Workers' Exposures to n-Propyl Bromide at a Hydraulic Power Control Component Manufacturer

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Abstract

The National Institute for Occupational Safety and Health (NIOSH) conducted a field study at a hydraulic power control components manufacturing plant where n-propyl bromide (nPB) was used as a vapor degreasing solvent. Workers' breathing zone, "in-mask" respirator, and exhaled breath concentrations of nPB and isopropyl bromide (iPB) were measured 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 Br-propanes, animal studies, and a few case studies.

Full-shift exposure to nPB in air samples collected in workers' breathing zones ranged from 0.078 to 2.0 parts per million (ppm) and from 0.33 to 4.0 ppm in the respirator/breathing zone samples. All of the workers were exposed to nPB at levels below the American Conference of Governmental Industrial Hygienist (ACGIH) Threshold Limit Value® of 10 ppm as well as the industrial guideline of 25 ppm published by the EPA in proposed rulemaking. Isopropyl bromide was not detected in air or respirator samples, or was detected in trace quantities. Exhaled breath concentrations of nPB ranged from 0.050 to 0.23 ppm and 0.053 to 0.55 ppm, respectively, for pre- and post-shift samples; iPB was not detected in any of the breath samples.

Respirators were used intermittently over 15 to 90 minute periods by assemblers when transferring parts in and out of the vapor degreaser room, and were only used continuously for a few minutes at a time in repetitive intervals ranging from 1 to 25 minutes. The respirator sample remained in the mask when worn around a worker's neck and placed in their breathing zone when respirator use was discontinued. Measured Program Protection Factors (PPF) for each sample pair were calculated by dividing full-shift levels *outside* the respirator by those measured *both inside and outside* the respirator. The PPFs ranged from 0.43 to 3.8 for five sample pairs, well below the laboratory "Assigned PF" of 10 for half-mask air purifying respirators. Lower measured PFs may be from face piece leakage, over-loaded cartridges, nPB in exhaled breath, or low respirator use time, which was a significant factor for this operation. Quantitative fit testing also showed two out of the three respirators users failed, attributed to the wrong size respirator or the presence of facial hair. However, two measured PFs were below 0.5, which implies that over-loaded cartridges or nPB in exhaled breath were important factors too.

Average urinary Br concentrations measured before the work week began were approximately 65% higher for workers than for unexposed controls who were not employed by this company, but the 24-hour concentrations for workers' were similar to control levels. The 24-hour average PMA concentrations from all workers were over an order of magnitude higher than the average PMA concentration in controls, suggesting that dermal absorption may contribute to exposure in addition to inhalation. The assembler with the lowest breathing zone concentration of nPB had urinary metabolite levels similar to those measured in controls.

Recommendations include substitution of nPB solvents with a less toxic solvent, periodic exposure monitoring, impermeable gloves to nPB, ventilation modifications, respiratory protection program improvements, and routine medical examinations.

Site Survey Record
Industrywide Studies Branch
Division of Surveillance, Hazard Evaluations and Field Studies
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

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Introduction

The Industrywide Studies Branch (IWSB) of the National Institute for Occupational Safety and Health (NIOSH) conducted a field study at Sargent Controls and Aerospace, a hydraulic power control component manufacturing plant in Tucson, Arizona on April 26-28, 2004. At this facility, n-propyl bromide (nPB) was used as a vapor degreasing solvent to remove oils and dirt from various parts and components prior to the inspection, milling, re-surfacing, lining, and assembly. In this research study, we measured workers' breathing zone and in-mask respirator 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

Sargent Controls and Aerospace, located in Tucson AZ, manufacturers specialty precision hydraulic power components and controls including landing gear actuators, steering/metering valves, air sealing joints, pneumatic valve seals, and precision hydraulic valves. These components are used in a large variety of military applications for aircraft, helicopters, Naval fleet, submarines, and tanks as well as in commercial aircraft and spacecraft. In addition to manufacturing, this facility performs testing for mechanical, hydraulic, pneumatic, temperature,

and destructive load capabilities as well as non-destructive inspections using ultra sound, magnetic particle, and dye penetration techniques.

Sargent Controls is approved to line, or strip and re-line bearings containing Teflon® fabric liner in accordance with FAA specifications. This facility also performs repair procedures on components utilizing Kahr-lon® liner and refurbishes self-lubricating bearings containing these liners. These tasks require intensive cleaning necessitating the use of a vapor degreaser.

A nPB-based solvent containing over 94% nPB (Solvon PB, Poly Systems USA, Inc.) is used as the vapor degreasing agent primarily by two departments to remove oils, grease, and dirt from casings, bearings, sleeves, and other hydraulic parts necessary for inspection, milling, surface treatments, and lining various components. One vapor degreaser is shared by approximately a dozen workers in the Teflon and Refurbishing departments. The actual number of assemblers who need to use the degreaser on a given day depends on the product line and work schedule. The production schedule for this company is dictated by customer orders. As such, the vapor degreaser is not continuously operated, rather parts are cleaned in batches on an "as-needed" basis prior to assembly.

In the Teflon department, new products are assembled after the parts are machined in other departments. Approximately six to eight assemblers may use the vapor degreaser for removing cutting oils prior to assembly. The Refurbishing department receives used Kahr bearings for re-conditioning and re-lining. The Kahr bearings are disassembled and the liner is removed. After inspection, the parts are sent to other departments to be either sand blasted or cut with a mechanical lathe. Reconditioned parts are then cleaned in the degreaser, re-assembled, and packaged for shipment. Three or four assemblers are authorized to use the degreaser in this department.

A medium capacity (17" x 44"), open-top vapor degreaser manufactured by Baron Blakeslee is located in a small ventilated room in the Refurbishing department. This degreaser utilized a refrigerated cooling coil (6") around the top of the interior of the vapor chamber with 14" of freeboard height. The cooling coil 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 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. The nPB degreasers also had a chamber cover that was closed when the degreaser was not in use.

A typical cleaning work cycle with the degreaser includes placing parts into baskets, attaching the basket to a hoist, and manually lowering the basket with a hand crank into the dirty side of nPB liquid solvent bath. After three minutes, the parts were transferred to a clean nPB liquid solvent bath for an additional three minutes. Before removing the parts out of the degreaser, the parts basket was staged in the vapor zone for one minute and lifted out of the chamber with the hoist. The parts were then transferred from the basket into process bins.

The room that contains the vapor degreaser is a small room (approximately 10' x 10') with a double door access and was exclusively dedicated for the cleaning operation. Local exhaust ventilation was not provided for the vapor degreaser but the room was maintained under negative pressure with general exhaust ventilation utilizing a 12" round duct located in the ceiling along the back wall. No additional plenums or hoods were attached to the ducting to aid with controlling solvent vapor emissions.

An additional liquid solvent wash tank (28" x 48"; 9" freeboard) containing Solvon PB is located outside in a chemical shed. This wash tank was reported to be used infrequently because it does not clean some product lines sufficiently to meet design specifications. The wash tank is primarily used to clean heavily soiled parts prior to inspection or to process parts that can tolerate some surface contamination.

Personal protective equipment used by employees were chemical resistant gloves made from poly vinyl alcohol [(PVA) Ansell Edmont], safety glasses, and safety shoes. Half-mask air purifying respirators (3M Comfo Classic) equipped with combination organic vapor cartridges and HEPA filters were required to use the vapor degreaser for protection against high nPB exposure. Maintenance personnel were required to use full face APF with organic vapor cartridges when emptying and cleaning the nPB solvent sump and replacing the solvent in the degreaser or wash tank.

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.

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, 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 four types of monitoring: 1) air sampling in their personal breathing zones; 2) air sampling inside their respirator when worn (or in their breathing zone when a respirator was not worn); 3) exhaled breath; and 4) urinary metabolites. Four workers voluntarily consented to participate, each of whom worked with or was expected to be in the vicinity of vapor degreasers using nPB. 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, respirator, 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.

Respirators were used intermittently by assemblers when using the vapor degreaser but were only used continuously for a few minutes at a time, ranging from 1 to 25 minutes when entering the degreaser room to transfer parts. In-mask respirator air sampling was conducted to assess workers' actual exposure while intermittently using a respirator, so that their breath, urine metabolite, and "air" sampling results could be analyzed with workers from other factories who did not use respiratory protection. Respirator monitoring was conducted using a Program Protection Factor (PPF) protocol (Myers et al., 1983; Guy, 1985) by simultaneously collecting air samples inside and outside of the respirator facepiece *"as it is used in the context of an existing respiratory protection program."* If any part of the respiratory protection program is deficient (i.e., proper fit, donning, facial hair, selection, maintenance, etc.) or otherwise compromised by a worker's activities, then the measured PPF will be adversely affected.

Personal respirators assigned to each individual worker were probed with a fitting midway between the nose and upper lip. The fitting was constructed of Kynar®, an inert plastic, to prevent chemical interaction with nPB. A 90 degree fitting was selected and vertically mounted downward to reduce the propensity for crimping the sampling pump tubing. The adsorbent tube end was affixed inside the fitting to ensure that the flexible tube connector was not exposed to the incoming air stream. The respirator air sample tube remained in the mask probe when the

respirator was used, even when worn around a worker's neck, and was placed in their breathing zone for the remainder of the work shift when respirator use was discontinued. Workers were observed when they operated the degreaser and the respirator donning and doffing times were recorded. Measured Program Protection Factors (PPF) for each pair of respirator and breathing zone trials were calculated by dividing the full-shift concentrations measured "only outside" the respirator by the concentrations measured "both inside and outside" the respirator.

Personal breathing zone, respirator, 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 0.7 μg which equates to a minimum detectable concentration (MDC) of 0.012 ppm in air using the maximum recommended air sampling volume of 12 liters and a MDC of 0.046 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. 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 cylinder. 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. 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 paired full-shift air sampling results collected exclusively in workers' breathing zones as well as in their breathing zone or within the respirator when it was used. Full-shift exposure to nPB in air samples collected in workers' breathing zones ranged from 0.078 to 2.0 parts per million (ppm) and from 0.33 to 4.0 ppm in the respirator/breathing zone samples. Daily averages to nPB were 0.85 and 0.86 outside the respirator, and 1.4 and 2.2 in the respirator/breathing zone composite samples, respectively, for day 1 and day 2. 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. Workers who used the vapor degreaser more frequently were exposed to the highest concentrations. The nPB breathing zone TWA for the assembler who spent 90 minutes degreasing parts was 2.0 ppm versus 0.078 ppm for the assembler who never needed to degrease parts.

Isopropyl bromide (iPB) was either not detected in the air or respirator samples, or was detected in trace quantities below the validated Limit of Quantification. Hence the values reported are estimates which could have considerable variability. Nonetheless, the highest iPB detected (~0.008 ppm) is well below the only criterion published for iPB (1 ppm).

Measured Program Protection Factors (PPF) for each pair of respirator and breathing zone trials were calculated by dividing the full-shift concentrations measured "only outside" the respirator by the concentrations measured "both inside and outside" the respirator. The PPFs ranged from 0.43 to 3.8 for five full-shift sample pairs, well below the *laboratory Assigned PF* of 10 for the half-mask air purifying respirators used at this plant. Measured respirator PFs equal to one shows that the same air contaminant level was found inside and outside of the respirator. PFs higher than one show the amount of protection the respirator provided over the sample period (e.g., full work shift). Lower measured PFs could be from facepiece leakage, over-loaded respirator cartridges, short time of respirator use, nPB in exhaled breath, or a combination of these factors. Total respirator use times for the five PF measurement trials were approximately 20 to 90 minutes per shift, which is a significant factor for the low PFs that were observed. Quantitative fit testing was also conducted after the exposure monitoring and two out of the three workers using respirators did not pass, attributed to the use of the wrong size respirator or the presence of facial hair (beard stubble). However, two of the measured PFs were less than 0.5, which shows that the nPB concentration inside the respirator was twice the outside concentration, suggesting that the other factors were important too (i.e., poor fit, loaded cartridges, or exhaled nPB).

Table 2 provides a summary of the breath concentrations of nPB for all five workers. The nPB concentrations ranged from non-detectable to 0.55 ppm. Only six (out of 25) breath samples had detectable levels of nPB, five of which came from the assembler with the longest degreaser use time and highest nPB exposures. Average breath concentrations were not calculated because of the paucity of detectable results. There are no criteria to compare breath concentrations because this is a new experimental method. Isopropyl bromide was not detected in any of the breath samples.

The average Br concentration from urine samples collected before the work-week began was 6.6 milligrams per liter (mg/l) for all four assemblers (Table 3). For comparison, the average Br concentration was 4.0 mg/l in spot samples from control subjects who were not employed by this company. However, the 24-hour average concentrations of urinary Br for assemblers was similar to the control average and within the range measured in control specimens. Bromide in urine can be influenced by non-occupational factors such as diet and medications, including over the counter medications. Propyl mercapturic acid (PMA) is a more specific metabolite for measuring exposure to nPB. The data for PMA are provided in Table 4. The average before work week concentrations for workers was approximately 350% 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 combined; fifteen and five times higher for day 1 and day 2, respectively.

The potential for solvent splashing and dermal contact exists with vapor degreasing processes, especially when the shape of the parts could carry solvent out of the degreaser vapor zone. The chemical resistant gloves observed to be used in these departments (e.g., PVA) do not provide adequate protection against nPB permeation for more than 30 minutes to a few hours. Furthermore, workers were also observed to wear latex or cotton gloves when handling parts recently immersed in nPB. These gloves don't provide any protection against nPB permeation or penetration. The assembler using latex gloves had the highest nPB in exhaled breath as well as the lowest measured PFs (less than 0.5), suggesting that dermal absorption of nPB is probably occurring in addition to inhalation from a poor fitting respirator.

Statistical analyses were not conducted for the data collected at this site since only four 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 to nPB were below the industrial guideline of 25 ppm proposed by the EPA as well as the ACGIH TLV® of 10 ppm.

- The condensing coil and exhaust ventilation provided for the vapor degreaser are relatively effective in controlling nPB air emissions, given the observed production rates. However, the ventilation duct in the degreaser room was orientated in a manner that did not effectively remove solvent vapors away from a worker's breathing zone. Increased work load for degreaser users may cause higher nPB exposure.

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

- The pre- and post-shift breath monitoring showed measurable levels of nPB but not iPB.

- Average "pre-week" concentrations of urinary Br were 65% higher for workers than for control subjects, possibly due in part to medications or food. The 24-hour concentrations of urinary Br during work days were similar to, or slightly higher than control concentrations.

- Average 24-hour concentrations of the urinary PMA measured in worker specimens for both work days combined were over 10 times higher than PMA concentrations measured in control specimens.

- Dermal contact with recently degreased parts may contribute to the workers' exposures. nPB is appreciably absorbed through workers' intact skin and some common glove materials, such as latex, which may contribute to their overall absorbed dose.

- Deficiencies in the respiratory protection program were observed and were discussed in

the closing conference. These include poor performance in quantitative fit testing due to the use of wrong-sized respirators; facial hair interfering with an adequate facepiece seal; worn straps; and straps fastened on the outside of hats and eye glass temple bars. An infrequent cartridge change-out schedule also increases the likelihood of nPB penetrating the sorbent bed of the cartridge if it becomes over loaded. The use of combination organic vapor with HEPA filters is not necessary for protection against nPB when particulates are not generated. (The HEPA filter creates more breathing resistance which may cause more face seal leakage.)

- 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 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. 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 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 and continue to meet this criterion.

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. Moreover, the ventilation system could be improved by installing a slotted plenum ventilation hood adjacent to the back of the degreaser so that it removes solvent vapor away from workers' breathing zones. Design specifications are available in the ACGIH Industrial Ventilation Manual, 25th edition (2006) or similar industrial ventilation textbook. In addition, a routine maintenance schedule is advised to ensure effective performance of the equipment.

3. Even though workers' exposure levels were below relevant criteria, their exposure could be reduced further with modifications to the degreaser. These include the use of a motorized hoist set at a pre-determined speed to prevent workers from lifting parts baskets too quickly through the vapor zone (and reduce the amount of time workers lean over the degreaser opening), and a secondary cooling coil installed above the principal coil to further contain the solvent vapors within the chamber.

4. 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.

5. 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 probably occurring 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., poly vinyl alcohol (PVA), latex, nitrile, neoprene, butyl rubber, poly vinyl chloride (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 at this plant. Hence, it is advisable to consult with technical experts and safety supply vendors to select an array of gloves needed throughout the facility. Periodic training of employees is important to prevent them from using the wrong gloves for different applications.

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 1.
Summary of workers' TWA[a] air sample and respirator concentrations of n-propyl bromide and isopropyl bromide.

Sargent Controls and Aerospace
Tucson, AZ
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
IWSB 232.13

Chemical	Measure	Breathing Zone Air Concentration *(ppm)*[b] (n = 4)	
		Day 1	Day 2
nPB[c]	Average	0.85	0.86
	Range	0.22 – 1.4	0.078 – 2.0
iPB[d]	Average	0.0030	0.00038
	Range	ND[e] – 0.0069	ND – 0.0015

Chemical	Measure	Day 1		Day 2	
		Respirator Concentration *(ppm)*	Protection Factor	Respirator Concentration *(ppm)*	Protection Factor
nPB	Average	1.4	1.2	2.2	2.1
	Range	0.46 – 2.9	0.43 – 2.1	0.33 – 4.0	0.49 – 3.8
iPB[d]	Average	0.0052	n.a.[f]	0.00083	n.a.
	Range	ND – 0.0080	n.a.	ND – 0.0025	n.a

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 = [(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). iPB measurements were either non-detectable or trace levels (between Limit of Detection and Limit of Quantification) so levels are estimates.

e) ND = non-detectable.

f) n.a. = not applicable. Protection factors for iPB were not calculated since levels were trace level estimates.

Table 2.
Summary of workers' breath concentrations of n-propyl bromide[a] for the assembly department.

Sargent Controls and Aerospace
Tucson, AZ
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
IWSB 232.13

Date	Measure	nPB Breath concentration *(ppm)*[b] (n = 4)	
		Pre-shift	**Post-Shift**
Day 1	Average	—	—
	Range	ND – 0.23[c]	ND – 0.20[c]
Day 2	Average	—	—[d]
	Range	ND – 0.050[c]	0.053[d] – 0.55
Day 3	Average	—	n.a[e]
	Range	ND – 0.13[c]	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) ND = not detected. nPB was only detected in one breath sample for this sample collection period.
d) Average was not calculated because only 2 breath samples had detectable levels and one sample was collected after 3 work hours due to early departure.
e) Not applicable. Only a "before work" breath sample (e.g. 16-hour post shift) was collected on day 3.

Table 3.
Summary of workers' bromine concentrations in urine for assembly department.

Sargent Controls and Aerospace
Tucson, AZ
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
IWSB 232.13

Chemical	Job	Day 1, Before Work[a]	
		Range	Average
Bromine (*mg/liter*)[b]	Assemblers (n = 4)	1.8 – 11	6.6
	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*)	Assemblers (n = 4)	1.1 – 7.9	3.9	1.2 – 6.7	3.5

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 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 4.
Summary of workers' propyl mercapturic acid concentrations in urine for the assembly department.

Sargent Controls and Aerospace
Tucson, AZ
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
IWSB 232.13

Chemical	Job	Day 1, Before Work	
		Range	Average
PMA[a] (μg/liter)[b]	Assemblers (n = 4)	31 – 686	218
	Controls[c]	ND[d] – 207	59.7

Chemical	Job	Day 1, 24-Hr. Concentration		Day 2, 24-Hr. Concentration	
		Range	Average	Range	Average
PMA (μg/liter)	Assemblers (n = 4)	150 – 3210	1010	119 – 655	356

Footnotes:
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.

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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