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Subject: Additional Information to Supplement the Files 8EHQ-02-15135 / 8EHQ-0502-15135A
and 8EHQ-0605-1513B

Dear Sir/Madam:

BASF Corporation is submitting the attached publication entitled "Investigation of Cancer Occurrences Associated with an Herbicide Manufacturing Facility" by M. Gerald Ott et. al. J La State Med Soc Vol 158 Sept/Oct 2006 as additional information.

If there are any technical questions regarding this publication, these should be addressed to our Corporate Epidemiologist, Gerald Ott, Ph.D., located at BASF Corporation, 333 Mount Hope Road, Rockaway, New Jersey 07866, telephone number (973) 895-8023.

Sincerely,

Janet Cerra

Janet Cerra
Product Regulatory Center of Excellence

/jc

Attachment



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301052

Investigation of Cancer Occurrences Associated with an Herbicide Manufacturing Facility

M. Gerald Ott, PhD; Sandra L. Poche, BSN; Julia E Klees, MD;
and Patrick R. Conner, MD

This study evaluated cancer incidence and mortality among 251 employees of a facility that synthesized a benzothiadiazin herbicide between 1979-1987. It was initiated in response to a perceived cancer cluster. Cancers were identified mainly by review of occupational medical records and personal interviews. Standardized incidence ratios (SIRs) were computed using comparison data provided by the Louisiana Tumor Registry.

Overall mortality was less than expected and did not vary by job type or duration of assignment in the facility. Total cancer incidence was marginally elevated [SIR = 1.4; 95% Confidence Interval (CI): 0.9 – 1.9] and was highest among men assigned to the unit during 1979 [SIR = 2.1; 95% CI: 1.3 – 3.3]. Thirteen of 20 cancers among these men were either prostate (9) or digestive system (4) cancers. Increased medical examinations and cancer awareness may have contributed to the detection of cancers at earlier ages than would be seen in a general population. No specific workplace agents were identified to account for the findings although a workplace role cannot be ruled out.

In 2001, the BASF Medical Department initiated a cancer cluster investigation after several employees raised concerns about cancer cases suspected of being linked to a former herbicide production unit. The unit, located in Geismar, Louisiana, was operated from 1979 until 1987. It had been subject to prior concerns related to two testicular cancer cases diagnosed in 1980 and 1983. A causal link with work was considered improbable because these cases were diagnosed 15 months and 4 years after start-up of the unit.

After gathering basic data regarding the newly reported and prior known cancers, a preliminary incidence study was begun in 2001 and completed in 2002. The findings were shared with site employees and provided to the U.S. Environmental Protection Agency (EPA). Briefly, there were 14 observed vs. 8.3 cases expected based on external age- and race-specific cancer incidence rates for South Louisiana. Half of the cases were due to prostate (4) or colorectal cancer (3). As a next step, a summary of the study findings was sent to unit employees no

longer working for the company and follow-up of their health status was initiated. In this article, we describe the overall study approach and findings of additional follow-up through 2003.

METHODS

Approach

In this study we used a phased approach to facilitate periodic updating of employees on study progress. Initially, occupational medical records were reviewed and interviews conducted to confirm the newly reported cancer cases. Toxicological profiles were reviewed for chemicals present in the unit and industrial hygiene (IH) and acute exposure incident data were examined. A retrospective cohort study was then conducted in two steps. First, employees were followed for cancer incidence during their years of active company employment and these findings were communicated to current employees. Sec-

ondly, cohort members who had left active employment with the company were provided with written findings of the initial study and interviewed by a health professional to update their cancer incidence experience. After the second follow-up, the study findings were again communicated to current and former employees.

Study group

The study group consisted of 251 production, maintenance, and service employees assigned to the bentazon unit for 3+ months between the start-up and shut down of the unit. Eligible employees were identified from annual census lists of production personnel, maintenance records, IH personal monitoring records [1979-87], job histories obtained during annual medical examinations, and through direct employee contacts. During the various communications with cohort members, several additional personnel with maintenance assignments of 3+ months in the unit were identified and added to the study cohort. A small number of women performing office work in the unit were not included in the study.

Assessment of work exposure

Bentazon was produced in a closed, multi-step, batch process. The process was brought on stream beginning in January 1979 with initial production of the final product occurring in April 1979. The unit was permanently shut down by April 1987. It was dedicated to a single product and operated about 10 months per year. The starting materials were diisopropylurea (DIPU), sulfur trioxide, and anthranilic acid. Process steps included sulfonation, chlorination, solvent removal, distillation, ring closure, and purification of the final product. Additional raw materials and process by-products included ethylene dichloride (EDC), monochlorobenzene (MCB), sulfuric acid, thionyl chloride, dimethylcyclohexylamine (DMCA), dimethylformamide (DMF), phosgene, caustic soda, sodium bisulfite, isopropyl amidosulfonylchloride (IPS), and vinyl chloride, generated as a side-reaction of EDC. The final product was an aqueous solution of the sodium salt of bentazon.

Assessment of potential exposures was based on 1) review of personal air sampling data, 2) discussions with IH, production, and supervisory personnel, 3) analysis of acute exposure incidents while performing duties in the unit, and 4) individual job histories of unit employees. For some maintenance and service employees, dates and time spent in the unit were reconstructed through personal interviews. Personal air samples (n=337) had been collected mainly between 1981-84. Approximately 2/3 of these samples were obtained using activated charcoal as the absorbing medium and analyzed for three analytes (EDC, MCB, and vinyl chloride) by gas chromatography employing a flame ionization detector. Air monitoring for DMCA (54 samples) was based on sample collection by Tenax® sorbent tube with analysis by gas

chromatograph/mass spectrometer. Short-term (10 minutes to <2 hours) and full shift samples (N=35) were collected to assess anthranilic acid concentrations based on gravimetric analysis. Continuous area monitors were used to alert employees to any phosgene releases. Limited personal sampling was also performed for phosgene, DMF, and several other materials.

Each job was categorized as involving a low or high likelihood of direct daily contact with process chemicals. Jobs with a high likelihood of direct process contact were unit operators, shift foremen/supervisors, mechanics, and instrument technicians. Engineers, control room operators, and plant maintenance supervisors were considered to have a low likelihood of daily process contact. The categorization was validated via IH sampling results, acute exposure incident reports, and discussions with employees. Jobs were also categorized as production vs. maintenance and service.

Collection of health outcome data

Vital status follow-up was available through 1992 for all employees¹ and through 2003 for active and retired employees. Additional follow-up of employees who left BASF was obtained using a search firm with verification by postal or telephone contact. Death certificates were coded according to the 9th Revision of the International Classification of Diseases. Cancer incidence follow-up was based on interviews and a review of each employee's occupational medical record including review of all routine medical examinations performed since 1979. The examinations included a health questionnaire, clinical laboratory tests, spirometry, vision and hearing testing, and physical examination by a physician. Digital rectal examinations performed routinely, and beginning in 1994, PSA testing was added for men aged 50 and above. These records were also used to determine the role, if any, that the Medical Department may have played in detection of the cancer. Chemical exposure incidents must be reported to the Medical Department regardless of whether any symptoms were noted. Basic information regarding each incident is captured in the medical record.

For former employees, cancer occurrences were ascertained by telephone interview initiated by a BASF health professional after receiving a return receipt of delivery of a letter describing the results of the preliminary study. For cancer cases, information was ascertained regarding date of diagnosis, site of cancer and cell type, treatment, and any indication of spread of the cancer to other organs. Individuals were also queried concerning second primary tumors. Interviews were conducted with a spouse if the former employee was ill or no longer alive. For persons with no listed telephone number, a follow-up letter was sent asking them to contact the Medical Department directly. The follow-up efforts were continued until February 2004.

Table 1. Demographic and employment characteristics of the study group.		
Characteristic	Study Group (N=251)	
	No.	%
Birth Year		
1916-39	49	19.5%
1940-49	95	37.9%
1950-65	107	42.6%
Race		
White	202	80.5%
African American	49	19.5%
Employment Status		
Current Employee*	83	33.1%
Retired	52	20.7%
Left	116	46.2%
Pay Status		
Hourly	178	70.9%
Exempt/Nonexempt	73	29.1%
Duration of Employment		
<1 year	8	3.2%
1-9 years	94	37.5%
10-19 years	61	24.3%
20+ years	88	35.1%

*As of 12/31/2003.

Methods of Analysis

Expected numbers of cancer cases and cause-specific deaths were assessed by a modified life-table approach, with person-years accumulated through last date known alive for mortality and through date of last employment or last contact for cancer incidence. Confidence Intervals (CIs) for standardized mortality ratios (SMRs) and standardized incidence ratios (SIRs)

were calculated based on Poisson distribution assumptions. For external mortality comparisons, we used age- and calendar-specific death rates for the U.S. male population and, for cancer incidence, age-, race- and calendar-specific incidence rates for South Louisiana.² The most recently available incidence data were for 1996-2000.

RESULTS

Demographic and employment characteristics of the study group are summarized in Table 1. The cohort included 71% hourly employees and 20% African Americans. At least one IH sample was collected for 46% of the 251 cohort members. Time-weighted-average (TWA) concentrations of EDC and MCB were generally below 1 part-per-million (ppm). In the case of EDC, 10% of the measurements exceeded 1 ppm and 5% (12 of 222) exceeded 2 ppm TWA. Two samples exceeded 10 ppm. All measurements exceeding 2 ppm occurred among individuals assigned to jobs classified as having a high likelihood (12 of 187) vs. a low likelihood (0 of 35) of daily contact with process chemicals. Similarly, 21 of 216 samples analyzed for MCB exceeded 1 ppm, and 3 samples exceeded 10 ppm. None of the 215 full-shift samples analyzed for vinyl chloride exceeded 0.5 ppm. Sampling for anthranilic acid during transfer operations revealed median dust concentrations of 2.7 mg/m³. Finally, long-term sampling results for DMCA were consistently below 1 ppm, although employees frequently detected its presence due to the intense fishy odor. Air sampling for bentazon was not carried out as the product was handled in an aqueous solution and was of low volatility.

A summary of acute exposure incidents is presented in Table 2. During the 8 years of operation, there had

Table 2. Summary of acute exposure incidents among 251 study group employees by agent and type of work.						
Agent	Total		Production		Maintenance and Service	
	No.	Rate ^A	No.	Rate ^A	No.	Rate
Total^B	198	0.238	139	0.259	59	0.200
Phosgene	58	0.070	51	0.095	7	0.024
Inorganic acids/bases	40	0.048	29	0.054	11	0.037
Dimethylcyclohexylamine	32	0.038	20	0.037	12	0.041
IPS + IPS residues^C	22	0.026	10	0.019	12	0.041
Monochlorobenzene	18	0.022	12	0.022	6	0.020
Thionyl chloride	12	0.014	6	0.011	6	0.020
Anthranilic acid	6	0.007	4	0.007	2	0.007
Ethylene dichloride	5	0.006	5	0.009	0	0.000
Others	2	0.002	1	0.002	1	0.003
Unknown	15	0.018	6	0.011	9	0.030

^A Rate = number of episodes per work-year in job category

^B Total is less than sum of specific agent totals because 12 incidents involved exposure to two different agents.

^C Isopropylamidofluoride (IPS) and IPS residues.

Table 3. Observed and expected deaths among bentazon unit employees (1979-2003).

	Obs/Exp ^A Deaths	SMR	95% CI
Total Study Group (N=251)	29/34.1	0.9	0.6 – 1.2
Production (N=142)	13/14.3	0.9	0.5 – 1.6
Maintenance and Service (N=109)	16/19.8	0.8	0.5 – 1.3
Time assigned to unit during 1979			
None (N=119)	13/14.8	0.9	0.5 – 1.5
>0 - <1 Year (N=32)	6/5.2	1.2	0.4 – 2.5
Full year (N=100)	10/14.1	0.7	0.3 – 1.3
Time in jobs with high likelihood of daily process contact			
None (N=39)	3/5.5	0.5	0.1 – 1.6
>0 - <1 Year (N=53)	9/8.5	1.1	0.5 – 2.0
1+ Years (N=159)	17/20.1	0.8	0.5 – 1.4

^A Expected deaths calculated based on age- and calendar-specific death rates for the U.S. general population.

been 198 exposure incidents. Approximately ½ of these incidents were attributed to phosgene exposure or exposure to inorganic acids/bases. Incidents occurred at a rate of 0.24 incidents per work-year with overall rates about 30% higher among production than maintenance or service employees. The distribution of incidents by chemical agent also varied by type of work with production personnel more frequently reporting phosgene exposures and maintenance and service personnel reporting exposure to IPS, IPS residues, or to unknown agents. The route of exposure was inhalation in 113, skin contact in 68, eye contact in 10, and other or unknown in 7 incidents. In 27%, no symptoms were reported in the medical record. Skin, respiratory, and gastrointestinal symptoms were reported in 30%, 25% and 12% of the incidents, respectively. Only one acute exposure event was ascribed to bentazon exposure. Overall incident rates are depicted by year and job category (high vs. low likelihood of daily contact with process chemicals) in Figure 1. The rates were highest during the first year of unit operation, and phosgene-related incidents were disproportionately higher during that year.

Mortality and cancer incidence findings

Vital status was known through 12/31/2002 for 244 of 251 employees (97.2%) assigned to the bentazon unit. Among 218 employees alive at the start of 2003, 3 died during the year; 149 were alive through 12/31/2003; and 66 were alive when contacted in 2003. Observed and expected deaths are summarized in Table 3. The overall SMR was 0.9 and there was no unusual trend relative to type of activity or exposure subgroup. There were 10 cancer deaths (8.8 expected) in the total study group. Death certificates were not obtained for 10 decedents; however, in four instances the surviving spouse reported that the former em-

ployee had never been diagnosed with cancer. Among employees assigned to the unit during all of 1979, there were 3 observed vs. 3.7 expected deaths due to cancer; for two decedents death certificates were not obtained, and there was no spouse interview.

Cancer incidence follow-up is summarized in Table 4. Sixteen of the 31 cancers identified during the study were reported during the period of active employment. Mailing of notification letters and subsequent telephone contact was attempted for 142 left and retired employees. For 7 individuals, no current address could be verified by return receipt. Telephone interviews were completed with 114 men and 6 spouses among the 135 individuals who had signed for the letter. Interviews with the spouse oc-

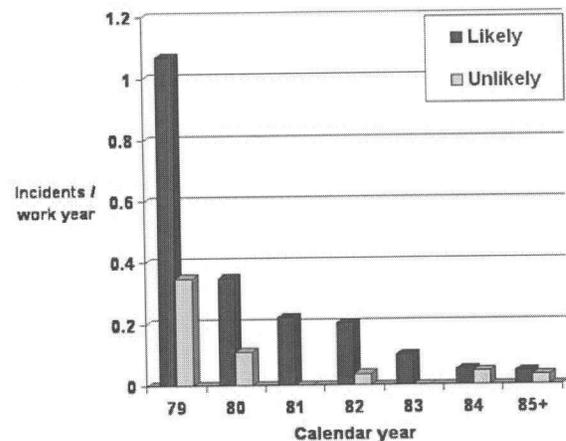


Figure. Acute exposure incidence rates by likelihood of direct daily contact with process chemicals and year.

Table 4. Cancer Incidence Follow-up of 251 bentazon unit employees.		
Employee Category	Number	Cumulative Follow-up %
Still working through 2003	83	33%
Deceased with death certificate (DC)	18	40%
Retired with examinations, 2002-2003	2	41%
Completed interview of employee (114) or spouse (6)	120	89%
Lost-to-follow-up		
Deceased with no spouse contact or DC	6	-
Refused to provide updated health history	1	-
Letter received but no contact by telephone	14	-
Lost-to-follow-up – No address	7	-

curred in four instances where the employee had died and in one instance where the employee was ill and later died. Only one interviewee refused to provide updated health status information. Fourteen men had unlisted telephone numbers or could not be reached after three attempted phone calls. Cancer incidence follow-up was thus completed for 223 of 251 individuals (89%) in the total study group and was 91% complete among employees assigned to the unit throughout 1979.

Observed and expected cancer incidence cases are shown in Table 5 by type of work activity and exposure subgroup. The overall SIR was 1.4 (95% CI: 0.9 – 1.9) based on 31 cases excluding non-melanoma skin cancer. There was no appreciable difference in results by type of activity and no notable difference based on time in high potential exposure jobs. Among employees assigned to the unit for all of 1979, there was an elevated SIR (SIR = 2.1; 95% CI: 1.3 – 3.3).

In Table 6, SIRs are presented by cancer site. An elevated SIR was observed for prostate cancer based on 11 observed vs. 5.0 expected cases. By age group there were 10 observed vs. 3.2 expected cases among men under age 65, but only 1 observed vs. 1.8 expected cases among men over age 65. Nine of the 11 prostate cancer cases were associated with assignment to the unit throughout 1979 (SIR = 4.3; 95% CI: 2.0 – 8.1). The age at diagnosis for these 9 cases ranged from 53 to 61 years and the year of diagnosis between 1994 and 2003.

There were also 8 digestive system cancers vs. 4.6 expected cases. These included one esophageal, five colon, and two pancreatic cancers. The colon cancer cases had worked for 1+ years in jobs with direct process contact and 4 cases (2 colon, 1 pancreas, and 1 esophagus) had worked in the unit throughout 1979. Among other site-specific cancers, there were three lymphomas, two lung cancer cases, and two bladder cancers. The all other

Table 5. Observed and expected cancer incidence cases among former bentazon unit employees (1979-2003).			
	Obs/Exp ^A Cases	SIR	95% CI
Total study group (N=251)	31/22.9	1.4	0.9 – 1.9
Production (N=142)	14/9.0	1.6	0.9 – 2.6
Maintenance and Service (N=109)	17/13.9	1.2	0.7 – 2.0
Time assigned to unit during 1979			
None (N=119)	8/10.0	0.8	0.3 – 1.6
>0 - < 1 Year (N=32)	3/3.3	0.9	0.2 – 2.7
Full year (N=100)	20/9.5	2.1	1.3 – 3.3
Time in jobs with high likelihood of daily process contact			
None (N=39)	5/3.5	1.4	0.5 – 3.3
>0 - < 1 Year (N=53)	6/5.7	1.1	0.4 – 2.3
1+ Years (N=159)	20/13.7	1.5	0.9 – 2.3

^A Expected cases calculated based on age-, race-, and calendar-specific cancer incidence rates for South Louisiana.

Table 6. Observed and expected cancer incidence cases by site among former bentazon unit employees (1979-2003).

	Total Study Group (N=251)			Worked all of 1979 (N=100)		
	Obs/Exp ^A Cases	SIR	95% CI	Obs/Exp ^A Cases	SIR	95% CI
Total cases^B	31/22.9	1.4	0.9 – 1.9	20/9.5	2.1	1.3 – 3.3
Total digestive system	8/4.6	1.7	0.8 – 3.4	4/1.9	2.1	0.6 – 5.4
Colorectal	5/2.6	1.9	0.6 – 4.5	2/1.1	1.8	0.2 – 6.5
Respiratory system	2/5.7	0.4	0.0 – 1.3	0/2.4	0.0	0.0 – 1.5
Prostate	11/5.0	2.2	1.1 – 3.9	9/2.1	4.3	2.0 – 8.1
Urinary system	2/1.9	1.1	0.1 – 3.8	2/0.8	2.5	0.3 – 9.0
Lymphatic + Hematopoietic tissue	3/1.9	1.6	0.3 – 4.6	2/0.8	2.5	0.3 – 9.0
All other^C	5/3.8	1.3	0.4 – 3.1	3/1.6	1.9	0.4 – 5.6

^A Expected cases calculated based on age-, race-, and calendar-specific cancer incidence rates for South Louisiana.

^B Excludes non-melanoma skin cancer.

^C All other includes two testicular, one throat, one melanoma of skin, and one brain cancer.

category consisted of one throat, one brain, and two testicular cancers and a melanoma of the skin. There had been no additional testicular cancers reported beyond the two cases reported in 1980 and 1983.

Study group employees had participated in over 1,550 occupational medical examinations or an average of 6.2 examinations per employee. Overall, these examinations led to physician referrals for further diagnostic work-ups in 8 of 16 cancer cases identified during active employment. In regard to prostate cancer, examination findings played a role in detecting all 4 cases diagnosed during active employment. Among men still employed by 1994, 72%, and of those over age 50 at last employment, 91% had at least one PSA test. Two medical referrals based on PSA results and two referrals based on other findings led to identification of prostate cancer cases in the study group. Among other cancers, occupational medical referrals played a role in detecting 3 of the 6 digestive cancers identified during active employment.

DISCUSSION

The overall mortality experience of the study group was comparable to that of all Geismar site employees as per the 1992 cohort study.¹ In that study, SMRs were 0.85 and 0.72 for hourly men employed for <10 and 10+ years at the site, respectively. In the present cohort, there was no relative increase in mortality either with respect to assignment to the bentazon unit during 1979 or time in jobs with direct daily process contact. There was also no difference in mortality by type of work activity. Ten deaths (8.8 expected) were due to cancer, and among employees assigned to the unit throughout 1979, there were 3 observed vs. 3.7 expected cancer deaths.

The overall cancer SIR was marginally, but not significantly, elevated relative to the external referent population. Results did not differ appreciably by work activity or time in jobs with daily process contact. The SIR was, however, statistically elevated for men assigned to the unit throughout 1979. Among specific cancer sites, prostate cancer was statistically elevated in the total cohort and among men who worked throughout 1979. Although the prostate cancer findings are compatible with a work-related effect, the elevated risk ratios could be due to other factors as well. First, the findings may be subject to detection bias due to both an active medical surveillance program and past concerns about cancer occurrences associated with work in the unit. Our program included annual digital rectal examinations and routine PSA testing that together can have a major impact on incidence rates. In a large randomized clinical trial, a five-fold higher incidence of prostate cancer was found in the screened group over a 4-year period of observation.³ A study conducted at a production facility in an adjacent parish also identified a relative excess of prostate cancer cases that was believed to have been due to frequent PSA testing.⁴ A subsequent nested case-control study supported this conclusion.⁵

In the present study, 3 of 9 prostate cancer cases among persons who had worked in the unit during all of 1979 were referred for diagnostic work-up based on BASF medical findings. The remaining cases were diagnosed after leaving employment and, except for one case in a former project manager, were detected between 2000 and 2003. The men were between 55 and 61 years of age. We do not have detailed information on how these latter cases came to be diagnosed; however, these are prime ages for early detection of prostate cancer through screening. Four of 9 cases were diagnosed among 53-61 year-old black

men between 1999 and 2002. Recent National Cancer Institute data indicate that prostate cancer incidence rates have risen more rapidly among black than white men since the advent of PSA testing.⁶ Between 1988 and 2002 the age-adjusted rates among 20-54 year-old black men rose from 10.3 to 56.0 per 100,000 and among 55-64 year-old black men rose from 289 to 818 per 100,000. These trends are not fully reflected in our comparisons because Louisiana Tumor Registry data were only available through 2000 at the time of our analyses. The relatively higher SIR for black men in our study group is again suggestive of a differential screening effect.

The established risk factors for prostate cancer are age, ethnicity, and a positive family history of the disease.⁷ Evidence linking prostate cancer to other factors has been inconclusive.⁸⁻¹² We are not aware of any data linking exposure to the chemical substances used in the bentazon process with prostate cancer either in animals or humans although several process materials have been identified as potential carcinogens based on animal bioassays or chemical reactivity. In particular, ethylene dichloride is recognized by the International Agency for Research on Cancer (IARC) as a multi-site animal carcinogen, but with inadequate evidence of carcinogenicity in humans.¹³ Vinyl chloride is a known human carcinogen capable of inducing liver and possibly brain cancer, but may not be associated with lung cancer, lymphoma, and leukemia as earlier thought.¹⁴ With chlorobenzene, equivocal evidence of carcinogenicity (neoplastic liver nodules) was seen in male rats; studies in male and female mice and female rats were negative.¹⁵ IH monitoring indicated that exposures to these substances were well-controlled in the unit. Exposure to strong inorganic acid mists containing sulfuric acid has also been identified as carcinogenic based on excess laryngeal and lung cancer findings.¹⁶ Other process chemicals, namely, phosgene, IPS, and thionyl chloride, can be damaging to lung tissue, if inhaled, and hence may also have a carcinogenic potential in the respiratory tract. In the present study, no cases of laryngeal and a deficit of lung cancer were observed. No evidence of carcinogenicity was seen in a bioassay study of anthranilic acid.¹⁷ Bentazon itself has been classified as non-carcinogenic to humans by the US EPA Office of Prevention, Pesticides and Toxic Substances.¹⁸ There were also no cancer cases identified in the study among 17 men whose job tasks specifically involved final product handling.

Among other cancers of interest, there were 3 lymphomas and 5 colorectal cancer cases. The lymphoma cases included a non-Hodgkin's lymphoma (NHL) of the abdomen and a lymphoma confined to one gland among men with long-term assignments in the unit. A third lymphoma case was identified as a cause of death in a former employee with <1 year of work in the unit. Since the early 1970s, NHL incidence rates have been increasing about 3.6% per year.¹⁹ The strongest risk fac-

tor for NHL is immune deficiency related to organ transplantation, HIV infection, or other immunologic disorders. We found no indication of acquired immunodeficiency among any of the lymphoma cases although one cohort member, who underwent a heart transplant, was subsequently diagnosed with prostate cancer. Aside from familial predisposition and exposure to other infectious organisms, increased risks have been observed in studies of rubber, aircraft maintenance and petroleum refinery workers, chemists, anesthesiologists, pathologists, woodworkers, and in association with solvent and agricultural and pesticide exposures.¹⁹ In the present study, there were potential exposures to solvents, however, none of the substances used in the unit has been specifically linked to NHL occurrence.

The colorectal cancer SIR was marginally elevated compared to that expected based on South Louisiana incidence rates. The five cases did not cluster with respect to work in the unit during 1979, but did occur among employees who had worked for 1+ years in jobs with a potential for direct contact with process chemicals. Colorectal cancer risk factors include a positive family history of the disease, meat consumption, smoking, and high alcohol intake.²⁰ In the present study, a positive family cancer history was reported by 4 of the 5 cases, with one case reporting multiple family members with colon cancer and another reporting a father with colon cancer.

Our study is subject to sample-size limitations, reliance on self-reported cancer diagnoses, and difficulties in judging the impact of medical surveillance on disease detection. However, an important goal has been to be responsive to employees and their health concerns. Based on communications with those employees following the 2002 study, colonoscopy examinations were offered and taken advantage of by 35% of the eligible employees. These examinations yielded no new cancer cases. A cancer incidence study was also undertaken among employees assigned to a bentazon production unit in Germany.²¹ An overall cancer SIR of 1.2 (95% CI: 0.6 - 2.0) was observed, and subsequent clinical examinations including sonography of the prostate and PSA testing identified 3 prostate cancers, consistent with the experience of European PSA testing programs.

CONCLUSIONS

We observed several associations between cancer incidence and work in this unit. However, no specific agents were identified to account for the relative increases in prostate and colon cancer. Annual medical examinations may have contributed to enhanced detection of both prostate and digestive tract cancers and the reported associations could also have occurred as a result of the potential biases discussed above. Cancer cluster investigations have not typically resulted in identifying clear-cut causal

relationships,²² but that does not detract from the desire or need to conduct such investigations in response to the expressed concerns of employees.

REFERENCES

1. Ott MG. Mortality experience among Louisiana chemical manufacturing employees, 1957-1992. *J La State Med Soc* 1996;148:260-266.
2. Chen VW, Craig JF, Fontham E, et al. *Cancer in Louisiana. Volume VI – Cancer incidence in South Louisiana, 1983-1986*, State of Louisiana Department of Health and Hospitals, 1990.
3. van der Crujjsen-Koeter IW, van der Kwast TH, Schröder FH. Interval carcinomas in the European Randomized Study of Screening for Prostate Cancer (ERSPC)-Rotterdam. *J Natl Cancer Inst* 2003;95:1462-1466.
4. MacLennan PA, Delzell E, Sathiakumar N, et al. Cancer incidence among triazine herbicide manufacturing workers. *J Occup Environ Med* 2002;44:1048-1058.
5. Hessel PA, Kalmes R, Smith TJ, et al. A nested case-control study of prostate cancer and atrazine exposure. *J Occup Environ Med* 2004;46:379-385.
6. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 9 Regs Public-Use, Nov 2004 Sub (1973-2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005.
7. Hsing AW, Devesa SS. Trends and patterns of prostate cancer: what do they suggest? *Epidemiol Rev.* 2001;23:3-13.
8. Haas GP, Sakr WA. Epidemiology of prostate cancer. *CA Cancer J Clin* 1997;47:273-287.
9. Parent ME, Siemiatycki J. Occupation and prostate cancer. *Epidemiol Rev* 2001;23:138-143.
10. Van Maele-Fabry G, Willems JL. Occupation related pesticide exposure and cancer of the prostate: a meta-analysis. *Occup Environ Med* 2003;60:634-642.
11. Alavanja MCR, Samanic C, Dosemeci M, et al. Use of agricultural pesticides and prostate cancer risk in the agricultural health study cohort. *Am J Epidemiol* 2003;157:800-814.
12. Mills PK, Yang R. Prostate cancer risk in California farm workers. *J Occup Environ Med* 2003;45:249-258.
13. IARC. *IARC Monographs on the evaluation of carcinogenic risks to humans, Vol 71, Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide (part two)*. Lyon, pp. 503-529.
14. Kielhorn J, Melber C, Wahnschaffe U, et al. Vinyl chloride: still a cause for concern. *Environ Health Perspect* 2000;108:579-588.
15. NTP. *Toxicology and carcinogenesis studies of chlorobenzene (CAS No. 108-90-7) in F344/N rats and B6C3F1 mice (gavage studies)*. National Toxicology Program, U.S. DHHS, October 1985, NIH publication No. 86-2517.
16. NTP. *Report on Carcinogens, Eleventh Edition*. U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program.
17. NTP. Bioassay of anthranilic acid for possible carcinogenicity (CAS No. 118-92-3). *Natl Toxicol Program Tech Rep Ser* 1978;36:1-92.
18. US EPA. *Toxicological Review of Bentazon (CAS No. 25057-89-0). In support of summary information on the Integrated Risk Information System (IRIS)*. U.S. Environmental Protection Agency, February 1998.
19. Vose JM, Chiu BC, Cheson BD, et al. Update on epidemiology and therapeutics for non-Hodgkin's lymphoma. *Hematology* 2002; 241-262.
20. Potter JD. Colorectal cancer: Molecules and populations. *J Natl Cancer Inst* 1999;91:916-932.
21. Nasterlack M, Hoffmann G, Messerer P, et al. Epidemiological and clinical investigations among employees in a former herbicide production process. *Int Arch Occup Environ Health* 2006, [Epub ahead of print].
22. Caldwell GG. Twenty-two years of cancer cluster investigations at the Centers for Disease Control. *Am J Epidemiol* 1990;132(1 Suppl):S43-S47.

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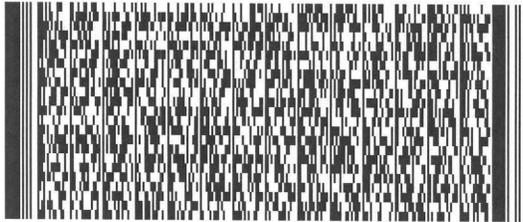
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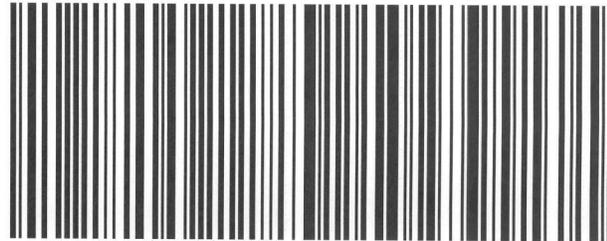
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