Workers' Exposures to n-Propyl Bromide at an Aerospace Components Manufacturer

Kevin W. Hanley, MSPH, CIH, REHS/RS

Kevin Dunn

Ron Sollberger

Industrywide Studies Branch
Division of Surveillance, Hazard Evaluations and Field Studies
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
US Public Health Service
Department of Health and Human Services

IWSB 232.12

November 2006

Abstract

The National Institute for Occupational Safety and Health (NIOSH) conducted a field study at an aerospace component manufacturing plant where n-propyl bromide (nPB) was used as a vapor degreasing solvent. Workers' breathing zone and exhaled breath concentrations of nPB and isopropyl bromide (iPB), and urinary metabolite concentrations of bromide and propyl mercapturic acid were measured.

n-Propyl bromide has been marketed to replace ozone depleting solvents 1,1,1-trichloroethane and freons®, as well as suspect carcinogens trichloroethylene and methylene chloride; chemicals that were commonly used in industry. Very little data are currently available to evaluate *human* exposure to nPB. However, there is concern that nPB may be a hematological, reproductive, or neurological toxin, based on analogy to other brominated-propanes, animal toxicity studies, and a limited number of case studies.

Full-shift exposure to nPB in air samples collected in workers' breathing zones ranged from 0.19 to 2.6 parts per million (ppm). All of the workers were exposed to nPB at levels below the American Conference of Governmental Industrial Hygienist (ACGIH) Threshold Limit Value® (10 ppm) as well as the industrial guideline of 25 ppm published by the EPA in their proposed rulemaking to accept nPB under the Clean Air Act. Isopropyl bromide was not detected in either the air or breath samples. Exhaled breath concentrations of n-propyl bromide ranged from ND to 0.13 ppm and ND to 0.38 ppm, respectively, for pre-shift samples and post-shift samples.

Average urinary bromide concentrations were approximately 77% higher for workers than for unexposed control subjects who were not employed by the company. Twenty-four hour average propyl mercapturic acid concentrations measured in urine specimens from workers were over an order of magnitude higher than that measured in control samples. Dermal absorption may have contributed to some of the workers' exposure in addition to inhalation exposure. Workers with the lowest breathing zone concentrations of nPB had urinary metabolite levels similar to those measured in control specimens. At this time, the health significance of these levels of urinary metabolites is unclear.

Recommendations include, but are not limited to, substitution of nPB solvents with a less toxic solvent (if feasible), periodic exposure monitoring, use of gloves that are impermeable to nPB, and routine medical examinations.

Introduction

The Industrywide Studies Branch of the National Institute for Occupational Safety and Health (NIOSH) conducted a field study at Hamilton Sundstrand, an aerospace component manufacturing plant in Rockford, Illinois on February 23-25, 2004. At this facility, n-propyl bromide (nPB) was used as a vapor degreasing solvent to remove oils, chemicals, and dirt from various parts and components prior to the inspection, surface treatments, painting, and assembly. In this research study, we measured workers' breathing zone concentrations to nPB and isopropyl bromide (iPB), an impurity, with standard air sampling methods in conjunction with new methods for measuring exhaled breath and urinary metabolites.

Background

The toxicity of nPB, also named 1-bromopropane (CAS no. 106-94-5), is not fully understood as there is limited information in the published literature. The Environmental Protection Agency (EPA, 1999; 2003) is evaluating nPB as an alternative to ozone-depleting solvents for vapor-degreasing and liquid cleaning of metal, precision, and electronic components as well as for use as a solvent in aerosol products and adhesives. n-Propyl bromide has been marketed to replace 1,1,1-trichloroethane, freons®, and suspect carcinogens trichloroethylene and methylene chloride, chemicals that were commonly used in industry. Very little data are currently available to evaluate *human* exposure to nPB. However, based on analogy to other brominated-propanes, animal toxicity studies, and a limited number of case studies, there is concern that nPB may be a hematological (blood), reproductive, or neurological toxin. (Refer to Attachment I for more detailed information regarding the toxicity of nPB and iPB.)

Based on the uncertainty regarding the toxicity of nPB, the Occupational Safety and Health Administration (OSHA) and NIOSH requested the National Toxicology Program (NTP) to evaluate the toxicity of this chemical (OSHA, 1999; NTP, 2004). The absence of nPB exposure assessment information has prompted this occupational exposure study to evaluate industrial exposures to nPB by measuring workers' personal breathing zone, exhaled breath, and urinary metabolite concentrations.

Process Description

Hamilton Sundstrand is a subsidiary of United Technologies, a diversified multi-industry corporation which manufactures aviation engines; power fuel cells; elevators and escalators; climate control, fire and security systems; and components for industrial and aerospace applications. The company that participated in this study is one of the largest global suppliers of advanced aerospace systems for commercial, regional, corporate, and military aircraft as well as for sea and spacecraft. This company has 10 manufacturing sites in the U.S. and additional facilities in Puerto Rico, Southeast Asia, and throughout Europe. Electric and flight control systems were the primary products manufactured at the Rockford site including, but not limited to, power generation, distribution, and control systems; constant speed drives; auxiliary generators; electric power conversion equipment; flight control actuation and electro-magnetic systems.

At this site, the main campus consists of three major manufacturing plants, with another industrial plant approximately two miles away. Twenty-five hundred employees work at these facilities; seven hundred workers are represented by the United Automobile Workers, UAW local 592.

A nPB-based solvent (Leksol, Amity International, Inc.) is used as a vapor degreasing agent in six departments to remove oils, chemicals, and dirt from casings, drive components, and other parts necessary for inspection, surface treatments, painting, and assembly tasks. Eight vapor degreasers of different makes, models, and capacities are available; however, three of the units are seldom used, only a few times per month. The production schedule for this company is dictated by customer orders, typically in small quantities of less than 10-20 units. As such, vapor degreasers are not continuously operated, rather parts are cleaned in batches on an "as-needed" basis. Although approximately 100 employees have access to the degreasers, only about 30 routinely clean parts.

Vapor degreasers utilize a refrigerated cooling coil around the top of the interior of the vapor chamber, which condenses nPB vapor into liquid droplets on the cool surface of parts to remove surface contamination. Excess solvent drips back into the solvent sump and is recycled as the parts slowly ascend from the vapor to condensing zones. A secondary function of the cooling coil is to control solvent vapor emissions by "capping" the heated vapor zone with a refrigerated air space, typically six to twelve inches in height. Some of the nPB degreasers also had a chamber cover that was closed when the degreaser was not in use, and mechanical hoists to remove the part racks at a programmed speed to minimize excessive vapor from being carried out of the unit.

Most of the parts cleaning occurred in plant 6 on the main campus for Assembly Prep (one worker was the principal user of the degreaser); Repair-Overhaul (two workers); Electric Systems – Paint & Wire departments (two shifts, six workers per shift), and at plant 1 for MXM cell/corrosion treatment and non-destructive testing (three shifts, six or seven per shift); and Engine Control Systems – Paint & Wire departments (two shifts, six workers per shift).

In the Assembly Prep area, parts needed for the main assembly floor are cleaned in a small (15" x 46") open-topped Delta Sonics vapor degreaser which was equipped with ultrasound vibration to aid with cleaning, and a back plenum-slot exhaust ventilation system for additional contaminant control. In the Repair-Overhaul room, an open-topped, medium size (~2.5' x 4') degreaser (Branson B3550R) was used for non-destructive testing which included fluorescent dye penetrant inspections. A chamber lid and local exhaust ducting was provided above the condensing zone to assist with vapor emission control.

Final assembly of components were conducted in the Paint & Wire locations for both the Electric Systems and Engine Control Systems departments. Assemblers' job tasks included degreasing, painting, and fastening wires and identification plates prior to shipment. Spray painting was performed with methyl ethyl ketone (MEK) and other organic solvent based paints in large ventilated spray booths; acetone, Stoddard solvent, and isopropyl alcohol were also present in

these locations for clean-up activities. The Paint & Wire vapor degreasers were large semi-enclosed units because of the size of some components. Components were loaded into baskets (~2.5 x 4') or crates and placed into an open framed rack. The rack was mechanically hoisted up and over the external wall of the degreaser, lowered into the vapor zone, and similarly removed at programmed rate for effective cleaning and to reduce solvent carry-out.

A similar vapor degreasing unit was present in the MXM Cell area, Plant 1 to service anti-corrosion surface treatment and non-destructive test procedures. Surface treatments were applied by immersing parts into a series of chemical solutions and water rinses with an overhead hoist. Phosphate coating was the principal anti-corrosion treatment; chemical solutions included Turco alkaline rust remover, sodium hydroxide, sodium fluoride, and phosphate fluoride. A number of non-destructive test procedures were employed in the MXM Cell room to evaluate the integrity of metal casings and housings: magnaflux (magnetic particles in Stoddard solvent); zyglo (fluorescent penetrant dye); metalnox with ultrasound; and X-ray radiation. The vapor degreaser used in MXM Cell was very similar in size and design to those installed in the Paint & Wire locations. Even though the degreaser was enclosed, the large size and shape of some casings caused solvent to pool in the parts and subsequently carried-out of the vapor control zone. As a response to this problem, an auxiliary push-pull slotted local exhaust ventilation system was installed on the sides of the exit conveyor to reduce workers' exposures to nPB vapors. The slot opening in the suction plenum was approximately 4" x 5'.

Personal protective equipment used by employees included nitrile, neoprene, or butyl rubber gloves, safety glasses, and safety shoes. Organic vapor half-face piece respirators were available for protection against high nPB exposures such as draining spent solvent from the degreaser sump and replenishing it with Leksol. Chemical aprons, and face shields were also required when using the degreaser in MXM cell room. Hearing protection was also available as specified by the Health & Safety department.

Evaluation Criteria

At present, occupational exposure limits (OELs) for nPB are not available from either OSHA (2006) or NIOSH (1992), and suggested manufacturers' guidelines are inconsistent, ranging from 10 to 100 parts per million (ppm) (Great Lakes Chemicals, 2005; Enviro-Tech International, 2005). The EPA initially reviewed industry-sponsored animal studies and suggested that 50 to 100 ppm should provide adequate protection, but cautioned that this was a preliminary decision since it was based on limited data with considerable uncertainty (EPA, 2000). This proposal was largely based on hepatic toxicity observed in rats, not on reproductive, hematopoietic, or neurologic effects. After reviewing industry studies (Clintrials Biorecherches1997a, 1997b; WIL Research Laboratories, 2000) and published literature, Rozman and Doull (2002) concluded that neurotoxicity is the most sensitive end point and an OEL for nPB in the range of 60 to 90 ppm should provide an adequate margin of safety.

On June 03, 2003, the EPA published a proposed rulemaking to accept nPB as a replacement solvent for ozone depleting substances for general metals, precision, and electronics cleaning, aerosol products, and adhesives (EPA, 2003). In this proposed rule, the EPA recommends an

industrial exposure guideline for nPB of 25 ppm over an 8-hr work shift. The proposed rulemaking is currently being re-assessed by the EPA. Albemarle Co. (2003), one of the domestic suppliers of nPB solvents, also recommends an exposure guideline for nPB equal to 25 ppm as an 8-hour time weighted average (TWA) concentration. In 2005, ACGIH published a recommended Threshold Limit Value® (TLV) for nPB as a 10 ppm, 8-hr TWA based on suspected neurological toxicity (ACGIH, 2006). As one can see from these exposure guidelines, the OELs for nPB recommended by different organizations vary by an order of magnitude.

Following a case study of reproductive and hematological health effects in workers exposed to iPB in an electronics plant (Kim et al., 1996; Park et al., 1997), the Republic of South Korea promulgated an OEL for iPB of 1 ppm, measured as an 8-hour TWA. No other OELs are presently published for iPB. Occupational exposure criteria for two of the urinary metabolites of nPB which were analyzed at these facilities (e.g., bromide and propyl mercapturic acid) are currently unavailable.

Methods

In this research study, we measured nPB inhalation exposures with standard air sampling methods in conjunction with new methods for measuring exhaled breath and urinary metabolites. Employees voluntarily participating in the study were informed of the study requirements and provided their written consent in accordance with Human Subjects Review Board protocol. A total of 11 workers were included, each of whom worked with or was expected to be in the vicinity of vapor degreasers using nPB. The workers also wore a light-weight air sampling device on 2 consecutive days, provided pre- and post-shift exhaled breath samples, and all of their urine specimens over a 48-hour period. The air and breath samples were analyzed for nPB as well as iPB, a low level contaminant in nPB solvents. The urine samples were analyzed for bromide (Br) ion and propyl mercapturic acid (PMA), also called N-acetyl-S-(n-propyl)-L-cysteine.

Personal breathing zone exposures and exhaled breath samples were collected with Anasorb carbon molecular sieve (CMS) sorbent tubes. The sorbent tubes were desorbed with 1 milliliter (ml) of carbon disulfide, and analyzed for nPB and iPB by gas chromatography with flame ionization detection (GC-FID) via NIOSH method 1025 (NIOSH, 2003a). The limit of detection (LOD) for this method is 1 μg which equates to a minimum detectable concentration (MDC) of 0.017 ppm in air using the maximum recommended air sampling volume of 12 liters and a MDC of 0.066 ppm in an exhaled breath volume of 3 liters. Qualitative evaluation of skin contact potential was conducted by visual observation of job tasks since effective quantitative skin exposure measurement methods do not exist for compounds, such as nPB, that are volatile and readily penetrate intact skin.

To obtain data on nPB metabolites excreted by humans, all of the workers' urine voids over a 48-hour period were collected, including the amount excreted while away from work. The specimens were collected as composite samples over sequential time intervals: 1) at work, 2) after work but before bedtime, and 3) upon awakening. Each sampling survey was intended to occur over a 48-hour period that started at the beginning of the work week (Monday, pre-shift),

following a weekend of no exposure and end before the work shift on Wednesday. [However, three (out of four) employees in plant 6, and one (out of seven) employees in plant 1 worked with nPB over the weekend.] For comparison, single "spot" control samples were collected from twenty-one unexposed office workers who were not employed by this company.

Urine specimens were collected in nitric acid rinsed Nalgene® bottles [high density polyethylene (HDPE)] and immediately chilled in 10 quart coolers with gel ice that were individually supplied to each participant. Upon the end of the collection period, three-25 ml sample aliquots were dispensed into nitric acid rinsed HDPE bottles and immediately frozen on carbonic acid (dry-ice). The total urine volume for this collection period was also measured with a graduated cyclinder. In addition to Br and PMA, the specimens were also analyzed for creatinine (cr).

Bromine

Bromine (Br) was measured with inductively coupled plasma/mass spectrometry (ICP/MS; Varion Ultra-mass 700) using yttrium as an internal standard (Allain et al., 1990; Ichihara et al., 2004; Kawai et al., 2001). The LOD for bromine was 90 micrograms per liter (μg/l). One ml of each sample was diluted to 10 ml with 1% nitric acid prior to analysis. Analytical standards and quality control samples were prepared using Uri-sub, a synthetic urine solution. This was necessary because background concentrations of bromine may be present in pooled urine from the general population.

Propyl mercapturic acid

The urine specimens were analyzed for PMA, one of the major mercapturic acid metabolites of nPB (Grenby and Young, 1960; Jones and Walsh, 1979). Four ml aliquots of the urine specimens were loaded onto a solid phase extraction cartridge, rinsed with three ml of a methanol-acidified water mixture (pH = 3); PMA was then extracted in four ml of acetone, dried under nitrogen, and reconstituted in one ml of methanol. Analysis was performed using high performance liquid chromatography (HPLC) with electrospray ionization-tandem mass spectrometry (ESI-MS/MS) for improved sensitivity and specificity (e.g., confirmation of chemical identity).

Creatinine

Creatinine was analyzed using Sigma diagnostics test kit, procedure #555. Room temperature urine specimens were diluted by a factor of 20 (or 40 if very concentrated) and mixed with six ml of alkaline picrate. After 10-15 minutes, color analysis of the creatinine-picrate complex was performed with a spectrophotometer (Milton Roy Spectronic 20 D). A 0.2 ml aliquot of acid reagent was then added and the specimen was re-analyzed after five minutes; positive results from the second analysis were subtracted from the first measurements as it is due to interfering compounds.

Creatinine is a protein by-product excreted in urine due to the metabolism of creatine from muscle exertion. It is often used to adjust urine data due to different levels of physical activity,

hydration, and urine concentrations between different individuals. The urine data in this report, however, are only presented as unadjusted concentrations, either mg/l or μg/l for Br and PMA, respectively. Once the data are compiled from multiple sites in this study, the urine data will be adjusted ("normalized") for creatinine (mg Br/gm creatinine or μg PMA/gm creatinine) for publication in scientific journals.

Results

Table 1A presents the air sampling results collected in workers' breathing zones over two full work shifts. Table 1B and 1C provide the data stratified separately for each plant. The TWA concentrations for all jobs in both plants ranged from 0.19 to 2.6 ppm with daily averages of 0.99 and 1.2 ppm. All workers' TWA exposures were less than 10 ppm. Iso-propyl bromide was not detected in any of the air samples. The two highest TWAs occurred in MXM cell department on a day when the degreaser was used thirteen times. Although the highest exposures occurred in MXM cell (plant 1) when conducting non-destructive testing, the average TWA exposure in plant 6 was greater than for plant 1 on both days (1.5 versus 0.69 and 1.5 versus 1.09, respectively for day 1 and day 2). One reason may be that three of the Assemblers who were monitored in plant 1, collectively used the degreaser once and only walked near theses areas on a few occasions. Workers in plant 6 reported infrequent use of the degreasers because they worked over the weekend.

Tables 2A, 2B, and 2C provide a summary of the breath concentrations for nPB, respectively for both plants combined, plant 1, and plant 6. The nPB concentrations measured in the post-shift samples ranged from non-detectable to 0.38 ppm. Ten (out of 22) samples had detectable levels of nPB in the pre-shift samples, ranging from ND to 0.13 ppm. Isopropyl bromide was not detected in any of the breath samples. The average breath concentrations measured in each building were nearly identical. However, nPB was detected in low concentrations (0.022-0.11 ppm) from air samples collected in the nurse's office during breath collection periods in Plant 1 but not Plant 6. This may have caused sample contamination.

The average Br concentration from urine samples collected before the work-week began was 8.8 milligrams per liter (mg/l) for both plants combined (Table 3A). For comparison, the average Br concentration was 4.0 mg/l in spot samples from control subjects who were not employed by this company. Moreover, the 24-hour average concentrations of urinary Br for all workers were approximately 77% greater than the control subjects. In plant 1, the average 24-hour Br concentrations were similar to the control average, but were two to three times higher in plant 6. The data for PMA are provided in Table 4A, 4B, and 4C, which show a similar trend as the average before work week concentrations for workers was approximately 44% higher than the average calculated from control specimens. Furthermore, the average 24-hour concentrations of PMA from all workers were an order of magnitude higher than controls for both work days. The most heavily exposed workers in plant 6 had the highest PMA in urine concentrations, however, the average 24-hour PMA levels in plant 1 were also at least four times as high as controls.

The potential for solvent splashing and dermal contact exists with vapor degreasing processes, especially in MXM cell department because of the shape of the parts. The gloves observed to be

used in these departments (nitrile and neoprene) do not provide adequate protection for more than a few hours.

Statistical analyses were not conducted for the data collected at this site since only 11 workers participated in the monitoring. Statistical analyses will be performed after all of the data collected at separate sites are pooled into larger data bases.

Conclusions

- All of the workers' full-shift exposures were below the industrial guideline of 25 ppm proposed by the EPA as well as the ACGIH TLV® of 10 ppm.

- The condensing coils and exhaust ventilation provided for the vapor degreasers is relatively effective in controlling nPB air emissions from these operations in both plants, given the observed production rates.

- Workers' exposures to iPB were not detected with a minimal detected concentration (MDC) well below 1 ppm, the only occupational exposure limit available (published by South Korea).

- The post-shift breath monitoring showed measureable levels of nPB but not iPB.

- With the exception of one sample, breath concentrations of nPB were not detected in pre-week samples.

- Dermal contact with recently degreased parts may contribute to the workers' exposures. nPB is appreciably absorbed through workers' intact skin, which contributes to their overall absorbed dose.

- Average 24-hour concentrations of the urinary Br were 77% higher for workers than for control subjects.

- Average 24-hour concentrations of the urinary PMA measured in worker specimens were at least 10 times as high as PMA concentrations measured in control specimens.

- The conclusions drawn are based on the data from the grouped population of workers. These data demonstrate that workers using degreasers are exposed to and are excreting nPB metaboles. However, the health significance of an individual's urine metabolite level is uncertain.

Recommendations

Human health effects from exposure to nPB are not fully understood as there are only a few reports in the published literature. The occupational exposure criteria of 25 ppm suggested by the EPA and some solvent manufacturers are largely based on limited data observed in animal

toxicity studies. As additional scientific information becomes available, the OEL currently proposed may, in fact, be lowered. Therefore, NIOSH scientists believe it is prudent to reduce occupational exposure of nPB to the lowest feasible levels.

To reduce the risk of hazardous exposures in the work environment, industrial hygiene principles incorporate the following hierarchy of exposure control, in decreasing order of preference (and effectiveness):

i) Eliminate a toxic substance by substituting it with a less toxic one or by process changes,

ii) Install engineering controls to remove or reduce the airborne contaminants, preferably at the point of emission using: local exhaust ventilation; isolation of contaminant emissions away from worker positions; or by process changes,

iii) Use of administrative controls to reduce individual exposures by altering or rotating job tasks and work schedules, thereby reducing high exposure durations, and

iv) Use of personal protective equipment (PPE), such as respiratory protection, gloves, aprons, etc., to reduce the absorbed dose from potential exposure. Although PPE is frequently used because it is a cheaper and easier method of control, it is the least desirable because it is not always effective. NIOSH policy is that PPE should only be used when engineering controls are infeasible; during the interim period when engineering controls are being installed or repaired; or when engineering controls are not effective in reducing exposure below hazardous levels.

More specific recommendations to minimize workers' exposures to nPB at this facility are provided below:

1. Eliminate nPB based solvents if feasible by using a less toxic substitute. It is advisable to consult with technical experts and solvent distributors to evaluate if there are any suitable alternative solvents that are less toxic which perform in accordance with engineering specifications.

2. Employee exposures to nPB should be periodically re-evaluated. If monitoring results exceed relevant criteria, install engineering controls consisting of local exhaust for the degreaser and provide make-up air ventilations systems to reduce airborne nPB concentrations. Design specifications are available in the ACGIH Industrial Ventilation Manual, 25th edition (2006). In addition, a routine maintenance schedule must be implemented to ensure effective performance of the equipment.

3. Respiratory protection should be provided for those workers who desire to use it when operating the vapor degreaser or if the controls are not effective in reducing exposures sufficiently. Only NIOSH approved air purifying respirators with organic vapor cartridges or NIOSH approved air supplied respirators should be used. The use of respiratory protection requires the implementation of a comprehensive respiratory protection program in accordance with OSHA regulations (29 CFR 1910.134) and NIOSH recommended procedures (NIOSH,

1987). A minimal acceptable program must be managed by a competent person and include: written procedures; proper selection; user training; routine cleaning and inspection; proper storage; surveillance of work conditions and worker exposures; program audits; medical determination of user fitness; and use of approved respirators.

4. n-Propyl bromide readily penetrates intact skin and common glove materials. The relatively low TWA air concentrations coupled with high PMA metabolites suggests that dermal contact and absorption of nPB is substantial for some workers using the vapor degreasers. When skin contact potential with nPB or parts recently removed from the degreaser is high, appropriate gloves, arm sleeves, aprons or other PPE should be used as appropriate. Solvent manufacturers recommend use of multiple layer laminates for protection against nPB. These include, but are not limited to, Viton™, 4H (PE/EVAL)™, and Silver Shield™. Other more common glove/PPE materials (e.g., latex, nitrile, neoprene, butyl rubber, PVC, etc.) do not adequately prevent nPB from penetrating the PPE material for more than 30 minutes to a few hours. This may include time after the glove is contaminated even though it is no longer worn by a worker. The more common gloves may still be required for protection against other chemicals used in these areas. Hence, it is advisable to consult with technical experts and safety supply vendors to select an array of gloves needed in these departments. Periodic training of employees is important to prevent them from using the wrong gloves for different applications.

5. If alternative solvents are not feasible, use nPB solvents that have the lowest iPB contamination as is possible. Based on the non-detectable iPB results, it appears that nPB solvents used at your facilities do not contain excessive iPB contamination. The ASTM (2001) standard for iPB contamination in nPB solvents is 0.10%. In the EPA proposed rulemaking (2003) to accept nPB solvents, a use restriction includes using nPB solvents with an iPB contamination not exceeding 0.05%, before blending into products. It is advisable to confirm that the nPB solvents at your sites meet this criterion.

6. Company management must maintain an awareness of the latest scientific information regarding occupational exposure guidelines for nPB as well as relevant health, safety, and environmental standards from regulatory agencies.

7. Employees potentially exposed to nPB should be provided with routine medical examinations. Reports of health effects should be referred to a health care provider who specializes in occupational or environmental medicine.

Table 1A.
Summary of workers' TWA[a] air sample concentrations of n-propyl bromide and isopropyl bromide for plants 1 and 6 combined.

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Chemical	Measure	TWA Air Concentration *(ppm)*[b] (n = 11)	
		Day 1	Day 2
nPB[c]	Average	0.99	1.2
	Range	0.19 – 2.1	0.11-2.6
iPB[d]	Average	–	–
	Range	ND[e]	ND

Table 1B.
Summary of workers' TWA[a] air sample concentrations of n-propyl bromide and isopropyl bromide for plant 1.

Chemical	Measure	TWA Air Concentration *(ppm)*[b] (n = 7)	
		Day 1	Day 2
nPB[c]	Average	0.69	1.1
	Range	0.19 – 1.1	0.11 – 2.6
iPB[d]	Average	—	—
	Range	ND[e]	ND

Table 1C.
Summary of workers' TWA[a] air sample concentrations of n-propyl bromide and isopropyl bromide for plant 6.

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Chemical	Measure	TWA Air Concentration *(ppm)*[b] (n = 4)	
		Day 1	Day 2
nPB[c]	Average	1.5	1.5
	Range	0.82 – 2.1	1.3 – 1.6
iPB[d]	Average	—	—
	Range	ND[e]	ND

Footnotes for Tables 1A, 1B, and 1C:

a) TWA = time weighted average. It is used when multiple samples are collected over the work shift to calculate the average exposure concentration "pro-rated" for time.

Example:

TWA = [(time 1 x conc. 1) + (time 2 x conc. 2)… + ($time_i$ x $conc._i$)] ÷ total time for both sample 1 and 2 plus all additional samples (i)

b) Units are in parts per million by volume; the amount of bromopropane per 1 million parts of air.

c) nPB = n-propyl bromide (also called 1-bromopropane).

d) iPB = isopropyl bromide (also called 2-bromopropane).

e) ND = non-detectable.

Table 2A.
Summary of workers' breath concentrations of n-propyl bromide[a] for plants 1 and 6 combined.

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Date	Measure	nPB Breath concentration *(ppm)*[b] (n = 11)	
		Pre-shift	Post-Shift
Day 1	Average	–	0.23
	Range	ND[c]	0.11 – 0.38
Day 2	Average[c]	0.11 (n = 5)[d]	0.17 (n = 8)[d]
	Range	ND – 0.13	ND – 0.21
Day 3	Average	0.097 (n = 5)[d]	n.a.[e]
	Range	ND – 0.13	n.a.

Table 2B.
Summary of workers' breath concentrations of n-propyl bromide[f] for plant 1.

Date	Measure	nPB Breath concentration *(ppm)*[g] (n = 7)	
		Pre-shift	Post-Shift
Day 1	Average	–	0.23
	Range	ND[h]	0.12 – 0.38
Day 2	Average[h]	0.11 (n = 4)	0.16 (n = 4)
	Range	ND – 0.13	ND – 0.19
Day 3	Average	0.096 (n = 2)	n.a.[i]
	Range	ND – 0.13	n.a.

Table 2C.
Summary of workers' breath concentrations of n-propyl bromide[a] for plant 6.

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Date	Measure	nPB Breath concentration *(ppm)*[b] (n = 4)	
		Pre-shift	Post-Shift
Day 1	Average	—	0.23
	Range	ND[c]	0.11 – 0.33
Day 2	Average	—[f]	0.18
	Range	ND – 0.12	0.13 – 0.21
Day 3	Average[c]	0.098 (n = 3)[d]	n.a.[e]
	Range	ND – 0.12	n.a.

Footnotes for Tables 2A, 2B, and 2C:
a) iPB was not detected in any of the breath samples.
b) Units are in parts per million by volume; the amount of bromopropane in 1 million parts of breath.
c) ND = non-detectable. Only detectable values were used to calculate averages.
d) n varies because only detectable values, in lieu of zero or imputed values, were used to calculate averages.
e) Not applicable. Only a "before work" breath sample (e.g. 16-hour post shift) was collected on day 3.
f) Average wasn't calculated because nPB was detected in only one breath sample from this collection period.

Table 3A.
Summary of workers' bromine concentrations in urine for plants 1 and 6 combined.

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Chemical	Job	Day 1, Before Work[a]	
		Range	Average
Bromine (*mg/liter*)[b]	Plants 1& 6 (n = 11)	1.8 – 22	8.8
	Controls[c]	0.98 - 16	4.0

Chemical	Job	Day 1, 24-Hr. Concentration[d]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
Bromine (*mg/liter*)	Plants 1& 6 (n = 11)	1.9 – 21	7.7	2.8 – 15	6.5

Table 3B.
Summary of workers' bromine concentrations in urine for plant 1.

Chemical	Job	Day 1, Before Work[a]	
		Range	Average
Bromine (*mg/liter*)[b]	Plant 1 (n = 7)	1.8 – 13	4.8
	Controls[c]	0.98 - 16	4.0

Chemical	Job	Day 1, 24-Hr. Concentration[d]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
Bromine (*mg/liter*)	Plant 1 (n = 7)	1.9 – 8.1	4.1	2.8 – 8.2	4.6

Table 3C.
Summary of workers' bromine concentrations in urine for plant 6.

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Chemical	Job	Day 1, Before Work[a]	
		Range	Average
Bromine (*mg/liter*)[b]	Plant 6 (n = 4)	8.7 – 22	16
	Controls[c]	0.98 – 16	4.0

Chemical	Job	Day 1, 24-Hr. Concentration[d]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
Bromine (*mg/liter*)	Plant 6 (n = 4)	7.6 – 21	14	4.2 – 15	9.7

Footnotes for Tables 3A, 3B, and 3C:

a) Sample was collected before or near the start of the work shift, after the weekend away from work.
b) Units are in milligrams of bromine per liter of urine.
c) Control samples were collected from 21office workers unexposed to nPB, not employed by this company.
d) 24-Hour concentrations were calculated from 3 combined samples of all urine specimens collected at work; after work before bedtime; and upon waking.

Table 4A.
Summary of workers' propyl mercapturic acid concentrations in urine for plants 1 and 6 combined.

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Chemical	Job	Day 1, Before Work	
		Range	Average
PMA[a] (μg/liter)[b]	Plants 1 & 6 (n = 11)	ND – 499	85.9
	Controls[c]	ND[d] – 207	59.7

Chemical	Job	Day 1, 24-Hr. Concentration[e]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
PMA (μg/liter)	Plants 1 & 6 (n = 11)	15.6 – 2390	649	4.99 – 2510	571

Table 4B.
Summary of workers' propyl mercapturic acid concentrations in urine for plant 1.

Chemical	Job	Day 1, Before Work	
		Range	Average
PMA[a] (μg/liter)[b]	Plant 1 (n = 7)	ND – 23.4	10.8
	Controls[c]	ND[d] – 207	59.7

Chemical	Job	Day 1, 24-Hr. Concentration[e]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
PMA (μg/liter)	Plant 1 (n = 7)	15.6 – 883	250	4.99 - 755	268

Table 4C.
Summary of workers' propyl mercapturic acid concentrations in urine for plant 6.

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Rockford, IL
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
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Chemical	Job	Day 1, Before Work	
		Range	Average
PMA[a] (μg/liter)[b]	Plant 6 (n = 4)	52.6 - 499	217
	Controls[c]	ND[d] – 207	59.7

Chemical	Job	Day 1, 24-Hr. Concentration[e]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
PMA (μg/liter)	Plant 6 (n = 4)	607 - 2390	1350	427 - 2510	1100

Footnotes for Tables 4A, 4B, and 4C:
a) PMA = propyl mercapturic acid.
b) Units are in micrograms of propyl mercapturic acid per liter of urine. (One microgram is one thousand times less than a milligram.)
c) Control samples were collected from 21office workers unexposed to nPB, not employed by this company.
d) ND = non-detectable.
e) 24-Hour concentrations were calculated from 3 combined samples of all urine specimens collected at work; after work before bedtime; and upon waking.

Attachment I
Toxicity of n-propyl bromide and isopropyl bromide

The molecular structure of bromopropanes is a simple three carbon alkane chain containing a single bromine substitution. There are two bromopropane isomers: n-propyl bromide [(nPB) also called 1-bromopropane; CAS No. 106-94-5] and isopropyl bromide [(iPB) also called 2-bromopropane; CAS No.75-26-3]. Prior to the last several years, nPB was primarily used to manufacture pharmaceuticals, pesticides, and other chemicals typically in well controlled closed processes. An international agreement between a number of industrial nations restricts the manufacture and use of ozone depleting substances including some compounds which were widely used throughout general industry: 1,1,1-trichloroethane and chlorofluorocarbons (freons®). In an effort to develop alternatives to replace these ozone depleting solvents, nPB products have been marketed, or are being considered, for metal cleaning/degreasing, automotive degreasing, electronics cleaning, precision cleaning (e.g., plastics, optics, and medical equipment), aerosol products, adhesive solvents, paint and coating solvents, textile dry cleaning, printing inks, and asphalt blending (EPA, 2003; Dead Sea Bromine, 1999; Petroferm, 2000). Products containing potential carcinogens trichloroethylene and methylene chloride are also candidates for alternative solvents, especially since the OSHA methylene chloride standard imposes more stringent occupational exposure and medical surveillance criteria with increased compliance costs. Currently, the principal application for nPB, in terms of quantities used, is for a vapor degreasing and liquid cleaning agent as well as spray adhesive solvent (EPA, 2003). However, the need to find suitable alternative solvents could expand nPB market applications, substantially increasing the quantities manufactured.

The first reports of health effects for bromopropanes occurred in 1996 in a Korean electronics plant where iPB was used as a cleaning solvent for electronic switches (Kim et al., 1996; Park et al., 1997). An epidemiology case study of 33 workers revealed that approximately two-thirds were experiencing reproductive disorders affecting both genders (e.g., low sperm concentrations, low motility or deformed sperm in men; and amenorrhea and elevated follicle stimulating hormone in women) (Kim et al., 1996). Further, seven workers had pancytopenia (e.g., reduced blood cell counts). An exposure-health effect association was obscured in this study since breathing zone monitoring was not performed, and the significance of reported dermal contact and brief short-term exposure to very high air concentrations is unclear. Ichihara et al. (1997; 1999) conducted a similar study at a chemical plant manufacturing iPB in China. Although severe reproductive disorders were not observed, reduced sperm concentrations and motility as well as decreased hemoglobin and hematocrit were suspected by the authors to be related to iPB exposure.

Subsequent to these occupational investigations, a series of rat studies were conducted in Japan with iPB to evaluate male reproductive and female reproductive or hematopoietic toxicity. In a review of the literature, Takeuchi et al. (1997) concluded that iPB impairs: *(i)* the testes, especially spermatogonia, *(ii)* ovarian function by disturbing the estrous cycle, damaging primordial follicles and oocytes, *(iii)* bone marrow causing pancytopenia. Neurologic effects in rats exposed to iPB were also discovered by Yu et al. (1999; 2001).

There has been incentive to use nPB in lieu of iPB because of the perception that nPB has lower toxicity. There are several reports in the published literature regarding epidemiological and toxicological studies of nPB which are contrary to this supposition. In a 2001 report, Yu et al. (2001) demonstrated peripheral and possibly central neurotoxicity in rats but did not show reproductive or hematologic effects. Several additional reports have concluded that nPB produces dose dependant estrous cycle irregularities (Yamada et al., 2003; Takeuchi et al., 2001); spermiation destruction (Takeuchi et al., 2001; Ichihara et al., 2000a); reproductive and developmental toxicity (NTP, 2002; 2004; Ichihara et al., 2005); increased liver enzymes (Lee et al., 2005); and peripheral and central neurotoxicity (Yu et al., 2001; Ichihara et al., 2000b) in rats at similar dose levels that produced these effects by iPB. Ichihara et al. (2000b) concluded that nPB appeared to be a more potent neurotoxin than iPB. This conclusion is supported by several rat studies which have shown ataxic gait and hyper-excitability of the central nervous system, particularly at higher doses (Fueta et al., 2000, 2002a, 2002b, 2004; Honma et al., 2003; Wang et al., 2003).

Garner et al. (2006) published a metabolism study which investigated the disposition and excretion of nPB following intravenous, inhalation and dermal administration using mice and rats of both genders, metabolic inhibitors, and genetically altered animals. The authors concluded that metabolism and excretion were independent of route of administration. Elimination of nPB was very rapid with a half life under one hour, mostly via exhalation. Urinary excretion occurred by two principal mechanisms: dehalogenation by cytochrome P-450 and conjugation with glutathione. Minor metabolites were also observed indicating several other pathways for elimination.

Two case studies in the US have been published which describe decreased peripheral nerve functioning for three foam cushion workers using spray adhesives containing over 50% nPB (Ichihara, et al. 2002) and a worker who performed metal stripping using a degreasing solvent with approximately 95% nPB (Sclar, 1999). Presenting symptoms included numbness, weakness of lower extremities, staggering, and parasthesia or dysesthesia. The authors concluded that nPB likely caused the peripheral and central nervous system defects in these workers.

NIOSH has conducted Health Hazard Evaluations (HHEs) at two foam cushion fabricators and an aircraft seat cushion manufacturer where nPB was used as a spray adhesive solvent (NIOSH, 2003b; 2002a; 2002b). Full-shift nPB exposures at these plants identified numerous excursions exceeding 100 ppm, one recommended exposure guideline by some solvent distributers. For comparison, the 2003 proposed EPA industrial exposure guideline is 25 ppm, and the ACGIH TLV® published in 2005 is 10 ppm, measured as an eight-hour time-weighted average (TWA). At the aircraft seat cushion plant, full-shift nPB exposures ranged from 60 to 381 ppm, and 67 of 69 measurements exceeded 100 ppm (NIOSH, 2002a). Analysis of complete blood counts obtained from 43 (61%) of the aircraft cushion workers did not establish nor exonerate abnormalities associated with nPB exposure. A reproductive health questionnaire was also administered but the results were also inconclusive.

Toraason et al. (2006) conducted genotoxic studies to assess DNA damage, in vitro, and from 64 workers employed at two of the above HHE foam fabricating plants NIOSH investigated using PB-based adhesives. The authors concluded that limited evidence existed at these facilities to show exposure to nPB was associated with increased DNA damage.

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