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Worker Exposures to Nitrosamines in a Rubber Vehicle Sealing Plant

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APPLIED STUDIES

Worker Exposures to Nitrosamines in a Rubber Vehicle Sealing Plant

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Occupational nitrosamine exposures were measured during a National Institute for Occupational Safety and Health (NIOSH) health hazard evaluation at a rubber vehicle sealing plant. All of the 28 personal breathing zone samples had detectable concentrations of nitrosodimethylamine (NDMA), nitrosodiethylamine, nitrosopiperidine (NPIP), and nitrosomorpholine; and 27 of the 28 samples had detectable concentrations of nitrosopyrrolidine. The NDMA exposures were the highest, ranging from 0.47 to 11.44 $\mu g/m^3$. The next highest exposures were to NPIP, ranging from 0.20 to 4.39 $\mu g/m^3$. Several general area air samples were also collected, which revealed concentrations of NDMA ranging from 2.29 to 88.47 $\mu g/m^3$ at the drills along the salt bath lines. The salt bath curing process appears to be the primary source of nitrosamine formation, and personal exposures were highest for the salt bath line operators and assistant operators. Although there are no numerical occupational nitrosamine standards in the United States to reference, the exposures in this plant were much higher than the German standard of 1 $\mu g/m^3$ total nitrosamines for general industry and 2.5 $\mu g/m^3$ total nitrosamines for certain processes such as vulcanization. NIOSH investigators recommended that the ventilation systems be improved to reduce the exposures to the lowest feasible concentrations until the process can be redesigned so that nitrosamines are not formed.

Keywords: nitrosamines, nitrosdimethylamine (NDMA), rubber vehicle sealing, salt bath curing process

Many nitrosamines are suspected of being human carcinogens, but direct causal associations have not yet been proven. The suspected mechanism of carcinogenesis is that nitrosamines from exogenous or endogenous sources are metabolized into reactive intermediates that can then covalently bind to macromolecules, including DNA. Although a causal association between nitrosamine exposure and human cancer has not yet been firmly established, there is circumstantial evidence that nitrosamines could cause cancer in humans. In 1956 Magee and Barnes demonstrated the carcinogenic potential of nitrosodimethylamine (NDMA) in rats.(1) Since then nitrosamines have been studied extensively in laboratory animals. Approximately 90% of the 300 tested nitrosamines have shown carcinogenic effects in bioassays and laboratory animals.(2) The animals that have been studied include mammals, birds, fish, and amphibia. Of the approximately 40 animal species tested, none has been resistant.(3) Nitrosamine effects have been demonstrated in 29 organs;(4) the tumor sites depend on the specific nitrosamine, the species tested, and the route of administration. Dose-response studies with rats have shown "no effect levels" corresponding to dietary concentrations of 1 ppm NDMA, 1 ppm nitrosodiethylamine (NDEA), and 5 ppm nitrosopyrrolidine (NPYR).(4)

All of the published biochemical, pathological, and experimental data provides little evidence that humans might be resistant to the carcinogenic potential of nitrosamines.(3) Human tissues from the trachea, bronchus (lung), esophagus, colon, pancreatic duct, bladder, and buccal mucosa have been shown to metabolize nitrosamines into DNA-binding compounds.(3) Human liver tissue appears to metabolize nitrosamines with a similar activity to rodent liver tissue, and rodents have acute symptoms of liver necrosis and cirrhosis similar to those observed in humans.(3) Human DNA adduct studies have revealed higher levels of nitrosamine-related DNA adducts in cancer cases than in controls.(5,6) Studies in experimental animals have shown similar DNA adduct formation to those detected in the human studies.(7–9)

The International Agency for Research on Cancer (IARC) has classified both NDMA and NDEA as group 2A carcinogens (probable human carcinogens), and nitrosodibutylamine (NDBA), nitrosodipropylamine (NDPA), nitrosomorpholine (NMOR), nitrosopiperidine (NPIP), and NPYR as group 2B carcinogens (possible human carcinogens).(10) The National Toxicology Program lists all seven of these nitrosamines as substances that may be reasonably anticipated to be human carcinogens.(11) Only one nitrosamine, NDMA, is regulated occupationally in the United States. Both the Occupational Safety and Health Administration (OSHA)(12) and the National Institute for Occupational Safety and Health (NIOSH)(13) consider NDMA to be an occupational carcinogen, and NIOSH recommends that its exposure be reduced to the lowest feasible concentration.(13) The American Conference of Government Industrial Hygienists also classifies NDMA as a suspected human carcinogen.(14) There are no established numerical exposure limits in the United States.

Germany, under the authority of the Ausschuss für Gefahrenstoffe, has regulations for occupational exposures to nitrosamines. In general industry the total exposure to all nitrosamines present may not exceed 1 $\mu g/m^3$. In certain specific operations, such as vulcanization, exposures to all nitrosamines present may not exceed 2.5 $\mu g/m^3$.(15)

Nitrosamines can be formed in the laboratory; in various food, household, or industrial products; in industrial processes; and in vivo. Because of the variety of amines and reaction conditions possible, there are hundreds of nitrosamines; and because of the large number of exposure sources, including formation in vivo, there is a complicated matrix of total nitrosamine exposure. Occupational exogenous exposures have been reported in rubber industries, leather tanning industries, metal working industries, chemical industries, mining, pesticide production, detergent production, and fish factories.(4)

This article presents the occupational nitrosamine exposures measured during a NIOSH health hazard evaluation at a rubber vehicle sealing plant. Two site visits—an initial one on February 16, 1994, and a follow-up on May 3–5, 1994—were performed to characterize the inhalation exposures to nitrosamines.

PROCESS DESCRIPTION

There were eight production lines that made continuous strands of automotive rubber vehicle sealing (VS), which were then cut and molded to fit the specific order. The process began with a strand of wire mesh being formed into a channel while dense rubber was extruded on top of it. Sponge rubber was extruded with the dense rubber to form the bulb portion of the vehicle sealing material.

The strand of rubber sealing was cured in a salt bath, an enclosed tunnel through which the rubber was mechanically pulled (Figure 1). A trough with slits in its bottom carried a combination of molten nitrate and nitrite salts along the inside of the top portion of the tunnel so that the molten salt showered the rubber as it was pulled through the tunnel. The entire salt bath was lined with access doors that remained open during start-up for 10 to 20 minutes (Figure 2). Throughout most of the workday these doors remained closed, except when each door was repeatedly opened and slammed shut to knock off the accumulated salt. This procedure occurred about twice a day, depending on the individual operator. Each salt bath had four ducted exhausts that exited the building through rooftop stacks.

As the rubber sealing exited the salt baths, it was cleaned with steam and high-pressure air and then cooled on a water drum. Next, small holes were drilled into the bulb portion at specified intervals. Also, the date, time, and specification number were printed on the rubber by a video ink jet marking process. The remainder of the process was varied depending on the specific order; the operations could include a preheating oven, a ventilated silicone spray booth, an infrared curing oven, or mastic injection, a process in which a starch and clay mixture was injected into the groove of some parts.

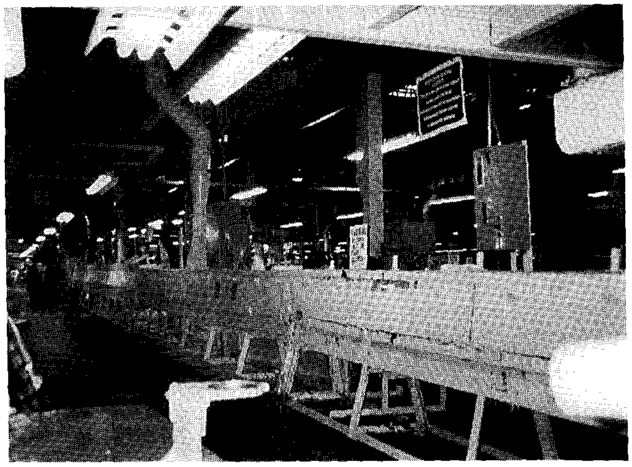

FIGURE 1. Salt bath with access doors closed, as during normal operations

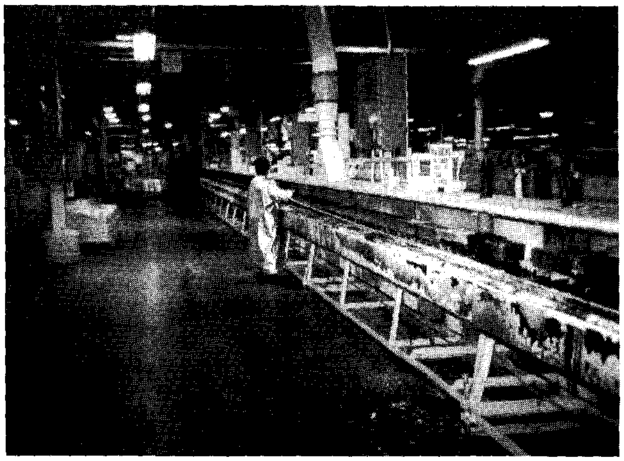

FIGURE 2. Salt bath with access doors open during start-up procedures

At the end of the line, the rubber was cut into the specified lengths and either boxed for shipping to the customer or further processed at this facility. Approximately 60% of the rubber sealing was shipped to customers as it came off the lines, and 40% was further processed before shipping. The rubber lines operated 24 hours a day with three 8-hour shifts, but the finishing procedures were usually performed only during the first shift.

Since different rubber stocks were used for different customer orders, depending on the current orders the salt bath lines could all be running different stocks. Likewise, one line could run one stock for a time, ranging from several hours to several days, and then be cleaned and set up to run a different stock.

The finishing processes included three types of joining procedures as well as adding tape and double-sided adhesive strips, cutting notches in the rubber, and spraying the new joints and notches with silicone. The three joining procedures were: (1) transfer molding, where small rubber pellets and a press were used to form a joint or molded details; (2) cold splicing, where glue and an accelerator were used to join two ends of the VS in a press; and (3) hot splicing, where glue and heat were used to join two ends of the VS in a press. The new notches and joints were then sprayed with silicone in a ventilated spray booth. Any exposed wire ends were then covered with a black adhesive and an accelerator to prevent rusting.

Some of the finishing processes, such as the hot presses, had local exhaust ventilation (LEV). The entire VS department was supplied by 11 make-up air units, three of which were added after 1989 when a test and balance ventilation survey revealed an imbalance of only 90,000 ft^3/min of make-up air compared to over 300,000 ft^3/min of exhausted air. The fourth new make-up air unit was added in 1992.

EVALUATION METHODS

During the first site visit general area (GA) nitrosamine samples were collected along Lines 5 and 6 on Thermosorb/N® air samplers over a 4-hour period using Gilian® high-flow air pumps at a flow rate of 2 L/ min. During the second site visit the nitrosamine samples were collected in the same manner as during the first visit except that the flow rate was 1 L/min. Over three consecutive days, 28 personal breathing zone (PBZ) air samples and 8 GA air samples were collected throughout the entire area. In addition, two bulk water samples were collected for nitrosamine analysis—one from the steam bath and one from the cooling drum.

All of the samples were analyzed by gas chromatography using a Hewlett Packard Innowax capillary column (30 m, 0.25 i.d., 0.25 μm film thickness). Also, a high-resolution mass spectrometer operated in the selected-ion-monitoring mode was used to confirm the identity of any compound that eluted at the same retention time as the nitrosamine standards by monitoring its molecular ion. In this way the chromatographic peak was confirmed as the nitrosamine compound of interest. The limit of detection for this method was 0.01 micrograms (μg) per sample.

RESULTS AND DISCUSSION

Nitrosamine Air Sampling

On February 16, 1994, three GA samples were collected and analyzed for nitrosamines, one by the drill press on Line 5, one just past the infrared oven on Line 6, and one midway along the salt bath on Line 6. All three samples had detectable amounts of NDMA, NPIP, and NMOR. The NDMA concentrations ranged from 6.3 μg/m^3 to 37.7 μg/m^3; the NPIP concentrations ranged from 3.9 μg/m^3 to 7.6 μg/m^3; and the NMOR concentrations ranged from 0.2 μg/m^3 and 0.37 μg/m^3. NDEA was also detected on two of the samples—0.16 μg/m^3 and 0.38 μg/m^3. All of these sample results are time-weighted averages and each sample was collected over approximately 4 hours.

These GA air sampling results suggested that volatile nitrosamines were present in this department and that further evaluation was warranted. Thus, a follow-up site visit was conducted on May 3–5, 1994. PBZ and GA samples were collected for nitrosamines on all three days of the site visit, and the sampling results are displayed in Tables I to IV. The highest PBZ exposures were to NDMA, ranging from 0.47 μg/m^3 to 11.44 μg/m^3; the next highest was to NPIP, ranging from 0.20 μg/m^3 to 4.39 μg/m^3. An amine-like odor was noticeable near the drill presses, and nitrosamine concentrations from the GA samples collected at various drill presses ranged from 2.29 μg/m^3 NDMA at Line 6 on May 5, 1994, to 88.47 μg/m^3 NDMA at Line 3 on May 5, 1994. The higher nitrosamine concentrations appeared to occur on the lines that were processing a rubber stock that contained dinitrosopentamethylene tetramine.

The highest PBZ exposures were collected on salt bath line operators and assistant operators. This would be expected, because these employees worked closest to the source. The operators were responsible for maintaining the extrusion and salt bath curing processes; they spent most of their shifts along the extrusion lines. The assistants performed other jobs along the extrusion line, such as packing the rubber stripping at the end of the lines and maintaining the silicone spray booths.

To estimate average exposure by job category, the results of NDMA concentrations were averaged. The exposures ranged from 1.2±0.4 μg/m^3 NDMA for the molding/finishing operators

TABLE I. Personal Breathing Zone Air Sampling Results for Salt Bath Line Operators

			Nitrosamine Concentration (μg/m^3)						
Job/Location	Date	Volume (L)	NDMA[A]	NDEA[B]	NDPA[C]	NDBA[D]	NPIP[E]	NPYR[F]	NMOR[G]
Line 6 operator	5/3/94	676	5.17	0.64	ND[H]	ND	2.57	0.06	0.1
Line 5 operator	5/3/94	870	5.69	0.25	ND	ND	2.44	0.08	0.09
Line 8 operator	5/3/94	672	1.68	0.19	ND	ND	1.1	0.04	0.04
Line 2 operator	5/3/94	566	6.48	0.28	ND	ND	2.54	0.05	0.09
Line 3 operator	5/4/94	844	4.35	0.10	ND	ND	1.88	0.06	0.18
Line 2 operator	5/4/94	854	3.90	0.07	ND	ND	1.59	0.04	0.16
Line 5 operator	5/5/94	846	5.58	0.20	ND	ND	3.25	0.08	0.16
Line 8 operator	5/5/94	822	1.40	0.81	ND	ND	1.03	0.04	0.08

[A] NDMA = nitrosodimethylamine
[B] NDEA = nitrosodiethylamine
[C] NDPA = nitrosodipropylamine
[D] NDBA = nitrosodibutylamine
[E] NPIP = nitrosopiperidine
[F] NPYR = nitrosopyrrolidine
[G] NMOR = nitrosomorpholine
[H] ND = none detected; minimal detectable concentration is 0.01 μg/m^3

TABLE II. Personal Breathing Zone Air Sampling Results for Salt Bath Line Feeders and Assistants

			Nitrosamine Concentration (µg/m³)						
Job/Location	**Date**	**Volume (L)**	**NDMA**[A]	**NDEA**[B]	**NDPA**[C]	**NDBA**[D]	**NPIP**[E]	**NPYR**[F]	**NMOR**[G]
Feeder	5/3/94	872	1.40	0.14	ND[H]	ND	0.64	0.01	0.07
Feeder	5/4/94	908	0.47	0.03	ND	ND	0.27	0.01	0.03
Feeder	5/5/94	898	2.89	0.32	ND	ND	1.18	ND	0.12
Line 5 coil packer	5/3/94	694	11.44	0.16	ND	ND	4.39	0.09	0.26
Line 2 coil packer	5/3/94	728	5.40	0.04	ND	ND	2.22	0.01	0.16
Line 8 coil packer	5/3/94	822	1.82	0.13	ND	ND	1.40	0.06	0.06
Line 2 coil packer	5/4/94	846	5.67	0.11	ND	ND	2.35	0.08	0.15
Line 8 assistant	5/4/94	814	2.96	0.07	ND	ND	1.72	0.12	0.18
Line 3 assistant	5/4/94	706	4.67	0.13	ND	ND	1.91	0.06	0.20
Line 7 assistant	5/5/94	768	1.10	0.04	ND	ND	0.64	0.03	0.06
Silicone booth operator	5/4/94	830	2.84	0.07	ND	ND	1.79	0.06	0.13
Silicone booth operator	5/5/94	818	3.80	0.21	ND	ND	2.61	0.06	0.15

[A] NDMA = nitrosodimethylamine
[B] NDEA = nitrosodiethylamine
[C] NDPA = nitrosodipropylamine
[D] NDBA = nitrosobutylamine
[E] NPIP = nitrosopiperidine
[F] NPYR = nitrosopyrrolidine
[G] NMOR = nitrosomorpholine
[H] ND = none detected; minimal detectable concentration is 0.01 µg/m³

to 4.4±3.1 µg/m³ NDMA for the salt bath operator assistants (Figure 3). These are only estimates of average exposure, because different workers in each job title were sampled on the different days, and also the rubber stock processed by each line varied from day to day. This also explains the high standard deviations.

A GA sample was collected inside the smoking break room on May 4, 1994, and in the nonsmoking break room on May 5, 1994. These samples both had detectable concentrations of NDMA, NDEA, NPIP, NPYR, and NMOR. A concentration of 4.17 µg/m³of NDMA was detected in the smoking break room; and a concentration of 10.37 µg/m³ of NDMA was detected in the nonsmoking break room. Since cigarette smoke contains nitrosamines, their presence was expected in the smoking room. The probable cause of the high amount in the nonsmoking room was that on May 5, 1994, the wind was out of the west/southwest. This wind direction blew the exhaust from the salt bath lines in the direction of the rooftop air handling units (AHUs) that served the offices and break rooms in the VS area. Specifically, the exhaust from Line 8, zone D was visually observed flowing directly into the AHUs. Also, the nonsmoking break room is located near the salt baths, across from the drill press of Line 1.

Two bulk samples were collected and analyzed for nitrosamines. One was a sample of the water in the bottom of the steam bath that cleans the rubber as it exits the salt bath. The other was a sample of water from the cooling drum. Neither bulk sample contained detectable amounts of nitrosamines—less than 0.02 µg per gram of water.

Ventilation Observations

Re-entrainment of exhaust appeared to be a problem in the offices and break areas in the VS department, and also in the entire work area. As previously mentioned, when the winds were from the west/southwest as was observed on May 5, 1994, salt bath exhaust flowed into the AHUs that supply the offices and break areas.

TABLE III. Personal Breathing Zone Air Sampling Results for Molding/Finishing Operators

			Nitrosamine Concentration (µg/m³)						
Job/Location	**Date**	**Volume (L)**	**NDMA**[A]	**NDEA**[B]	**NDPA**[C]	**NDBA**[D]	**NPIP**[E]	**NPYR**[F]	**NMOR**[G]
Injection press operator	5/3/94	808	0.53	0.01	ND[H]	ND	0.20	0.01	0.01
Press operator	5/3/94	670	1.07	0.03	ND	ND	1.02	0.03	0.09
Press operator	5/4/94	810	1.35	0.03	ND	ND	1.62	0.04	0.06
Press operator	5/4/94	776	1.47	0.12	ND	ND	0.98	0.06	0.17
Press operator	5/5/94	724	1.18	0.40	ND	ND	1.31	0.05	0.10
Punch press operator	5/5/94	780	1.12	0.05	ND	ND	1.35	0.03	0.07
C-pillar press operator	5/5/94	768	1.94	0.08	ND	ND	1.71	0.03	2.42
A-pillar press operator	5/5/94	766	1.19	0.05	ND	ND	1.12	0.03	0.10

[A] NDMA = nitrosodimethylamine
[B] NDEA = nitrosodiethylamine
[C] NDPA = nitrosodipropylamine
[D] NDBA = nitrosobutylamine
[E] NPIP = nitrosopiperidine
[F] NPYR = nitrosopyrrolidine
[G] NMOR = nitrosomorpholine
[H] ND = none detected; minimal detectable concentration is 0.01 µg/m³

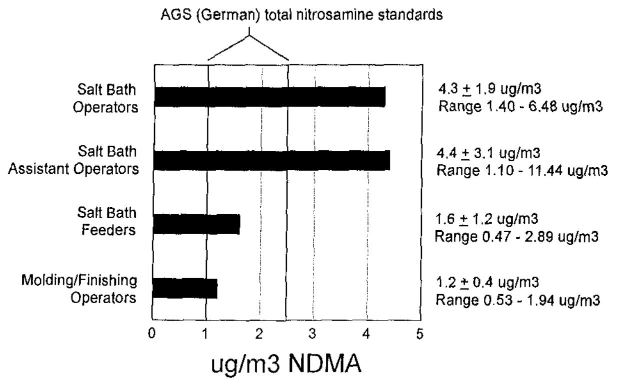

FIGURE 3. Average nitrosodimethylamine (NDMA) exposure by job title. Averages are estimates because different workers were sampled on different days and the rubber stocks processed by each line varied from day to day. These variations explain the high standard deviations.

When the winds were from the north, the exhaust was blown into the courtyard between the VS building and the empty warehouse. There are two AHUs in this courtyard that supply make-up air to the VS area. Also, there is a large garage door on the side of the VS building that opens to this courtyard. Exhaust was visually observed flowing into the AHUs and into the garage door opening on May 4, 1994. Similarly, when the wind was from the south, exhaust was blown to the other side of the VS building. A large water tank was located approximately 20 feet from this side of the building, and exhaust became trapped in eddies between the water tank and the building. There is another make-up air AHU in this area, and exhaust was seen flowing into it on February 16, 1994.

Inside the VS building some of the local exhaust ventilation (LEV) was not working properly. In some cases the exhaust was overpowered by floor fans or make-up air currents, such as along Line 8 at the ink spray jet. The LEV along the salt bath lines was working in some areas, but not others. Some local exhaust fans that were not working included Line 7, zone D on May 3, 1994; and Line 3, zone A, Line 7, zone D, and Line 8, zone D on May 4, 1994. In zones where the LEV fans were not working, emissions could be seen flowing out of the salt baths into the work area.

CONCLUSIONS AND RECOMMENDATIONS

Occupational exposure to nitrosamines appears to have been occurring in this rubber VS plant, and the primary source of exposure was the salt bath lines. A combination of insufficient LEV and salt bath exhaust re-entering the work area resulted in exposures to volatile nitrosamines in this workplace.

NIOSH considers NDMA to be an occupational carcinogen and recommends that its exposure be reduced to the lowest feasible concentration.(13) Since most nitrosamines have similar properties to NDMA and are suspected of being human carcinogens, the exposures to all nitrosamines in the VS plant should be reduced as low as feasibly possible. The best solution is elimination of the source. A few of the rubber stocks contain dinitrosopentamethylene tetramine, and those stocks appear to produce higher concentrations of nitrosamines. Also, the various rubber curatives and additives, such as alkyl carbamates, alkyl thiurams, and secondary amine derivatives, contain amines that can combine with the nitrite salts from the salt baths to form nitrosamines. Using a curing process other than salt baths and developing different rubber stocks that do not contain nitrosamines or secondary amines are two ways of eliminating the source.

Until the source of nitrosamines can be eliminated, better engineering controls are necessary. Better LEV along the salt baths and adding a LEV system at each drill press along the lines should reduce the volatile nitrosamine concentrations. Routine maintenance is necessary to ensure that the LEV systems are always functioning properly.

During the start-up procedures and the cleaning procedures, the salt bath access doors remain open, which alters the ventilation system. Workers involved in the start-up or cleaning should be provided with adequate respirators to ensure protection. NIOSH recommends full-face supplied-air or self-contained breathing apparatus respirators for protection from chemicals considered by either OSHA or NIOSH to be potential occupational carcinogens.(16) The required use of any respirators must be accompanied by an entire respiratory protection program.(16,17)

The ventilation system should be redesigned to ensure that no exhaust re-enters the workplace. Introducing contaminated outside air into the building negates the function of the exhaust

TABLE IV. General Area Air Sampling Results

			Nitrosamine Concentration (µg/m^3)						
Job/Location	**Date**	**Volume (L)**	**NDMA^A**	**NDEA^B**	**NDPA^C**	**NDBA^D**	**NPIP^E**	**NPYR^F**	**NMOR^G**
Line 5 drill	5/4/94	766	9.99	0.03	ND^H	ND	2.92	0.15	0.25
Line 3 drill	5/5/94	718	88.47	0.19	ND	ND	10.17	0.14	0.55
Line 5 drill	5/5/94	814	13.08	ND	ND	ND	4.03	0.16	0.06
Line 6 drill	5/5/94	368	2.29	ND	ND	ND	1.98	0.15	0.08
Line 7 drill	5/5/94	804	20.50	0.04	ND	ND	4.13	0.12	0.33
Line 8 drill	5/5/94	428	4.84	ND	ND	ND	2.20	0.05	0.13
Smoking break room	5/4/94	738	4.17	0.71	ND	ND	1.35	0.05	0.14
Nonsmoking break room	5/5/94	708	10.37	1.03	ND	ND	4.32	0.06	0.55

^{A}NDMA = nitrosodimethylamine
^{B}NDEA = nitrosodiethylamine
^{C}NDPA = nitrosodipropylamine
^{D}NDBA = nitrosobutylamine
^{E}NPIP = nitrosopiperidine
^{F}NPYR = nitrosopyrrolidine
^{G}NMOR = nitrosomorpholine
^{H}ND = none detected; minimal detectable concentration is 0.01 µg/m^3

systems. Outside air intakes, such as the ones on the rooftop AHUs or on the outside of the VS building, should be located in areas where exhaust does not flow directly into them or where it is not likely that exhaust will accumulate.

Future Evaluation

NIOSH investigated the nitrosamine exposure in the VS department in more depth. The total exposure and body burden of nitrosamines cannot be ascertained solely by air monitoring. Hence, a second evaluation was conducted to perform biological monitoring techniques along with air monitoring. Blood and urine samples were collected to measure nitrosamine-specific DNA adducts in peripheral blood cells and urothelial cells, the activity of the DNA repair enzyme that repairs these adducts, and the excised DNA adducts in the urine. Also, to help explain the expected interindividual variations, the genetic variability of the enzyme that activates nitrosamines in the body was assessed by a restriction fragment length polymorphism technique. Specifically, this study will assess whether the amount of occupational nitrosamine exposure is related to an increase in DNA adducts and a decrease in the bodily enzyme that repairs these adducts in exposed employees, allowing an estimation of the biologically effective dose (the amount that has interacted with cellular macromolecules) of nitrosamines in the exposed workers. Also, since the question of the human carcinogenicity of nitrosamines is still unresolved, the association of exposure with genotoxic events such as formation of DNA adducts and interference with DNA repair activity will provide useful information on the subject. The results of this second evaluation will be presented when the data analyses are complete.

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REFERENCES

1. **Magee, P.N. and J.M. Barnes:** The production of malignant primary hepatic tumors in the rat by feeding dimethylnitrosamine. *Br. J. Cancer 10*:114–122 (1956).

2. **Preussman, R.:** N-nitroso compounds. In *Environemental Carcinogens. Selected Methods of Analysis*, vol. 6. (IARC scientific pub. no. 45). Lyon, France: World Health Organization, International Agency for Research on Cancer, 1983. p. 4.

3. **Bartsch, H. and R. Montesano:** Relevance of N-nitrosamines to human cancer. *Carcinogenesis 5(11)*:1381–1393 (1984).

4. **National Institute for Occupational Safety and Health (NIOSH):** *N-nitroso Compounds in the Factory Environment*, by D.P. Rounbehler and J.M. Fajen (DHHS/ NIOSH pub. no. 83- 114). Cincinnati, OH: Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, NIOSH, 1983.

5. **Umbenhauer, D., C.P. Wild, R. Montesano, R. Saffhill, et al.:** O^6-methylguanosine in oesophageal DNA among individuals at high risk of oesophageal cancer. *Int. J. Cancer 37*:661–665 (1985).

6. **Saffhill, R., A.F. Badawi, and C.N. Hall:** Detection of O^6-methylguanine in human DNA. In *Methods for Detecting DNA Damaging Agents in Humans: Applications in Cancer Epidemiology and Prevention*, H. Bartsch, K. Hemminki, and I.K. O'Neill, eds. (IARC scientific pub. no. 89). Lyon, France: International Agency for Research on Cancer, 1988. pp. 301–305.

7. **Boucheron, J.A., F.C. Richardson, P.H. Morgan, and J.A. Swenberg:** Molecular dosimetry of O^4-ethyldeoxythymidine in rats continuously exposed to diethylnitrosamine. *Cancer Res. 47*:1577–1581 (1987).

8. **Deal, F.H., F.C. Richardson, and J.A. Swenberg:** Dose response of hepatocyte replication in rats following continuous exposure to diethylnitrosamine. *Cancer Res. 49*:6985–6988 (1989).

9. **Belinsky, S.A., J.F. Foley, C.M. White, M.W. Anderson, et al.:** Dose-response relationship between O^6-methylguanine formation in Clara cells and induction of pulmonary neoplasia in the rat by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. *Cancer Res. 50*:3772–3780 (1990).

10. **International Agency for Research on Cancer (IARC):** *IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans* (ISBN 92-832-1411-0, ISSN 0250-9555). Lyon, France: World Health Organization, IARC, 1987.

11. **National Toxicology Program:** *Sixth Annual Report on Carcinogens.* Rockville, MD: Department of Health and Human Services, Public Health Service, National Toxicology Program, 1991.

12. 29 *CFR* 1910.1016.

13. **National Institute for Occupational Safety and Health (NIOSH):** *NIOSH Recommendations for Occupational Safety and Health: Compendium of Policy Documents and Statements.* (DHHS/NIOSH pub. no. 92-100) Cincinnati, OH: Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, NIOSH, 1992.

14. **American Conference of Governmental Industrial Hygienists (ACGIH):** *1994-1995 Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices.* Cincinnati, OH: ACGIH, 1994.

15. **Bek. des BMA:** *German Technical Regulations for Hazardous Materials: N-nitrosamines* (no. 552). German technical regulations for hazardous materials, Bundesarbeitsblatt, no. 6, 1994.

16. **National Institute for Occupational Safety and Health (NIOSH):** *NIOSH Guide to Industrial Respiratory Protection.* (DHHS/NIOSH pub. no. 87-116) Cincinnati, OH: Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, NIOSH, 1987.

17. 29 *CFR* 1910.134.