates, and to develop other ancillary data such as is alluded to here, in time for submission to the hearing record."[14] Thus, Shell proceeded full-speed with a new research study to be completed in time for the February hearings, the Benzene Historical Exposure Study.

Benzene History Exposure Study

In the fall of 1983, Shell launched the Benzene Historic Exposure Study (BHES) at WRMC and DPMC. The study sought to "assess the historical workplace benzene exposure for the diagnosed cases of leukemia" and "estimate the historical benzene exposure for all jobs at WRMC and DPMC where benzene may have been encountered."[20] This study would either implicate benzene by demonstrating that workers with leukemia clustered in high-benzene-exposure jobs or fail to find an explanation for the leukemia excess. The subsequent BHES report stated that nine of the 23 identified leukemia cases at Wood River and Deer Park had "nil" exposures to benzene when calculating career parts-per-million (ppm) days, and eleven of 23 cases had "nil" exposures when calculating peak ppm minutes per year. Thus, without evidence of a dose–response, Shell's BHES study concluded, "At this time, the excess leukemia is unexplained."[12]

Shell submitted the BHES report to OSHA and published two papers that relied on the BHES study data: a "brief communication" on the SMR analysis in 1985[21] and a 1986 case–control study.[22] Both papers limited their data to the Wood River refinery and excluded the Deer Park cases. Both of these two papers echoed the conclusion in Shell's report to OSHA that "the excess of leukemia remains unexplained."[21,22] Later, in 1989 and 1995, Shell published two further papers expanding the BHES Wood River cohort into larger mortality studies.[23,24]

SYSTEMATICALLY UNDERESTIMATING EXPOSURE IN BHES

Shell Oil Company utilized a two-pronged approach to estimate exposures to benzene at the Wood River and Deer Park refineries. First, Shell estimated the possible exposure for each job within the refinery; second, it constructed a detailed case exposure history for each of the Shell employees with leukemia using personnel records of job titles and interviews with co-workers. Shell had no contemporaneous exposure-monitoring information. Shell's method hinged upon extensive historical recall as well as subjective indications of dose, odor recognition, and detectable exposure. Furthermore, the analysis was not blinded; the Shell personnel who conducted the assessments knew the disease status of the leukemia cases. The study design and execution flaws are enumerated in the following sections.

Worksite Study Fundamentally Flawed

In Dr. Cole's original review of the nine previous research activities conducted at Wood River, one study was labeled the "'Follow-back' study of worksites."[15] Dr. Cole cautioned that the "study's negative result will not be perceived as highly persuasive" in part because "benzene, being highly volatile, may permeate nearly the entire facility and affect just "susceptible" individuals."[15] Yet within months of this caution, Dr. Cole and Shell launched the BHES, a study built on worksite exposure analyses, and later used the absence of findings to discredit any possible benzene–leukemia link. Expansion of this flawed study design biased the final results towards the null.

Shell Made Limited or No Corrections for Olfactory Fatigue

Since Shell had failed to monitor benzene exposure levels, it relied on retrospective recognition of benzene odor to estimate exposures. Odor recognition refers to the parts per million concentrations at which a substance can be detected by smell. At the outset of data collection for BHES, Shell determined that "the lowest detectable exposure level for [background] benzene has reportably [sic] been identified as 1.5 ppm."[25] Therefore, it concluded that if a worker smelled benzene he was exposed to at least 1.5 ppm. Shell devel-

		PPM Estimate To Be Used
1. No liquid visible but odor of benzene is detectable Examples: Downwind odors Fugitive emissions		1.5–5.0 ppm (3.0)
2. No liquid visible but an obvious source of benzene vapor is nearby Examples: Vessels, Tanks, Vents		5.0–10.0 ppm (7.5)
3. No liquid visible, possibly strong odor at times		10–25 ppm (17.5)
4. Liquid visible and odor of benzene is present, possibly strong at time	4A	25–50 ppm (37.5)
	4B	25–75 ppm (50.0)
5. Liquid visible, strong odor present, contact with liquid	5A	50–100 ppm (75.0)
	5B	50–100 ppm (100.0)
6. Odor and/or liquid contact so significant so as to require "backing out of it" or getting fresh air	6A	150–200 ppm (175.0)
	6B	150–400 ppm (275.0)
7. No detectable odor.		< 1.5 ppm

Figure 1—"Categorization of odor recognition," Shell Oil Company.

oped a ranking system to estimate exposures for greater intensities of odor perception and modified the estimated exposures based on visual cues such as liquid benzene or visible vapor. Shell divided benzene air exposures into seven categories based on these characteristics[26] (see Figure 1).

This ranking system relies on the false premise that an individual's perception of benzene can determine a relatively precise exposure level. However, olfactory fatigue or "adaptation" refers to an individual's progressive inability to detect an odor with continued exposure to that odor. A worker with daily exposure to benzene is unlikely to perceive a rise in ambient benzene concentration. Furthermore, not all benzene-like odors are benzene. For these reasons, odor threshold is a subjective, variable, and ambiguous way to estimate benzene exposure, especially in a refinery. Shell made no effort to standardize its method and did not include any positive or negative control cases to assess the accuracy of the exposure estimates.

Knowlton Caplan, of Industrial Health Engineering Associates, Inc. (IHEA), the industrial hygiene firm hired to consult on the BHES, warned Shell of flaws in this design; "the operable odor threshold for a refinery worker may very well be significantly higher than the official threshold of 1.5 pp, due to olfactory fatigue or olfactory adaptation. Further, although benzene has a distinct odor, it is likely that other petroleum hydrocarbons also present would mask or confuse that odor."[27] Caplan emphasized, "If we estimate mere odor perception as a 1.5 ppm exposure, I fear we will be seriously underestimating the exposure. . . . I urge that a serious effort be made to determine what the 'adaptation' factor may be for benzene. If a thorough literature search does not yield this, perhaps you may want to consult a real odor expert on this subject."[27] Shell and its consultants intentionally omitted any discussion of these problems from their reports and published papers. In the BHES report sent to OSHA, Shell discussed the problem of olfactory fatigue but misleadingly commented, "A specific literature search during the project development phase had not turned up any applicable information."[12] Random exposure misclassification biased the results towards the null.

Shell Ignored Better Methods for Estimating Exposure

As an industry expert, Shell had the capacity to assemble an unprecedented quantity of accurate exposure information. Caplan criticized Shell's reliance upon subjective memories of odors and particular tasks drawn from interviews and records.[28] Instead, he recommended a strategy based upon models of air-pollution dispersion presented at a NIOSH symposium in 1979.[29] In this method, a count of the valves, lines, pump seals, flanges, et cetera, in the refinery was synthesized with data about known vapor-emission factors for petroleum refinery equipment.[30] As Caplan informed Shell, "I do not know of any other industry for which leak rate or emission data exists in as complete and thorough a form as it does for petroleum refining."[28] While admittedly imprecise, "this approach at reconstructing historical benzene concentrations appears to be more meritorious than any other approach. . . ."[30] Shell responded with disinterest to Caplan's recommendations. In reply, Caplan stated,

> The notable lack of enthusiasm among your experts concerns me. . . . It is pure assumption on my part that reluctance to embark on this project is based on the departure from the usual criteria of precision. If there is some more fundamental objection, I do not understand what it would be.[28]

In fact, the BHES study plan originally included exposure-simulation studies,[20] but these were deferred indefinitely because "the desire for an expeditious study was not consistent with an experimental program that may take months to complete."[12] The 'usual criteria of precision' were apparently jettisoned in favor of obtaining results before the February deadline.

Shifting Combined Exposures Down

Shell did not account for the different benzene concentrations in various product mixtures (blends). Without measuring actual exposures, Shell automatically and arbitrarily reduced exposure estimates when workers were exposed to mixtures that included benzene. Its report explains, "Where the exposures reported primarily reflects [sic] the odor substances other than benzene (although benzene is present) then the highest odor exposure values reported for each task is lowered to the next category. . . . For example: Phenol odor 'C' lowered to 'B'."[31] This inappropriately lowered exposure estimates by converting "Categorization of Odor Recognition" into arbitrary ranges not based on workers' actual perceived odors. The presumption that the presence of another odor reduced the ambient benzene level contravenes Caplan's warning that other odors would "mask or confuse that [benzene] odor."[28] [Emphasis added]

No Inquiry into Possible Exposures at "Compounding House"

The BHES reported that it was "noteworthy" that "Three of the leukemia cases had extensive work histories in the area known as the compounding house. In addition, two other cases had short term assignments in compounding . . . no benzene was encountered in the compounding operations."[12] However, in Shell's exposure analysis, Caplan deliberately put quotes around the claim that there was no benzene at this location and encouraged Shell to pursue the issue further.

> A great number of additives have been used in that department over the years and the possibility exists that some of them may have been causative factors for leukemia even though that may have been unknown at the time. I suggest that a strenuous effort be made to determine what those additives were, and the chemical composition.[32]

Shell did not follow this suggestion and maintained that there was "no benzene" in the compounding house.

SMR Analysis Classification Errors in Individual Leukemia Cases

Before beginning the BHES, Shell knew that it had statistically significant excesses of leukemia incidence at two of its refineries. We have presented the way their study design systematically underestimated the benzene-exposure estimates. Descriptions of two further strategies used in the SMR analysis to underestimate the benzene exposure follow.

Paradigm shift—converting undeterminable exposures to "nil." Shell designated certain employees, including laborers, craftspeople, inspectors, and security personnel, as having refinery-wide exposures. For these refinery-wide jobs, employee records contained little information on the duration or location of work. For these cases, Shell routinely biased findings towards the null by haphazardly estimating refinery-wide exposures and converting "none determinable" refinery-wide exposures into the category of "nil exposure."

Cases XI and VIII demonstrate the haphazard methods used to classify exposures for refinery-wide jobs.[33,34] Both cases were laborers/yardmen with identical information in their case reports for "Duties and Work Practices," a summary of potential exposure situations derived from the interviews with living peers. The peers' limited recall of Case XI's actual work assignments substantiate the generic Duties and Work Practices developed for all laborer/yardmen, listing both high- and low-exposure worksites.[33] There were no specific worksites obtained from Case VIII peer interviews. Yet, despite almost identical profiling of their risks as laborer/yardmen, Case XI, with 33 years in this position, is listed as having a smaller career total exposure of "360–950 ppm-days,"[33] and Case VIII, with only 18 years, is listed as having a larger career total exposure of "800–1900 ppm days."[34]

Even more troublesome is the paradigm shift between yielding a "none determinable" exposure estimate and a final "nil" exposure estimate. Table 2 shows that, of the 16 leukemia cases at Wood River, 11 had worked at least some time in refinery-wide jobs, for which there was little or no actual information about the specific assignment areas. Therefore there was no basis to rule out exposure, and in most cases, it is likely that these cases were exposed. As the table shows, Shell determined the exposure to be "none determinable" for six of these cases. These exposure values were later converted to "nil." Both in the BHES report and in later published studies, the significance of the "nil" exposure cases became the main underpinning of the claim that "The excess leukemia remains unexplained." Yet, as Table 2 illustrates, there is evidence of likely or actual benzene exposures in 15 of 16 Wood River cases.

Unblinded cases and biased interviewers. Shell used interviews with up to three peer co-workers for each leukemia case to supplement their data on potential benzene exposure for each job. The interviewers knew both that the cases had leukemia and that benzene was the suspected cause. No attempt was made to blind the interviewers or provide any control cases. Moreover, national and local press coverage of the cancer excess may have affected the interviews.[12,19,35–37] Shell staff interviewed the co-workers, who were pensioned Shell employees, creating a strong potential for a social-desirability bias. Shell staff used haphazard and biased methods to accomplish these interviews; positive recall of exposures was weighted differently than negative recall; it appears that some interviewee statements that eliminated benzene exposure were prompted; and in

TABLE 2 Faulty Exposure Estimates

	Reported Exposure Category	Raw Data Show . . .
Case I	"None determinable to very slight" later "nil"	Worked refinery-wide (1956–73)
Case II	"1,300–10,400 ppm days"	
Case III	"None determinable" later "nil"	Worked refinery-wide (intermittent, duration approximately 1 year)
Case IV	"25–70 ppm days"	Worked refinery-wide (1932–51)
Case V	"None determinable" later "nil"	Worked refinery-wide (1937–54)
Case VI	"Very slight" later "nil"	Worked refinery-wide (1947–48 and 1962–63)
Case VII	"230–480 ppm days"	Worked refinery-wide (1923–63)
Case VIII	"800–1900 ppm days"	Worked refinery-wide (1942–51)
Case IX	"10,000–26,000 ppm days"	
Case X	"2,500–5,800 ppm days"	
Case XI	"360–950 ppm days"	Worked refinery-wide (1941–74)
Case XII	"None determinable" later "nil"	
Case XIII	"21,000–43,000 ppm days"	Worked refinery-wide (1942–57)
Case XIV	"None determinable" later "nil"	Worked refinery-wide (13 weeks)
Case XV	"None determinable" later "nil"	Worked refinery-wide (1943–70)
Case XVI	"640–1,300 ppm days"	

one live case, the interview concentrated more on avoiding litigation than on collecting any health data.

Dismissing Positive Reports of Exposures

BHES documents contain repeated references to the use of benzene as a cleaning solvent. In the Historical Overview of Wood River Research Laboratory, Shell noted that benzene was, "the clean up solvent of choice for the asphalt workers in the 40s and 50s. . . . Careful control of exposure to material was not practiced widely until the middle or the late 1960s."[38] A review of the Wood River case data reveals that the peer interviews specifically mentioned the use of a cleaning agent for cases IV, VII, X, XI, and XIV.[33,39–42] The potential use of benzene as a cleaning solvent is particularly notable, since direct skin contact with 100% benzene would be classified as one of the top two exposure categories in Shell's ranking system. In Shell's peer interviews, positive recall and negative recall about benzene as a cleaning agent were treated very differently. Table 3 shows how three interviewees noted probable benzene use for Case IV.

Despite this repeated positive recall about the highest level of benzene exposure, Shell dismissed this evidence with the baseless argument that "benzene was not available in the refinery" at the time of employment.[40] If this were true, why did Shell ask the coworker about potential benzene exposures in the first place? In fact, not only does Shell state that benzene was the cleaning solvent of choice during most of this time, but their BHES study report indicates that benzene was available in the refinery proper from 1942 on; Case IV had worked from 1932 to 1951.[12,40]

This pattern is repeated in Case VII and CaseXI; again, interviewees reported probable exposures to benzene as a cleaning agent. Yet, without explanation, the final exposure estimates do not accommodate any possible direct exposure.[12,33,41]

No comment or consideration is given to the potential use of benzene as a cleaning solvent by the two leukemia cases who worked in the research laboratory (Case IX, Case II) despite the fact that interview responses indicated that, "benzene was used widely as a solvent in the laboratory." Caplan criticized this dose underestimation and stated that "this discrepancy should be clarified if at all possible."[32] While records for Case IX are less clear, Case II's final worksheet shows no upward adjustment for use of benzene as a cleaning solvent.[12]

TABLE 3 Data for Case IV

Reported Exposure	Raw Data Show. . .
"25-70 ppm days" (not high enough to account for any possible direct exposure through cleaning of tools)	"Interviewee A: . . . He did use benzene to clean tools, gloves and shoes, especially when working at the asphalt plant."
	"Interviewee B: . . . .It was stated that most craftsmen used 'benzene' to clean tools."
	"Interviewee D: " . . . benzene might be used as a cleaning agent."

TABLE 4 Records of Interviews for Litigation Avoidance

	Reported Exposure	Benzene as Cleaner?	Was This Included in Total Exposure Estimate?
Case II	"1,300–10,400 ppm days"	Very likely in laboratory	No
Case IV	"25–70 ppm days"	Reported by interviewees	No
Case VII	"230–480 ppm days"	Reported by interviewees	No
Case IX	"10,000–26,000 ppm days"	Very likely in laboratory	Unknown
Case X	"2,500–5,800 ppm days"	Very likely with asphalt	Unknown
Case XI	"360–950 ppm days"	Reported by interviewees	No
Case XIV	"None determinable"	Peer reports frequent use of cleaning solvent but rules out benzene repeatedly	No

Crediting and Possibly Prompting Negative Reports of Exposure

In each case where the interviewees could rule out benzene use as a cleaning solvent, this information was given full credit. In some interviews, the peers demonstrated an uncanny ability to rule out benzene as the cleaning solvent used decades earlier by the deceased co-worker, creating the suspicion that responses were either prompted or significantly influenced by desirability bias.[39] The interviewers' reports that Case X did not clean with benzene are particularly suspect, since Case X worked with asphalt, and by Shell's admission, benzene was the cleaner of choice for these workers.[42]

In all, six of 16 cases had reported or very likely exposures to 100% benzene as a cleaning solvent. These exposures are most likely to have spanned years, sometimes decades. Yet, the exposure worksheets for four of these six cases excluded even the possibility of any high short-term exposures that would reflect this practice (Cases II, IV, VII, and XI) (Table 4).[12] The failure to include exposures from the frequent and common use of benzene as a cleaning solvent skewed the exposure estimates downward, again biasing the research to the null hypothesis and clearly demonstrating the bias in the methods used to interpret the co-worker interviews.

In the most extreme example of interviewer bias, Shell used an interview with a live leukemia case to suppress potential litigation and then arbitrarily categorized his exposure as "nil."[43] For the two living leukemia cases (Case XV and Case XVI), Shell had an opportunity to corroborate its methods for reconstructing past exposure potential with firsthand information.[43,44] Case XVI's data file is constructed based on two personal interviews and three supplemental peer interviews.[44] However, the file for the other live case (Case XV) is markedly different. Despite Case XV's having been assigned to refinery-wide jobs from 1943 to 1970, the file shows no evidence of any attempt by interviewers to identify the specific work locations or recall of benzene exposures. They seem focused on a different topic altogether:

> [Case XV] was questioned about a "call from some lawyer" that he had told Schenk about in a previous phone call. . . . We advised him that if he was called again under similar circumstances, to obtain his name and get in touch with Richard Gerth, Shell Wood River. Davidson also gave him his own personal card with his home phone number. This was an excellent interview. His attitude towards Shell is wonderful.

Applying the same method as was used with Case VIII (est. exposure 100–237 ppm/days/yr) would result in Case XV's having a cumulative exposure of 2,700–6,400 ppm days over his 27 year career. However, the later BHES report categorized his exposure without justification as "probably insignificant" or "nil."[12]

REPORTING MISLEADING BHES FINDINGS

1984—Report to OSHA

In February 1984, Shell submitted the BHES study report to OSHA. In this report, it used the many data-manipulation strategies outlined to conclude, "At this time, the excess leukemia remains unexplained." Shortly thereafter, in an exchange with OSHA staff, Shell admitted that the BHES methods did not produce reliable results.

> At best, we would have to take each employee with known post-1975 exposure and try to estimate pre-1975 exposure with the methods we used in the historical exposure study we recently submitted to OSHA. This would require an extremely heavy commitment of resources on our part, and *the resulting data would still be clouded with uncertainty.*[45] [Emphasis added]

Prior communication from Dr. Infante demonstrates a climate of antagonism between Shell and OSHA during this time:

> Rather than providing the requested information, or explaining why it was not available, you both seem to have engaged in a personal attack on my scientific integrity. . . . Such unfounded accusations and personal attacks can only create a bad image for the Shell Oil company and industry in general and serve to divert attention from vital issues related to the protection of industrial workers from the toxic

effects of benzene. Your response to my requests also gives the impression that you might be withholding information.[18]

1985—"Brief Communication: Excess Leukemia in a Refinery Population"

In 1985, Shell published an SMR analysis from BHES in a *Journal of Occupational Medicine* article entitled, "Brief Communication: Excess Leukemia in a Refinery Population."[21] In this paper, Shell reported only 14 of 24 BHES leukemia cases.[21] The authors accomplished this reduction in part by limiting reporting to mortality (eliminating two live Wood River leukemia cases) and by omitting all the Deer Park cases. Shell's exclusion of these cases eliminated the few people who could give direct (instead of reconstructed) evidence about their benzene exposures. Shell reported a statistically significant excess of leukemia at Wood River but with the false and misleading caveat that "Although specificity of the work histories was limited, the investigation has shown that the subjects did not work in jobs identified as having the highest benzene exposures. At this time the excess of leukemia remains unexplained."[21] In fact, their earlier report to OSHA admits one of the Wood River cases worked in one of the highest-exposure jobs (Cumene plant)[12] and they omit to mention that subjects logged over 100 years of worktime in refinery-wide positions.

1986—"A Case–Control Study of Leukemia at an Oil Refinery"

In late 1984, Dr. Cole and Dr. Harland Austin submitted the more complete treatment of the BHES data, entitled "A Case–Control Study of Leukemia at an Oil Refinery," to NIOSH. This study, published in 1986, sought to "use the case–control design to identify the jobs or departments at the refinery responsible for the excess of cases of acute myelogeous leukemia." Cole and Austin tested the same hypothesis as the BHES study but with a modified case–control study design to test whether or not, "the men with leukemia had longer durations of exposure or higher levels of exposure [to benzene] than did comparable workers who did not develop leukemia."[22] The submission of the draft paper to NIOSH and OSHA in 1984 spurred both agencies to criticize not only the study but the underlying BHES data as well. Dr. J. Donald Miller, Director of NIOSH, summarized the criticism:

> We are concerned that the statement 'The study produced no distinctly positive result, not even for benzene, and the reason for the excess leukemia among refinery workers remains unexplained,' could serve to imply that benzene has adequately been ruled out as a cause for the observed excess. We do not agree with that implication. The small size of the study population and the lack of good information on which to estimate exposures for the subjects, do not support this implication. We believe exposure to benzene is the most likely explanation for the excess incidence of leukemia.[46]

This is followed by pages of detailed criticisms from the staff, including recommendations to combine Wood River and Deer Park data into a single study.[46] Despite these concerns, Shell published the study unchanged, failed to mention the NIOSH critique, and never fully followed up NIOSH's recommendations.

Unfortunately, neither the internal nor the published case–control study report provides individual exposure information, so it is unclear to what degree the case-level misclassification errors of BHES were carried forward to this later study.[22,47] Other study design flaws are apparent. First, as has been shown, Shell's BHES classification of exposure potential by job or department contained so many unknown assignments with refinery-wide staff as to mask any possible exposure differences between cases and controls. Second, living leukemia cases were excluded, but controls could be either living or dead.[47] Third, despite Shell's assertion that the industrial hygienists were blinded, at least one key researcher developing exposure estimates knew which participants were cases and which were controls.[14,22]

1989 and 1995—Follow-up Mortality Studies

In 1989, Wongsrichanalai, Delzell, and Cole, in part in response to NIOSH's recommendations, published a mortality study that significantly expanded the Wood River cohort to include most workers, not just active or retired, and expanded the follow-up to 1984.[23] They did not pursue the second NIOSH recommendation, to combine Wood River and Deer Park data to improve the power of the investigation. In this publication, the authors reported a statistically significant 50% excess of leukemia deaths (44 observed versus 29.6 expected) and discussed benzene, a known leukemogen at the plant, as a possible casual factor in these cases.[23]

While the researchers could not avoid reporting an excess of leukemia for this study, several strategies were used to minimize the import of this finding. The authors admitted that occupational exposure to benzene was one possible hypothesis, but claimed "several observations argue to some extent against the hypothesis that the excess is due to refinery exposures."[23] They reviewed previous research on this cohort, the 1985 SMR analysis and the 1989 case–control study, reiterating that neither found an occupational link between leukemia and benzene. They theorized that hourly workers should have higher benzene exposures than salaried ones, and argued that the lack of correlation between leukemia and hourly work was evidence that occupational exposure had not caused this excess. However, this theory would place office janitors in the

same exposure category as the hourly laborers cleaning benzene lines. The authors admitted that these observations "do not detract greatly" from the causal association.[23] Finally, the authors pointed to a potential decline in recent cases to argue that Shell had corrected the benzene-exposure problem. They acknowledged, however, that the time period was too short to arrive at definite conclusions.[23]

In 1995, Delzell, Cole, and Honda published another mortality study, "undertaken primarily to evaluate more thoroughly the apparent disappearance of the earlier leukemia excess."[24] The authors expanded the cohort to 1989 and concluded after analysis, "These results indicate that any occupational leukemogenic exposures at the plant have been reduced to a point at which they are insufficient to cause leukemia."[24] However, the authors again relied on a flawed method. They determined exposure status in salaried employees by separating them into production versus non-production jobs.[24] Documents from Shell again demonstrate serious exposure misclassifications inherent in this method. For example, the following quote from the BHES peer interviews described the job of a refinery patrolman: "at times the fumes and smell on some units would cause the patrolman to cough and gag. Many times a person would blindly leave a unit with tears in his eyes."[48] Yet, the authors classified the patrolman as "unexposed."[49]

A comparison of the study publication and the internal report also demonstrates a bias towards publishing the beneficial findings. For instance, Shell's internal version of this study has a chart labeled, "Characteristics of WRMC employees who had leukemia and who died in the 1980s."[49] Sixteen leukemia deaths are listed on this chart, although only eight were reported in the published paper, due to the post hoc decision to exclude workers employed for fewer than six months. This post hoc decision contradicts contemporaneous scientific literature that shows the dose–response curve between benzene and leukemia is not linear but instead might be more dependent on high short-term or intermittent exposures.[50]

The authors incorporate yet another design flaw in the publication (but not the internal report) by disaggregating homogeneous pathologic conditions. The authors admit, "there may have been a local shift in diagnosis or reporting practices in the 1980s, with some persons designated as having [myelodysplasia/myelofibrosis] MF/MDS, who, if diagnosed in earlier time periods, would have been designated as having leukemia."[24]

As a result of these flaws, Cole et al. under-reported Shell's benzene-associated disease mortality statistics for 1980–1989. Shell's internal study report showed greater diligence in pursuing a probable link to benzene through the following methods: including people employed for fewer than six months, recording incidence, reporting contributing causes of death, and aggregating a broader spectrum of homogeneous conditions. Yet, the authors failed to report any of this information in the published paper.

CONCLUSION

In the words of Gennaro and Tomatis, "In spite of claiming primary prevention as their aim, studies of potential occupational and environmental health hazards that are funded either directly or indirectly by industry are likely to have negative results."[13] Shell's research on leukemia and the occupational exposures to benzene at their refineries demonstrates this phenomenon.

First, Shell distributed press and employee communications designed to assuage concerns about occupational exposure to benzene. These texts incorporated the healthy-worker effect flaw and directly contradicted their own internal data. Second, Shell rushed the BHES study report in order to influence rule making. The BHES study incorporated a host of design flaws, including repeatedly ignoring suggestions for better design, biased treatment of data, and multiple (and sometimes blatant) strategies for underreporting benzene exposures in leukemia cases. Two publications quickly followed this report, each further building the scientific base of industry-friendly findings. In the 1984 SMR analysis publication, Shell not only carried forward the many flaws of the original study, but it also reported on only one refinery, a strategy that reduced the potential to obtain statistical significance. In the 1986 case–control study, some of the flaws in the SMR analysis might have been corrected, but the use of unblinded researchers alone invalidates the study. In 1987, despite data from Shell and other benzene manufacturers arguing against a lower PEL, OSHA had gathered enough evidence to support reestablishing the 1978 PEL. Undeterred, Shell continued to build the legacy of BHES misdirection with the 1992 and 1995 WRMC mortality studies. Both studies repeat the previous flaws of not aggregating similar data (both the WRMC and the DPMC refineries), incorporating the healthy-worker effect, and misclassifying workers between exposure categories. BHES and related reports on leukemia show a pattern of attempting to influence regulation and litigation through biased research. The early BHES research was part of a larger group of tactics used to delay restrictive benzene regulation, resulting in an estimated 30 to 490 extra deaths.[11]

COMMENTARY

Exposure Standards

> "It must be recognized that this study's negative result will generally be perceived as not highly persuasive" because . . . Benzene, being highly volatile, may permeate nearly the entire facility and affect just 'susceptible' individuals."[15]

Dr. Cole's statement reveals a profound understanding that standardized risk assessments and therefore, standardized regulations do not protect real world populations of workers. It is an admission that the risks of contracting cancer (or any other disease) from exposures to a chemical substance are not equally distributed in a population. In other words, Shell's consultant tells them that because of genetic and other factors (other exposures, age, gender, diet, etc.) some individuals have much greater risks of contracting cancer from exposure to a particular carcinogen than do others.

Unfortunately, all risk assessments and regulations are based on epidemiologic studies that assume that population risks are equally distributed. This is not so. Some individuals contract cancer from particular exposures at lower doses.

Because exposure standards are based on average exposures that produce disease in average populations, all standards underestimate the real risks of contracting cancers of the vulnerable subpopulations who, for the most part, are the only individuals at risk for contracting the disease in question. It is clear that this systematic under protection of populations is a phenomenon well known to petroleum industry managers and their consultants.

Publication Standards

Shell's actions related to the BHES study are hardly atypical; the record of corporations manipulating science to maximize profit is significant and appears to be growing.[51–56] Seeding the literature with pro-industry findings is a strategy with far-reaching effects on regulation, as well as compensation.

There is enough evidence to demonstrate that the integrity of industry-funded research cannot be ensured by the current system of oversight.[51–56] We propose two simple strategies to remedy this situation. First, the interpretation of the Toxic Substance Control Act must be expanded, to require all source data be provided to regulatory agencies along with summary reports. Second, these same source data should be posted online, available to reviewers, and subject to random audits when used as a basis for a peer-reviewed journal article. Although the current voluntary "peer-review" process never looks at raw data, journals could learn from the IRS and leverage compliance (quality) by randomly auditing papers. Like the IRS, journals could weight the selection process to select a higher percentage of industry-conducted studies.

Not one of us knows the level to which medical and scientific literature has been influenced by deliberately biased publications. The longer we allow this problem to stand unchallenged, the greater suspicion we throw on the full body of scientific work built over so many years. The solutions we propose are neither difficult, nor costly; they should be implemented as soon as possible.

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