Workers' Exposures to n-Propyl Bromide at an Adhesives and Coatings Manufacturer

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Abstract

The National Institute for Occupational Safety and Health (NIOSH) conducted a field study at an adhesive and coating manufacturing plant where n-propyl bromide (nPB) was used as a solvent carrier. Workers' breathing zone, and exhaled breath concentrations of nPB and isopropyl bromide (iPB) were measured on two consecutive days, as were urinary metabolite concentrations of bromide (Br) and propyl mercapturic acid (PMA).

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 commonly used in industry. Sparse 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 studies, and a few case studies.

Full-shift time weighted average (TWA) exposure to nPB collected in workers' breathing zone air samples ranged from 0.072 to 19 parts per million (ppm) and from 0.077 to 9.1 ppm, respectively, for day 1 and day 2. All of the workers were exposed to nPB at levels below the industrial guideline of 25 ppm published by the EPA in their proposed rulemaking to accept nPB under the Clean Air Act. However, three (out of 22) TWA nPB measurements exceeded or approached (> 75%) the American Conference of Governmental Industrial Hygienist (ACGIH) Threshold Limit Value® of 10 ppm. The average TWA exposure for all workers on both days combined was 2.5 ppm. The cement makers and packagers working directly with nPB based adhesives had the highest breathing zone exposures; they wore air purifying or air-supplied respirators for protection. Exhaled breath concentrations of nPB ranged from non-detectable (ND) to 0.056 ppm and ND to 0.32 ppm, respectively, for pre- and post-shift samples. Isopropyl bromide (iPB), a low level contaminant in nPB solvents, was detected in all but one of the air sample TWA measurements and ranged from 0.006 to 1.0 ppm; iPB was not detected in any of the breath samples. However, the highest iPB levels were found in workers who were remote from the nPB adhesives operation, and their iPB concentrations were close to or greater than their nPB exposure levels. The workers who worked directly with the nPB adhesive had the highest nPB exposures, but also had much lower iPB levels than the highest that were measured. This suggests that a chemical mixture other than the nPB solvent was the source of the iPB, or there was a positive interference with the analytical method.

Workers' average urinary Br concentrations, as measured by 24 hour composite samples, were slightly higher than for unexposed controls who were not employed by this company [0.52 versus 0.4 milligrams per liter (mg/l)]. The low urinary bromide concentration in exposed workers may be due, in part, to the infrequent manufacturing schedule for nPB adhesives at this facility (approximately every 45 days). Bromide in urine can be influenced in general and working populations by non-occupational factors such as diet and medications, including over the counter medications. Propyl mercapturic acid is a more specific metabolite for measuring exposure to nPB. The workers' 24-hour PMA concentrations determined for both workdays ranged from ND to 2370 micrograms per liter (µg/l) and the average was nearly an order of magnitude greater than the average PMA concentration in controls. Dermal absorption, in addition to inhalation exposure, may contribute to the observed urinary metabolite levels.

Recommendations provided in this report include substitution of nPB solvents with a less toxic solvent, periodic exposure monitoring, improved exhaust ventilation, continued use of respiratory protection, impermeable gloves to nPB, and routine medical examinations.

Site Survey Record
Industrywide Studies Branch
Division of Surveillance, Hazard Evaluations and Field Studies
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Introduction

The Industrywide Studies Branch (IWSB) of the National Institute for Occupational Safety and Health (NIOSH) conducted a field study on September 14-16, 2004, at SIA Adhesives, Sovereign Specialty Chemicals, Inc., manufacturing plant in Akron, Ohio. At this facility, n-propyl bromide (nPB) was used as a carrier solvent for manufacturing Whisper Spray® adhesive. 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.

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 NIOSH to conduct a multi-industry occupational exposure study to evaluate workers' industrial exposures to nPB. One objective is to evaluate a variety of industries listed by the Environmental Protection Agency (EPA) for review of nPB approval under the Clean Air Act. This study is an exposure assessment study, not a health study; as such it will not provide medical determinations. This site report describes the monitoring performed at one of these facilities which will be compiled into the larger NIOSH-IWSB study regarding occupational exposure to nPB in multiple industries.

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.)

Process Description

SIA Adhesives is a subsidiary of Sovereign Specialty Chemicals, Inc., one of the largest adhesive manufacturers in the world. (Sovereign was purchased by Henkel Corp. on December 28, 2004.) SIA Adhesives manufactures a large variety of adhesives and coatings for aerospace, automotive, construction, furniture, and other industrial applications. In addition to liquid and spray adhesives, the company's product lines include caulks, sealants, films, epoxies, urethanes, acrylates, thermoplastics, flame retardant and UV curable adhesives. SIA Adhesives has been making adhesives at the Akron plant since 1950; this industrial complex has been at this site for over a hundred years.

A nPB-based solvent containing over 96% nPB (Solvon PBA®, PolySystems USA, Inc.) was introduced in early 2003 and is used as the principal solvent in manufacturing Whisper Spray®, once every 30-45 days. The production schedule depends on customer orders and warehouse supplies; approximately 6000 gallons of Solvon PBA® were used per month. Whisper Spray® was mixed and packaged in the Solvent building, a class IA flammable location, where a large variety of solvent-, water-, and epoxy-based adhesives are manufactured in "batch" mixers.

The mixing vessels were installed near the ceiling of the first floor so that hatch openings penetrate the floor on the second level of the building. The charging of the mixing vessels occurred on the second floor of the Solvent building by cement makers. Large volume *liquid* solvents are received by tanker trucks, transferred to an outdoor tank farm, and pumped into holding tanks within the building. An enclosed piping manifold system is then used to charge the mixing vessels. High volume solvents used at this facility include methyl ethyl ketone, toluene, heptane, nPB, and petroleum distillates (rubber solvent, mineral spirits, and textile spirits).

Solid chemicals are added to the vessels manually by the Cement Makers through the hatch openings, which otherwise remain closed during mixing. Solids include rubber particles, acrylates, stabilizers, anti-oxidants, and other additives. After passing quality control testing, the adhesive is transferred out of mixing vessels by Packers using semi-closed methods. The finished adhesive is packaged in 5 gallon buckets, 55 gallon drums, or 250 gallon bulk tank totes, and moved to the chemical warehouse for shipment. Whisper Spray® is made infrequently, approximately every 45 days, based on customer orders and warehouse supplies.

Local exhaust ventilation was not provided for the mixing vessels or packaging dispensing locations. Instead, each bay on the charging and packing floors were serviced with high volume dilution ventilation consisting of air supply and exhaust ventilation systems located on opposite walls to produce directional air flow. These systems provided eleven room-air changes per hour which was reduced to six room-air changers per hour during the cold winter months.

The personal protective equipment utilized by employees included safety glasses, safety shoes, coveralls/aprons, and faceshields when there was the potential for splashing. Neoprene and butyl rubber industrial gloves were also available and each cement maker and packer were issued half-facepiece respirators (MSA comfo-classic) with combination air purifying cartridges for organic vapors, halogens, chlorine, acid mist, hydrocarbons, sulfur dioxide, and hydrogen sulfide. The Cement Makers working directly with nPB also used Bullard air supplied respirators (model CC20) when charging the mixing vessel with nPB and solids requiring an open hatch. Packers wore the MSA half mask air purifying respirators when transferring nPB adhesive into drums.

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 5 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. These authors are re-assessing the data.

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; Japan has published an OEL consistent with S. Korea. 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., Br and PMA) are currently unavailable.

Methods

In this research study, nPB exposures were determined with standard air sampling methods in conjunction with new methods for 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.

At this facility, workers' exposures to nPB and isopropyl bromide (iPB) were measured over two consecutive workdays using three types of monitoring: 1) air sampling in their personal breathing zones; 2) exhaled breath; and 3) urinary metabolites. Eleven workers voluntarily consented to participate, each of whom either worked with nPB or was expected to be in the Solvent building during nPB adhesive mixing and packaging. The jobs monitored include Cement Makers (5), Packers (Drum Fillers) (4), Supervisor (1) and a Production Manager (1). The workers wore two light-weight air sampling pumps on 2 consecutive days; provided exhaled breath samples before and after their work shifts; and provided all of their urine collected over a 48-hour period, both while at and away from work. 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 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 0.5 μg which equates to a minimum detectable concentration (MDC) of 0.0083 ppm in air using the maximum recommended air sampling volume of 12 liters and a MDC of 0.033 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, which 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. The sampling survey occurred over a 48-hour period that started at the beginning of the work week, following a weekend of no exposure, and ended before the work shift began on the third day. 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 which 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

Bromide (Br) ion 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 Br 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 or time periods. 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 1 presents the time weighted average (TWA) air sampling results collected in workers' breathing zones over 2 full work shifts. Full-shift exposure to nPB ranged from 0.072 to 19 parts per million (ppm) and from 0.0.77 to 9.1 ppm, for the first and second monitoring days, respectively. Daily averages for all workers combined were 3.5 ppm on day 1, and 1.5 ppm on day 2. The higher nPB levels observed on day 1 were consistent with the production schedule: two batches were mixed and packed on the first monitoring day whereas only a single batch was manufactured on the second day. All of the workers were exposed to nPB at levels below the industrial guideline of 25 ppm published by the EPA in their proposed rulemaking to accept nPB under the Clean Air Act and recommended by several solvent distributors. However, three (out of 22) TWA measurements exceeded or approached (> 75%) the American Conference of Governmental Industrial Hygienist (ACGIH) Threshold Limit Value (TLV®) of 10 ppm, measured over an 8-hour workshift.

Iso-propyl bromide, a low level contaminant in nPB solvents, was detected in every TWA measurement except for one, ranging from non-detectable (ND) to 1.0 ppm. The only published occupational exposure limit (OEL) for iPB is 1 ppm, published by S. Korea and Japan. The source of iPB is questionable, however, since the two highest iPB concentrations were found from workers' who were remote from the Whisper Spray® operation in concentrations close to (0.98; 1.0 ppm) or greater than their nPB exposure (0.76; 1.3 ppm). Moreover, these iPB levels were considerably greater than the iPB concentrations measured from the workers who were directly using nPB and Whisper Spray® and who also had the highest nPB exposure concentrations. Hence, it appears that Solvon PBA® was not the source of the iPB. Given the

large variety of chemicals at this facility, it is possible that there was an interfering compound with the analytical method or iPB emission may have come from another chemical mixture.

Table 2 provides a summary of the exhaled breath concentrations for nPB. The nPB concentrations measured in the pre-shift breath samples ranged from ND to 0.056 ppm, and from ND to 0.32 in the post-shift samples. The average pre-shift breath concentrations of nPB were less than the respective post-shift average for both monitoring days (i.e., average pre-shift and post-shift concentration pairs were ND versus 0.10 for day 1; and ND versus 0.12 for day 2). Iso-propyl bromide was not detected in any of the breath samples with a minimum detectable concentration above 0.033 ppm for a 3 liter sample. There are no criteria to compare breath concentrations because this is a new experimental method.

The average Br concentration from urine samples collected before the work-week began was 5.9 milligrams per liter (mg/l) for all eleven workers (Table 3). The 24-hour average concentrations of urinary Br ranged from 1.4 to 21 mg/l, and both daily averages were 5.2 mg/l. For comparison, the average Br concentration was 4.0 mg/l in spot samples from control subjects who were not employed by this company. Hence, workers average urinary Br levels on work days were slightly higher than the control average.

Bromide in urine can be influenced by non-occupational factors such as diet and medications, including over the counter medications. Propyl mercapturic acid is a more specific metabolite for measuring exposure to nPB. The data for PMA are provided in Table 4. Before the work week began, the PMA concentrations for workers ranged from ND to 243 microgram per liter (μg/l), and ND to 207 μg/l for controls; workers' pre-week average was also less than the average calculated from control specimens. However, the average 24-hour concentrations of PMA from all workers over both workdays were nearly ten times higher than the control average. (The factors were 10.6; 8.2; and 9.4 times greater for day 1; day 2; and both days combined, respectively.)

The potential for solvent splashing and dermal contact exists with cement mixing and dispensing into 5 gallon buckets, 55 gallon drums, and bulk tote containers. The chemical resistant gloves that were used in these departments (neoprene and butyl rubber), do not provide sufficient protection against nPB permeation for more than 30 minutes to a few hours.

Statistical analyses were not conducted for the data collected at this single site since only eleven 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 TWA exposures to nPB were below the industrial guideline of 25 ppm proposed by the EPA and several solvent distributors, however, several TWAs exceeded or approached (> 75%) the ACGIH TLV® of 10 ppm. Bullard air-supplied or MSA air purifying respirators were used for protection during these operations.

- Given the observed daily production rate on the first monitoring day, the air supply and exhaust ventilation did not control nPB breathing zone exposure below 10 ppm for those workers engaged in mixing and packaging Whisper Spray®. Furthermore, exposures to nPB in the winter may increase because the "dilution" exhaust and make-up air supply ventilation is operated at six room-air changes per hour in lieu of eleven during the summer months, when this monitoring was conducted.

- Two workers' exposures to iPB were detected at a concentration close to 1 ppm, the occupational exposure limit published by South Korea and Japan. The source of the observed iPB air concentrations is unclear but is likely due to another chemical mixture other than Solvon NPA® or analytical interference.

- The post-shift breath monitoring showed measurable levels of nPB but not iPB, and the post-shift averages were greater than the pre-shift averages on both work days. The employees working directly with nPB adhesive had breathing zone exposure concentrations of nPB that exceeded or approached the TLV; those same employees also had the highest post-shift nPB breath concentrations.

- Average workday concentrations of the urinary Br were slightly higher for workers than for control subjects.

- Average 24-hour concentrations of the urinary PMA measured in worker specimens during both work days combined were nearly an order of magnitude greater than the average PMA concentration measured in control specimens.

- The use of neoprene and butyl rubber gloves for the Whisper Spray ® manufacturing may contribute to the workers' urinary metabolites of PMA since these glove materials are permeable to nPB. This solvent is appreciably absorbed through workers' intact skin, which may contribute to their overall absorbed dose and subsequent metabolite excretion.

- The conclusions drawn are based on the data from the grouped population of workers. These data demonstrate that workers in the Solvent building where nPB adhesives were manufactured were exposed to measurable levels of nPB and were excreting nPB metabolites. 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. The ACGIH TLV of 10 ppm for nPB is based on suspected neurological toxicity. 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:

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

b) 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,

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

d) Use 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. If alternative solvents are not feasible, use nPB solvents that have the lowest iPB contamination as is possible. Based on the iPB results, it appears that nPB solvents used at your facilities may 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 used at your facility meet, and continue to meet, this criterion.

2. Employee exposures when manufacturing and packaging nPB adhesives should be periodically re-evaluated. If monitoring results continue to exceed relevant criteria, improve the existing engineering controls (i.e., dilution supply and exhaust ventilation systems) to reduce airborne nPB concentrations. It is advisable to ensure that an adequate, uncontaminated make-up air volume is provided to optimize the performance of the exhaust ventilation. Moreover, installation of local exhaust ventilation (with a slotted plenum design) should be considered to remove the air contaminants at the point of emission and away from workers' breathing zones. Suitable locations could be around the perimeter of hatch openings and dispensing locations for filling drums, bulk totes, and buckets.

Design specifications are available in the ACGIH Industrial Ventilation Manual, 25th edition (2006) or similar industrial ventilation textbook. In addition, a routine maintenance schedule for ventilation systems is necessary to ensure effective performance of the equipment.

3. Respiratory protection should continue to be provided for those workers who desire to use it, or if the controls are not effective or feasible in reducing exposures. 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; use of NIOSH approved respirators; 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 observed work practices coupled with high nPB metabolites (i.e., urinary PMA) suggests that dermal contact and absorption of nPB may be occurring for some workers. When skin contact potential with nPB 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, poly vinyl chloride (PVC), etc.] do not adequately prevent nPB from penetrating the PPE material for more than a few minutes to a few hours. This may include time after the glove is contaminated even though it is no longer worn by a worker.

5. 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.

6. 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 1.
Summary of workers' TWA[a] air sample concentrations of n-propyl bromide and isopropyl bromide for cement making and can filling.

SIA Adhesives, Sovereign Specialty Chemicals, Inc.
Akron, OH

National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
IWSB 232.16

Chemical	Measure	TWA Air Concentration *(ppm)*[b] (n = 11)	
		Day 1	Day 2
nPB[c]	Average	3.5	1.5
	Range	0.072 – 19	0.077 – 9.1
iPB[d]	Average	0.19[e]	0.19
	Range	ND[f] – 0.98	0.051 – 1.0

Footnotes:

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:

$TWA = [(\text{time 1} \times \text{conc. 1}) + (\text{time 2} \times \text{conc. 2}) \ldots + (\text{time}_i \times \text{conc.}_i)] \div$ 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) Average was calculated only with detectable results (n = 10).

f) ND = non-detectable.

Table 2.
Summary of workers' breath concentrations of n-propyl bromide[a] for cement making and can filling.

SIA Adhesives, Sovereign Specialty Chemicals, Inc.
Akron, OH

National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
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Date	Measure	nPB Breath concentration *(ppm)*[b] (n = 11)	
		Pre-shift	**Post-Shift**
Day 1	Average	—	0.10[c]
	Range	ND[d]	ND – 0.18
Day 2	Average	—	0.12[e]
	Range	ND	ND – 0.32
Day 3	Average	0.055[f]	n.a.[g]
	Range	ND – 0.056	n.a.

Footnotes:
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) Average was calculated only with detectable results (n = 7).
d) ND = non-detectable.
e) Average was calculated only with detectable results (n = 8).
f) Average was calculated only with detectable results (n = 2).
g) Not applicable. Only a "before work" breath sample (e.g. 16-hour post shift) was collected on day 3.

Table 3.
Summary of workers' bromide concentrations in urine for cement making and can filling.

SIA Adhesives, Sovereign Specialty Chemicals, Inc.
Akron, OH

National Institute for Occupational Safety and Health
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Chemical	Job	Day 1, Before Work[a]	
		Range	Average
Bromide (*mg/liter*)[b]	Workers (n = 11)	0.48 – 26	5.9
	Controls[c]	0.98 – 16	4.0

Chemical	Job	Day 1, 24-Hr. Concentration[d]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
Bromide (*mg/liter*)	Workers (n = 11)	1.4 – 21	5.2	1.9 – 21	5.2

Footnotes:
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 bromide 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 awakening.

Table 4.
Summary of workers' propyl mercapturic acid concentrations in urine for cement making and can filling.

SIA Adhesives, Sovereign Specialty Chemicals, Inc.
Akron, OH

National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
IWSB 232.16

Chemical	Job	Day 1, Before Work[a]	
		Range	Average
PMA[b] (μg/liter)[c]	Workers (n = 11)	ND[d] – 243	50.5
	Controls[e]	ND – 207	59.7

Chemical	Job	Day 1, 24-Hr. Concentration[f]		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
PMA (μg/liter)	Workers (n = 11)	32.3 – 2370	631	ND – 1920	489

Footnotes:
a) Sample was collected before or near the start of the work shift, after the weekend away from work.
b) PMA = propyl mercapturic acid.
c) Units are in micrograms of propyl mercapturic acid per liter of urine. (One microgram is one thousand times less than a milligram).
d) ND = non-detectable.
e) Control samples were collected from 21office workers unexposed to nPB, not employed by this company.
f) 24-Hour concentrations were calculated from 3 combined samples of all urine specimens collected at work; after work before bedtime; and upon awakening.

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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