AIR MANAGEMENT REGULATION XIV - CONTROL OF EMISSIONS FROM DRY CLEANING FACILITIES

COMMENT/RESPONSE DOCUMENT
November 17, 2010

City of Philadelphia
Department of Public Health
Air Management Services

CITY OF PHILADELPHIA
LAW DEPARTMENT

Date Approved November 23, 2010
Approved by Martha Johnston

Comment/Response Document for Air Management Regulation XIV – Control of Emissions From Dry Cleaning Facilities

On September 4, 2007, the Air Pollution Control Board, APCB, directed the City of Philadelphia, Department of Public Health, Air Management Services (AMS) to draft a regulation to govern the use of Perchloroethylene (Perc) by dry cleaning facilities. On June 24, 2010, the APCB voted and passed the proposed Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities (AMR XIV). AMR XIV aims to minimize Perc exposure for individuals who live or work next to dry cleaning establishments, reduce the amount of Perc entering the environment, and prohibit the use of potentially more toxic / hazardous dry cleaning solvents in place of Perc.

On July 6, 2010, notice that AMR XIV was approved by the APCB and filed with the Department of Records was published in the *Philadelphia Inquirer*, the *Philadelphia Daily News*, the *Legal Intelligencer*, and on the AMS website. In response to written comments and requests, the APCB held a public hearing on AMR XIV on August 12, 2010. In addition to comments made at the hearing, the APCB accepted written comments on AMR XIV until August 20, 2010. The APCB also met separately with, and took further comment from, n-Propyl Bromide (n-PB) dry cleaning solvent producers Enviro Tech International Inc. and Poly Systems USA, on October 7, 2010. A brief excerpt from all of these comments, and the APCB's responses, follow below. After consideration of all of the comments, AMS has modified AMR XIV in some respects, as discussed in this report. A copy of the Regulation as modified is attached in the Appendix.

COMMENT #1:

AMR XIV – Section II. Prohibitions (a)(3) - Use of any Perc Dry Cleaning Equipment as a Transfer Machine, Section III. Work Practice Standards (b)(1)(i), and Section IV. Leak Detection & Repair (a)(2)(iii)

Nora Nealis from the National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS
Jon Meijer from the Drycleaning & Laundry Institute - Hearing Testimony and E-mail received on August 19, 2010

"Given that the City will be prohibiting the use of transfer equipment, industry repeats its opposition to the use of the 20°F temperature differential set forth in the Federal NESHAP that refers to a refrigerated vapor condenser controlling emissions from cold washer in a transfer (first generation) system. …The requirement re: the proper operation of the refrigerated condenser should be limited to the exit air temperature check of 45°F or less. …Similarly, requiring the cleaner to check for a temperature differential when the standard does not apply to the generation of equipment in service will undoubtedly prove confusing. …The requirement to inspect weekly for the 45° exit air temperature should suffice. The 20°F temperature differential does not apply to 3rd or 4th generation equipment and MUST not be cited as a performance standard in the rule. …Most third or fourth generation dry-to-dry machines are not equipped

with temperature gauges before and after the condensing coil, which makes it impossible for cleaners to take differential readings. If it is the intention of AMS to distinguish fourth and fifth generation machines from earlier generations that might use ad on refrigeration technology, then AMS should make this section more clear." (See Appendix)

APCB RESPONSE TO COMMENT #1:

The provisions of AMR XIV have been modified to be consistent with the requirements imposed by 40 CFR § 63.322(e)(2) and 63.323(a)(1). As modified, AMR XIV requires dry cleaners who operate Perc Dry-to-Dry Machines equipped with refrigerated condensers as a control device to: 1) monitor and ensure the temperature of the air-Perc stream on the outlet side of the refrigerated condenser is less than or equal to 45° F, and 2) monitor and ensure the refrigeration system pressure during the drying phase remains within the range specified by the manufacturer. Dry cleaners will only have to comply with the refrigeration system pressure requirement if the Perc Dry-to-Dry Machine in question is equipped with pressure gauges. See Sections III.(b)(1)(i), IV.(a)(2)(iii).

COMMENT #2:

AMR XIV – Section II. Prohibitions (a)(7) and Section III. Work Practice Standards (b)(3)

Nora Nealis from the National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS

"…no work place standard has been established for vaporizing treated water or treating vaporized water that meets the 20 ppb standard set forth for sewered water. Industry would like to suggest that vaporization of such water be added as an option in III.(b)(3)ii. Due to the development of new technologies currently underway in the industry, vaporize, treat and emit may prove to be most environmentally friendly option." (See Appendix)

APCB RESPONSE TO COMMENT #2:

In consideration of the above comment, AMR XIV requirements for handling Perc contaminated wastewater have been revised. Pursuant to Section II.(a)(7) as modified, vaporization of Perc contaminated wastewater will be permitted if control devices, as approved by AMS, are used to prevent the release of Perc into the air. Wastewater that is treated through the use of water separators, double carbon filtration, or other alternative technology approved by AMS (such as vaporization with an appropriate control device) may be discharged into the public sewer in accordance with Philadelphia Water Department Regulations. Id. See Section III.(b)(3)(ii).

COMMENT #3:

AMR XIV Section III. Work Practice Standards (a)(2)(i)

Jon Meijer from the Drycleaning & Laundry Institute - Hearing Testimony and E-mail received on August 19, 2010
Carol Memberg from PA & DE Cleaners Association - Hearing Testimony and letter submitted at the hearing

"The minimum 25 ft. buffer may not be feasible in all plants. …It has been told to us that many of the plants physically because of their locations are going to be well in the twenty-five foot buffer. …Some areas may only allow for a foot or two less. …There should be some allowance for difficult urban settings …you have already established performance criteria that all cleaners have to achieve. We believe that should be sufficient to meet the needs of AMS. …it probably should not make a difference simply because we are talking about performance based. If the dry cleaner is performing, the buffer itself probably does not have any meaning as long as the dry cleaner is in actual compliance with the numbers that are described in the regulation." (See Appendix)

APCB RESPONSE TO COMMENT #3:

In consideration of the above comments, the 25 foot buffer requirement has been revised. Section III.(a)(2)(i) now requires the airborne concentration of Perc at any air intake, window, doorway, or similar penetration of neighboring residential, commercial, or sensitive facilities be less than or equal to 40 ppb. This requirement can be met by the proper placement of Process Ventilation Emission Points and through the installation of emission controls as approved by AMS on a case-by-case basis.

COMMENT #4

AMR XIV Section III. Work Practice Standards (b)(1)(v)

Nuk Youl Kim from Happy Cleaners - Hearing Testimony

"…replace the door gasket every two years. Because of the gasket, there is almost an eight or ten gaskets every machinery. …Why do we have to replace that gasket? …We have to check with the manufacturer." (See Appendix)

APCB RESPONSE TO COMMENT #4:

Upon further review, the two year door gaskets replacement requirement has been revised. Pursuant to Section III.(b)(1)(vi), Perc Dry Cleaners will now be required to replace door gaskets in accordance with manufacturer's specifications. Records of such replacement must be kept. See Section VI.(a)(7).

COMMENT #5

AMR XIV Section IV. Leak Detection and Repairs (b) - Repair of detected leaks

Nora Nealis from National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS

"Industry suggests that the stated exception to 'short term maintenance' should be expanded to include the loading and unloading of the clothing/textiles into the machine." (See Appendix)

APCB RESPONSE TO COMMENT #5:

The APCB has reviewed your comment, and upon further consideration, has modified AMR XIV to address fugitive Perc emissions at the time clothing/textiles are loaded and unloaded from any Dry Cleaning System. Fugitive Perc emissions emanating from a Dry Cleaning System, during loading and unloading of textiles following the completion of the Drying Cycle, are not considered a violation of AMR XIV, Section IV(b) Leak Detection and Repair provisions.

COMMENT #6:

AMR XIV Section V. Monitoring (a)(1)

Nora Nealis from National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS

"The cleaner's ability to monitor rests on his ability to gain access to the space in question. This is likely to be an area he has neither control nor custody over. Some provision must be made or some remedy offered if a cleaner is prohibited from conducting the required monitoring through no fault of his own." (See Appendix)

APCB RESPONSE TO COMMENT #6:

Pursuant to Sections II.(b)(2) and V, only the owners or operators of Co-Commercial Dry Cleaning Facilities who wish to continue using Perc beyond the December 31, 2013 phase out date must take quarterly air samples from the adjoining Co-Commercial site where the airborne concentration of Perc is highest. Such owners and / or operators will be expected to take all reasonable steps to contact the owner / occupants of adjacent Co-commercial sites to obtain permission to conduct the necessary sampling. AMS will work with the owner / occupants of adjacent Co-Commercial sites to explain the rationale behind the sampling. In the event that such permission is not forth coming, affected Dry Cleaners must contact AMS for assistance. AMS has certain limited legal and administrative authority to conduct sampling on Co-Commercial sites. However, the full costs of the sampling and subsequent laboratory analysis, if performed by AMS, will be assessed to the owner / operator of the Co-Commercial Dry Cleaning Facility in question.

The following letter, or a similar draft, will be provided to the affected Co-Commercial sites:

Dear Business Owner:

Air Management Regulation XIV – Control of Emissions from Dry Cleaning Facilities (AMR XIV) was adopted by the Air Pollution Control Board on June 24, 2010, and went into effect on XX/XX/2010. The City of Philadelphia, Department of Public Health, Air Management Services (AMS) is the local air pollution control agency charged with enforcing AMR XIV.

AMR XIV imposes restrictions on the use of dry cleaning solvents containing Perchloroethylene (Perc) and n-Propyl Bromide (n-PB). Scientific studies show exposure to Perc and n-PB is linked to increased incidents of neurological damage, cancer, and other serious health problems. To minimize the public's exposure to Perc and n-PB, AMR XIV mandates that the owners or operators of Dry Cleaning Establishments that use dry cleaning solvents containing either chemical must test the air in adjacent industrial / commercial sites every three months. The air testing requires that a suitable sampling device (e.g. a charcoal tube & pump, canister, or passive sampler) be placed inside your place of business for 24 hours. The air testing will not interfere with your business and shall be completed at no cost to you or your business.

Accordingly, AMS seeks your cooperation and permission to permit the neighboring Dry Cleaning Establishment to conduct quarterly air sampling at your business. AMS wants to ensure that there are no negative health impacts from Dry Cleaning Establishments in the City. This testing will ensure that the Perc and n-PB levels in your business remain below dangerous levels. Additional information regarding AMR XIV can be found on the AMS website at: http://www.phila.gov/health/AirManagement/index.html.

Thank you,

Thomas Huynh
AMS - Director
321 University Avenue, 2nd Floor
Philadelphia, PA 19104

COMMENT #7:

AMR XIV Section V. Monitoring (a)(1)

Nora Nealis from National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS

"…industry would like to suggest that the Board consider modifying their 24 hour standard to the two hour passive monitoring badge protocol employed by both the NYS and NYC Departments of Health. …need for a protocol on the testing of adjacent spaces to ensure that (1) no products are being stored or used that contain perc on those premises. …perc can be found in any number of consumer products and it is important that the cleaner be protected against the possibility that these products are in use by neighbors and are therefore tainting the test results;

(2) that the monitoring equipment is not tampered with during the testing period (this is another reason for the two hour sampling…)" (See Appendix)

APCB RESPONSE TO COMMENT #7:

The APCB, after reviewing the raised concerns, has decided not to change the air sampling protocol provided in Section V. The 24-hour sampling protocol is a compromise that balances both economic and practical concerns. Sampling over a 24-hour period minimizes the uncertainty in the results attributed to variations in environmental and operating conditions. To achieve the same degree of confidence with a shorter sampling period, the APCB would have to require Dry Cleaners to conduct multiple tests. As the cost of analyzing an air sample is fixed, requiring the owners and operators of Perc Dry Cleaning Facilities to conduct and pay for multiple samples would be overly burdensome. The APCB is aware that Perc contamination in Co-located commercial sites may not be 100% attributable to the operation of neighboring Perc Dry Cleaning Facilities. In implementing AMR XIV, AMS will investigate, and eliminate, other sources of Perc contamination before pursuing enforcement action against Co-located Perc Dry Cleaning Facilities.

COMMENT #8:

General Comment on AMR XIV

Nora Nealis from National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS

"In all appropriate places, industry would suggest the language 'or equivalent control technology' be used to allow for the possibility of technology advances that are not currently available and therefore not addressed in the current proposal." (See Appendix)

APCB RESPONSE TO COMMENT #8:

In response to the above comment, AMR XIV Sections II.(a)(7) (vaporization of Perc from wastewater with control devices), III.(b)(3)(ii) (discharge of wastewater to public sewer), and III.(a)(2)(i) (placement and emissions control of Process Ventilation Emission points) have been modified to allow for the use of alternative control technology. All alternatives must be approved by AMS on a case-by-case basis before they can be implemented.

COMMENT #9:

AMR XIV Section VI. Recordkeeping (a)(3) and (4)

Dale Kaplan from PA Dry Cleaners - Hearing Testimony
Carol Memberg from PA & DE Cleaners Association - Hearing Testimony and letter submitted at the hearing

Jon Meijer from the Drycleaning & Laundry Institute - Hearing Testimony and e-mail received on August 19, 2010

"Since regeneration is computerized and automatic, how does the dry cleaner count the loads processed? …regarding the number of loads processed between generations, I do not know what it means. What kind of exhaust fan has to be replaced? There are fans in the machines that help with the drying. Those machines I have been told by an equipment company may sometimes have to be replaced once but most of them last the life of the unit. …If it's an external exhaust fan through the wall through the building, yes, obviously that can be done, but we don't have an exhaust fan on our fourth generation dry cleaning machines. With PERC, it does not exhaust to the atmosphere at all. It's a total closed loop system. So, there is no such thing as an exhaust fan on that. Cleaning and replacement of lint filters, it's just not there anymore. …You don't change lint filters. …Carbon Absorber pre-filters, I've called a few manufacturers and none of them understand that terminology. …we don't have pre-filters on our carbon absorbers; …the amount of activated carbon in the carbon absorbers dry weight in pounds. There is no way to do that. …Cleaners cannot empty their cartridge, weigh the contents and then refill it. There are also no standards on how much carbon should be in it. So, what is the goal of the measurement? It would make much more sense to require the replacement of the cartridges after eighteen months or two years. Quite frankly, we have no idea. …what AMS's intension is with this section. Simply put, this section makes no sense and should be removed." (See Appendix)

APCB RESPONSE TO COMMENT #9:

Upon further review, AMR XIV has been revised to eliminate regular reporting of the dry weight of activated Carbon in Carbon Adsorbers and recording of the number of loads processed between regenerations. Instead, Perc Dry Cleaners will be required to repair or replace Carbon Adsorbers, lint filters, and exhaust fans according to manufacturer's specifications. See Section III.(b)(1)(iii). Manuals for the Dry Cleaning System installed detailing repair / replacement schedules for the Carbon Adsorbers, lint filters, and exhaust fans must be kept onsite. See Section VI.(d). Records of repairs to and replacement of the Carbon Adsorbers, lint filters, and exhaust fans must be kept. See Section VI.(a)(3).

COMMENT #10:

General Recordkeeping

Dale Kaplan from PA Dry Cleaners - Hearing Testimony
Carol Memberg from PA & DE Cleaners Association - Hearing Testimony and letter submitted at the hearing
Jon Meijer from the Drycleaning & Laundry Institute - Hearing Testimony and e-mail received on August 19, 2010

"Drycleaners are already obligated to keep the vast majority of the records AMS is requiring in the new regulations. Unfortunately, the actual regulation does not always mirror what is contained in other well establish rules for perc drycleaners. This creates regulatory duplication,

an additional paperwork burden, and just general havoc for the drycleaner. Already, the current perc drycleaning regulation brought forth by AMS also includes elements from other regulations, including RCRA with regard to hazardous waste, including manifesting, storage, spill containment, and other record keeping requirements, Additionally, drycleaners are already required to report spills and releases to the environment based on current "reportable quantity" rules, and follow strict NESHAP requirements. Simply put, there is absolutely no need to add, change or modify recordkeeping requirements over and above what is already in existence. It is a tremendous burden to ask a small business owner, who does not have a staff or attorneys to duplicate all that paperwork. …The air quality reports must be maintained on their Pennsylvania Department of Environmental Protection calendar, on which they must record their perc usage and maintenance for each machine. This calendar should be sufficient and meets your requirements. Any duplication is a waste of time and effort. We suggest that it be mandatory for the calendar be used and be available for inspection. …It would be a good idea to require cleaners to subscribe to or affiliate with an association that would provide them with the information and assistance they need for compliance." (See Appendix)

APCB RESPONSE TO COMMENT #10:

The majority of AMR XIV recordkeeping requirements are identical to existing Federal and Pennsylvania requirements for Perc Dry Cleaners. Accordingly, Perc Dry Cleaners can comply with a majority of AMR XIV recordkeeping requirements by filling out the annual "Dry Cleaner Compliance Calendar" produced by the Pennsylvania Department of Environmental Protection (http://www.elibrary.dep.state.pa.us/dsweb/View/Collection-7981). Aside from the items already tracked by the Compliance Calendar, AMR XIV requires recording of the following:

1) Date, the amount, and nature of any spill originating from the Dry Cleaning System, the notification procedures followed, and the corrective actions taken.
2) Quarterly air samples from an adjoining Co-commercial business/site for Co-commercial Perc Dry Cleaning Facilities.
3) The time of inspection of the components of the Dry Cleaning System inspected weekly and the quarterly air samples from an adjoining Co-commercial business/site for Co-commercial Perc Dry Cleaning Facilities.

Compliance assistance is available through the Small Business Development Center of Pennsylvania, which is associated with the Wharton School at the University of Pennsylvania (877.ASK.EMAP). AMS will set up Compliance Assistance Workshops to educate Dry Cleaners as to their recordkeeping responsibilities once AMR XIV enters into effect.

COMMENT #11:

AMR XIV Section VII. Reporting (a)(4)

Dale Kaplan from PA Dry Cleaners - Hearing Testimony

"…when you're inspecting dry cleaners, you want to use the term still residue waste, not still oil waste because they are going to understand what you are asking for if you are saying still residue rather than a still oil." (See Appendix)

APCB RESPONSE TO COMMENT #11:

In consideration of the above comment, the term "still residue waste" has been substituted for "still oil." See Section VII.(a)(4).

COMMENT #12:

Perc Health Effects Compared to Other Pollution

Seung Jo Lee from Lee's Cleaners - Letter dated July 25, 2010
Soo Lee from KYL Dry Cleaners - E-mail received by AMS on July 28, 2010
Nuk Youl Kim from Happy Cleaners - Hearing Testimony
Jason Kim from Korean Dry Cleaners Association - Hearing Testimony
Mia Nam from Lee's Cleaners - Hearing Testimony
Soo Lee from KYL Dry Cleaners - Hearing Testimony
Rich Morford from Enviro Tech - Hearing Testimony

"The price for Perc has been sky rocketing. It is almost precious as gold so we are using it very carefully. It is true that Perc is harmful to human body if you are exposed for a long period of time. In my opinion, it is almost safe since Perc is fully dried inside the machine. Sometimes, you can smell polluting gas from big trucks. In comparison to truck polluting, Perc merely affects not even 0.001% of air pollution. …as long as the PERC is being properly disposed of, the affect is already minimal. It's not like they are just dumping it out in the river or just, you know, throwing it out in buckets, and we have to think of other causes that cause pollution like the millions of people who smoke. …the millions of cars that are being driven. The buses and trains and factories. People who use hair spray. Pesticides being used in our agriculture. The million household cleaning products that are being used. …If you look at the whole scope of the whole City, a hundred dry cleaners, maybe less than sixty stores that has PERC that might be pertained by this particular regulation that may need to change to a different solvent or different equipment. Even if there was pollution, how much does that really affect? Why a small group of dry cleaners? I just don't understand why the City is paying so much focus, time and effort on the dry cleaning industry.…I have gotten my dry cleaning done from my parents, and I'm not sick. No one in my family is sick. My parents have been doing this over thirty years, and they are both healthy. I would like to see a study if it is so-called harmful to the human body. …they need to have a study of dry cleaning business owners who are sick because I can probably tell you that in the City of Philadelphia, everyone is well and healthy. …to the point that PERC is a cancer causing chemical, the proof is in this room. We are all independently owned family business dry cleaners. Not one of us have been diagnosed with so-called affects that you put forth in your findings. We mostly spend six days a week, ten to twelve hours a day doing this business. All you have to show for your study is inconclusive findings. …Defining some PERC testing on animals after human studies have been inconclusive; and in addition, for every study proven

PERC is a toxic substance, there is another study that refutes it. The jury is still out on the health risks. I would also like to point out that a study by the American Council of Sciences and Health. It proves that seven hundred and seventy-one people that died from active smoking versus five point eight million Americans would yield one death from PERC. Additionally, there is no consensus in the scientific and regulatory community voting the likelihood of PERC as a carcinogen in humans. …Based on the Environmental Protection Agency's Chemical Fact Sheet on Perc "Perchloroethylene by itself is not likely to cause environmental harm at levels normally found in the environment." (749-F-94-020, August 1994) In addition, based on the United States of (sic) National Library of Medicine, TOXMAP, National Priorities List (NPL) release of the Perc chemical is minimal in Philadelphia. Additionally, the Hazardous Substances Data Bank (HSDB) (enc.) Human Health Effects study indicates that "Although tetrachloroethylene is known to induce peroxisome proliferation in mouse liver, a poor quantitative correlation was seen between peroxisome proliferation and tumor formation in the liver after administration of tetrachloroethylene by inhalation." ((1995))" (See Appendix)

APCB RESPONSE TO COMMENT #12:

The APCB commissioned a review of the current scientific research available on Perc and has concluded that Perc exposure has significant, negative health effects. The reviewed studies collectively appear to link Perc exposure to significantly increased risk of certain cancers and a variety of neurological, liver, and kidney problems. These studies and their findings are discussed, in depth in, the "Evaluation of Perchloroethylene Risks and Philadelphia Dry-Cleaning Proposal Report," dated January 13, 2010 (http://www.phila.gov/health /pdfs/Finkel_Perc_Report.pdf).

Despite these studies and sources cited by the commentators above, the APCB continues to believe that Perc Dry Cleaning must be regulated to protect human health. In particular, the APCB would note that the American Council on Science and Health's study relied upon by the commentators fails to consider chronic health effects that are linked to exposure to high levels of Perc over long periods of time. Such conditions, as confirmed through testing conducted by various government agencies including the City of Philadelphia, Department of Public Health, Air Management Services, are currently present in Residential, Commercial, and Sensitive sites that are situated next to existing Perc Dry Cleaning Facilities.

COMMENT #13:

Economy and Financial Assistance

Seung Jo Lee from Lee's Cleaners - Letter dated July 25, 2010
Kwikleen Cleaners - Letter received July 27, 2010 by Department of Records
Westbury Cleaners - Letter received July 27, 2010 by Department of Records
Royal Cleaners - Letter received August 2, 2010 by Department of Records
Cornell Brown from Germantown and Lehigh Business and Merchants Association - Hearing Testimony and letter submitted at the hearing
Nuk Youl Kim from Happy Cleaners - Hearing Testimony

Mia Nam from Lee's Cleaners - Hearing Testimony
Soo Lee from KYL Dry Cleaners - Hearing Testimony (Spoke for Il Hyon Nam of New Hollywood Cleaners as well)
Joseph Iannarelli from Enviro Tech - Hearing Testimony
Rich Morford from Enviro Tech - Hearing Testimony
Jason Kim from Korean Dry Cleaners Association - Hearing Testimony

Consider the "…deteriorating economy: …business has been very slow due to economic conditions. …we can't even afford to buy new machines because of struggling through the bad economy. …changing new equipments in such a short period of time will be difficult. …the need for financial assistance for the new machines. The City of Philadelphia can create a special budget for providing 10 year interest free loan to the owners of small drycleaners; …grant a small business loan at a very low interest rate, and/or extend the time period for us to pass these regulations; …the City of Philadelphia consider many ways to help small businesses for the better future. …replace the door gasket every two years. This costs more than a thousand dollars. I don't know how much they are going to charge for this labor. Maybe two thousand dollars. In this kind of economy, we can't handle that kind of metal. …many cleaners, they start the wet cleaning. Certain items we cannot wet clean. We have to pay back so much money. We charge maybe ten dollars for a suit. If we mess up the one suit, maybe it costs sometimes two hundred, sometimes three hundred dollars. This is scary. We have to make money. We don't want to lose the money. If we mess the garment, people they are not going to come. …Like the State of New Jersey right now, we all heard that they are passing it; and when they pass it, the dry cleaners that are being affected, there is four million dollars in a system money set up. The City, you flat out already told us that there is no money for it. So, without considering these business people and how to cope with this situation if the regulation changes, without any assistance, I don't understand how you can just set a rule and throw it at them and say you have to live by this. …if the City of Philadelphia should pass this law, then, the City of Philadelphia should be the ones paying for the new machines and not putting this burden on the small business owners or it should have been able to be written as a hundred percent tax deductible or there should be a fund for these dry cleaners. There is so many programs to help the people of Philadelphia. For example, Welfare. Unemployment benefits. Health insurance. Medicaid. Child care programs. Disability benefits, and this should be a program as well. We have been paying taxes to the City of Philadelphia. The taxes paid are used for the good of its people, and these dry cleaner owners are people, too. It's now time for the City of Philadelphia to help us as well. …we are demanding subsidies from the City and state in order to carry out the requirements. The cost of replacing the machine alone including the cleaning system will run each business about one hundred thousand dollars. There is a cost of disposing of the prior machines, disposal of the PERC and the purchase of the replacement chemicals. In light of these economic times, I think it's prudent that the City if they are going to impose this restriction, they should also help pay for the costs. …Will there be a grant or low interest loan available for purchasing the new cleaning technology? The State of PA and Philadelphia have complained about a (sic) funded mandates imposed by federal governments. Yet the City is turning around imposing the same to a small business. Does the City recognize how hard it is for us? We do not have luxuries the City employees take for granted such as paid holidays, vacation days, sick days and pension programs. The average cost of an alternative cleaning machine is about forty to sixty thousand dollars. …Most of the small cleaners do between a hundred and fifty and two hundred thousand

dollars per year. At a ten percent profit, that comes out that they make twenty thousand dollars a year. That's after working sixty hours a week. The cost of the hydrocarbon machine is basically fifty thousand dollars. The cost of CO2 is over a hundred thousand dollars. Fifty thousand dollars over a five year payment plan is about nine hundred dollars a months. That's interest free. If the City does not want to come up with any money to help these people out, those are not viable alternatives to most cleaners. You have to be an extremely large cleaner to be able to afford that. …no bank or lending institution in this economy in this day is going to give a one hundred thousand dollar loan to a business that does two hundred thousand dollars gross in a year. …We want to walk the fine line to make sure the environment is safe, sound and businesses can still operate without going out-of-business. …any regulations or exemptions, we would like to work with you so it would not be a hardship for any business. We want the businesses to stay open in Pennsylvania and Philadelphia. (See Appendix)

APCB RESPONSE TO COMMENT #13:

In drafting AMR XIV, the APCB took economic considerations and other upcoming regulatory requirements into account. The existing federal regulation has, since July 26, 2006, prohibited the installation of new Perc Dry Cleaning Equipment in Dry Cleaning Facilities that are located in residential buildings. As written, AMR XIV only prohibits the use of Perc in newly constructed Co-located Dry Cleaning Facilities, and existing Co-residential / Co-sensitive Dry Cleaning Facilities after December 31, 2013. Existing Stand-alone Dry Cleaning Facilities, and Co-commercial Dry Cleaning Facilities with permission pursuant to Section II.(b)(2), may continue using Perc beyond the phase out date.

The State of Pennsylvania offers financial assistance to Small Businesses under two separate programs, the Small Business Advantage Grant Program and the Pollution Prevention Assistance Account Loan Program. The owners or operators of Dry Cleaning Facilities may be eligible for funding to cover equipment upgrades to comply with AMR XIV under these programs. Letters regarding Financial Assistance for Dry Cleaners were sent to all dry cleaners and associations in Philadelphia on October 14, 2010. For more information on these programs please refer to these websites:

Small Business Advantage Grant Program:
http://www.portal.state.pa.us/portal/server.pt/community/financial_assistance/10495/advantage_grant/553249

Small Business Pollution Prevention Assistance Account (PPAA) Loan Program:
http://www.portal.state.pa.us/portal/server.pt/community/financial_assistance/10495/ppaa_loan/553247

Core Industries/Machinery and Equipment Load Fund:
http://www.armstrongidc.org/docs/MELF_3-10.pdf

COMMENT #14

Advanced Machines

Kwikleen Cleaners - Letter received July 27, 2010 by Department of Records
Westbury Cleaners - Letter received July 27, 2010 by Department of Records
Soo Lee from KYL Dry Cleaners - Hearing Testimony (Spoke for Il Hyon Nam as well – New Hollywood Cleaners)
Mia Nam from Lee's Cleaners - Hearing Testimony
Cornell Brown from Germantown and Lehigh Business and Merchants Association - Hearing Testimony and letter submitted at the hearing

Consider "Allowing the usage of advanced perc machines (4th and 5th generation) …we have all converted to dry-to-dry machines. This eliminates the PERC emissions that the Department is so concerned about, and in addition, regulations that govern disposal of PERC waste matter is strictly adhered to. This is evident in the US National Library of Medicine Tax Map, National Priorities List where it proves that leaks in the PERC chemical is minimal in Philadelphia. …my parents are still making payments on their machine that they recently replaced. So, if this proposal passes, they will be stuck with the payments that they have to pay for this machine that they cannot be using. It's imaging that you are buying a car that is like a forty or fifty thousand car and the City of Philadelphia is saying that because of pollution, you are not allowed to drive it, then, you know, it's unfair. Also, the machines that my parents have now is considered to be fairly new. It is the Real Star Dry Cleaning System, and the Real Star Dry Cleaning System meets and exceeds all current federal, state and local regulations for the use of PERC, and it is a fourth generation equipped with air clean carbon unit. The emission levels for Real Star Ultra-Diamond Systems are tested to be consistently lower than those required by the federal regulation. All systems are totally closed with no atmospheric venting. Solvent and solvent vapors are recleaned and regenerated. It also has a filtration system consisting of the Real Star Echo Filter Plus. Therefore, it meets the required regulation. …my parents should not be affected by the proposal because of their machine, their current machine which is considered new and they are still making the payments on which is the fourth generation system equipped with the air clean carbon unit. …All are proven operated throughout America as well in Europe. Each of these features air clean units incorporated in the machine, double water separators and automatic still cleanout systems. We believe that Lee Cleaners poses the standard state-of-the-art equipment that is mentioned in this regulation and experiences and desires to the best practices in the area of dry cleaning utilizing environmentally friendly-conscious equipment." (See Appendix)

APCB RESPONSE TO COMMENT #14:

AMR XIV, after December 31, 2013, permits the use of 4th and 5th generation Perc Dry Cleaning Equipment in existing Stand-alone and, with a permit from AMS, existing Co-Commercial Dry Cleaning Facilities. However, the use of Perc Dry Cleaning Machines in existing Co-residential and Co-sensitive Dry Cleaning Facilities after December 31, 2013 is likewise prohibited. While cleaner than prior models, Perc emissions from 4th and 5th generation Perc Dry Cleaning Equipment greatly exceed the 40 ppb limit that was determined by the APCB to be sufficiently

protective of human health. Accordingly, the unrestricted operation of 4th and 5th generation Perc Dry Cleaning Equipment would still pose a health risk to the occupants of neighboring residential and sensitive structures.

COMMENT #15

Commercial Location

Mia Nam from Lee's Cleaners - Hearing Testimony

"I also understand that this proposal gives exceptions to commercial and single dwelling locations. Then, my parents should be at this exception. Why? Because they are located on a commercial street and in between them is an empty lot and a vacant building that was out of business for about twenty years with no intent to re-open. There is no buildings behind the cleaners as well. I know it is difficult for someone to go out to each location that is being affected, but because this is a serious part, the time to go out to these locations is needed. …they should be an exception because they are on a commercial street. This is not a street full of houses and they are on the corner. This is all just a commercial location." (See Appendix)

APCB RESPONSE TO COMMENT #15:

AMR XIV permits the use of 4th and 5th generation Perc Dry Cleaning Equipment in existing Stand-alone and, with a permit from AMS, existing Co-Commercial Dry Cleaning Facilities. The Dry Cleaning Facility described in the this comment may fall within the AMR XIV Stand-alone or Co-Commercial definitions, and accordingly may continue to operate 4th and 5th generation Perc Dry Cleaning Equipment. However, without further information, a definitive classification cannot be made. Anyone with such questions are encouraged to contact AMS if you have questions or concerns about how a particular Dry Cleaning Facility is classified pursuant to AMR XIV.

COMMENT #16:

Why is Philadelphia stricter than the Federal Government?

Nuk Youl Kim from Happy Cleaners - Hearing Testimony
Jason Kim from Korean Dry Cleaners Association - Hearing Testimony
Mia Nam from Lee's Cleaners - Hearing Testimony
Isaac An from Broad Street Cleaners - Hearing Testimony

"This is the United States. They have all the regulation over there. We got everybody ready to do this regulation. Then, 2020 everybody we cannot use the PERC anymore. …the whole initiation of this new regulation that needed to be set in the City of Philadelphia, we just don't understand why because, you know, there is a federal guideline and also there is a state inspection and outside of the City of Philadelphia, the rest of the area under the Department of Environmental

Protection Agency, DEP, they get inspected yearly. …I'm not even sure if it's constitutionally right, why the Board has picked a small business. …If this regulation passes, a lot of the dry cleaners will probably operate a dry cleaning facility, but they will probably turn it into a drop store and take the business outside of the city limit. If you do that, the City will lose revenue, employment, …We believe that the timetable set forth by the City is very aggressive. …pushing to 2013 is very short of time. From I believe 1980 the Superfund, the waste, since then, they set the date for 2020. …If you give us some time, the industry will study more about hydrocarbons. They will make better equipment for us, and we can make a better City. …Basically my parents are literally being punished for having a business in Philadelphia. It's not fair just based on location, you know, that they are being affected. This is like discrimination. It's like discrimination of location. If there is two dry cleaners with the same situation, same machine, you know, both of course paying taxes, but one is being affected just because it is in Philadelphia and the other may be in the suburbs, it's not fair." (See Appendix)

APCB RESPONSE TO COMMENT #16:

The APCB is charged under the City Code with the responsibility to promulgate regulations to the emissions of air pollutants. See Philadelphia Code Section 3-302. In developing such regulations, the APCB must consider the effects that exposure to air pollutants, such as Perc, has on human health, commerce, recreation, and industrial activities. Id. The existence of federal regulations does not prevent the City from adopting more stringent standards to protect the public from Perc exposure. See e.g. 42 U.S.C. § 7516; 42 P.S. 4012(a).

The APCB is aware that the EPA has prohibited the installation of Perc Dry Cleaning Machines in Residential Structures since 2006 and has, after 30 years, finally set a 13-year clock to phase out Perc in some settings by 2020. However, the APCB is under no obligation to wait for the federal government to act before taking measures to protect the health of City residents. Id. In promulgating AMR XIV, the City joins other jurisdictions around the country such as California, North Carolina, New York, Massachusetts, Illinois, and New Jersey that have enacted, or are contemplating, restrictions on the use of Perc in dry cleaning despite existing federal regulation and the associated 2020 ban. The APCB has considered the economic ramifications in the drafting process and believes that AMR XIV balances the City's interest in protecting public health without being overly burdensome on the owners and operators of Dry Cleaning Facilities.

COMMENT #17:

Alternatives

Soo Lee from KYL Dry Cleaners - Hearing Testimony
Isaac An from Broad Street Cleaners - Hearing Testimony
Ray Roccon from Enviro Tech - Hearing Testimony
Rich Morford from Enviro Tech - Hearing Testimony
Dov Shellef from Poly Systems USA - Hearing Testimony

"…wet cleaning. Instead of complete replacement for PERC cleaning, there would be fabric duration thus compromising the structure composition of fabric. Sensitive fibers are subject to shrinkage. Bleeding of dyes. Large quantities of contaminated waste water which should be a high priority, petroleum based dry cleaning, highly flammable presenting a fire hazard. Fire codes will limit where some shops using the solvent can be located encourages bacteria to thrive because of solvent additives. Higher insurance premiums due to the higher risk and liquid CO2 which we all know what that is. Safety hazards. High pressure system. Asphyxiation. More expensive replacement of PERC machines. Effectiveness of use not proven as it is to the relatively new application, i.e. removal of proteins, grass, lipstick, any dirt you have on your clothes. None of these alternatives have proven to be an appropriate substitute for PERC. …how long did you guys study the alternative solvent? …I've been following hydrocarbons, CO2 wet cleaning, but hydrocarbon, they are very flammable. They can be very explosive. Last year in Chicago, I'm not going to say the brand name of the hydrocarbon machine, but the hydrocarbon machine exploded because during the drying cycle because their safety system did not work. …There is so many alternative solvents, we don't know which to choose. We do not know which hydrocarbon we should choose. There are one hydrocarbon solvent, but there are four, five different kinds of hydrocarbon machines. …studies conducted by the manufacturer shows that the Green Earth silicone solvent caused cancer in a rat. ...The hydrocarbons are VOC, volatile organic compound. That can also contribute to air pollution. They can destroy the ozone layer. I mean if we use hydrocarbon and if that's going to break the ozone layer, what is the purpose of going for green? …If we all use the wet cleaning, we are going to make a tremendous waste water. …On the PERC machine, we use one solvent and one equipment. Everything runs the same. Hydrocarbons so complicated to choose. …That is the energy consumption that you are going to be mandating on these cleaners. The alternative choices that they have being Petroleum, Green Earth, CO2 or wet cleaning, three out of those four alternatives have much higher energy consumption costs. …Green Earth. It's a Siloxin. Basically D5. This chemical is on the road to being banned in Canada because it bio-accumulates in the environment. It also has its own cancer and reproductive issues. …Hydrocarbons as you can tell, we have already heard, they can blow-up. They are combustible. They are very flammable. They are petroleum based. We are from the Chicago area. So was our guy whose machine blew up. Two employees in the business were injured in the blast and resulting fire. One of them came out with his clothes on fire and had to be put out by the people at the restaurant next door. I'm wondering what your Fire Marshall and firemen are going to think about a hundred stores moving to highly flammable, highly combustible machinery. All of those machines, yes, can be operated safely. All of those machines, yes, can malfunction, and you no longer have just a vapor issue. An inhalation issue. You have explosion and fire issues. Happened in 2009 with new machinery and new solvents. C02 no better really. It operates at between four hundred to six hundred PSI. Have never been able to, maybe some of our industry people can tell us, have not been able to verify it, but there are rumors all through the industry, I'm sure everybody here has heard them, of that pressure blowing off the submarine door that is installed on those to keep the pressure in and blowing it through a brick wall. I don't believe any of the health and safety people in Philadelphia would like that in a co-residential or co-sensitive building. These are risks that they are going to be taking. We talked about wet cleaning. I doubt that your Water Department is going to be happy with a hundred new cleaners using water and then emitting into the waste treatment system non-bio-degradable surfactants and other chemicals that are going to cause, could cause havoc for

their waste treatment facilities. …If you use hydrocarbon or CO2 or Green Earth, all your detergents contain a certain solvent that will do the job because Green Earth does not dry green. It's the detergent inside the dry clean. (See Appendix).

APCB RESPONSE TO COMMENT #17

AMR XIV regulates the use of Perc and n-PB in dry cleaning. Viable alternatives to Perc Dry Cleaning Solvents such as Wet Cleaning, Volatile Methyl Siloxane, Carbon dioxide cleaning, and various Hydrocarbon solvent mixtures exist. These alternatives are discussed in greater detail in the California South Coast Air Quality Management District (SCAQMD) Rule 1421 - Control of Perc Emissions from Dry Cleaning Systems, amended on December 6, 2002, (http://www.aqmd.gov/rules/reg/reg14/r1421.pdf) and in the Institute for Research and Technical Assistance Reports (See various reports at http://irta.us/reports.htm). Use of any of the identified dry cleaning solvent alternatives would otherwise be permitted. All Dry Cleaning Facilities, no matter what solvent is used, must comply with existing Philadelphia fire and water standards provided in the Philadelphia Code and relevant regulations promulgated thereunder.

COMMENT #18:

Due Process for n-PB

Rich Morford from Enviro Tech International, Inc. (manufacturer of DrySolv dry cleaning solvent) - Letter received July 30, 2010 by Department of Records and Hearing Testimony
Nora Nealis from National Cleaners Association - Letter dated July 21, 2010 and received July 27, 2010 by AMS
Jon Meijer from the Drycleaning & Laundry Institute - Hearing Testimony
Carol Memberg – PA & DE Cleaners Association - Hearing Testimony and letter submitted at the hearing
Dr. Mark Stelljes from SLR International Corp. - Hearing Testimony
Scott Mondi from Poly Systems USA - Letter dated August 19, 2010 and received August 30, 2010 by Department of Records

"…the Department was fully aware that a complete ban on the use of nPB in dry cleaning facilities would be detrimental to Enviro Tech. However, Enviro Tech was never contacted in any form by any representative from the Department regarding health and safety matters or the use of DrySolv in dry cleaning establishment. No notice of the proposed rule itself and no notice of the one meeting held which discussed Dr. Finkel's report regarding the proposed rule were sent to Enviro Tech, nor were they published in a form which could be reasonably expected to adequately inform Enviro Tech, or anyone else, on the proposed ban. Further the letter of July 13, 2010 sent to Dry Cleaning Professionals by the Department clearly mentions the rule as Control of Perchloroethylene (PERC) from Dry Cleaning Facilities but again does not mention the ban on nPB based dry cleaning solvents. Enviro Tech and users of DrySolv within Philadelphia had no reason to know or even assume that nPB would be included in a rule specifically aimed at PERC. …Since Mr. Finkel's report was not presented until June, 2010…less than one month was given to the consideration of the proposed ban on nPB. …Due to

the total lack of notice and the deficiency of the Notices actually published, we are seriously concerned about the lack of due process afforded by the Department to a company with employees in and paying taxes to the State of Pennsylvania. On this basis alone, the proposed ban on nPB should be stricken from the proposed rule. …it should be pointed out that Regulation XIV, control of Perchloroethylene from dry cleaning facilities, is not and was never developed to control emissions from other alternative processes. ...you have been working on PERC since 2007. It's 2010, and you are coming up with a proposed final rule. And yet, you based a complete ban on a solvent from February 2010 to June, July 2010. …The solvent has been banned without a proper hearing. We feel that this is unfair, since there has not been due process allowed. There should be further studies to determine its acceptability." (See Appendix)

APCB RESPONSE TO COMMENT #18:

The Philadelphia Code empowers the APCB to promulgate regulations aimed at "preventing degradation of air quality, preventing air pollution nuisances, and limiting, controlling, or prohibiting the emission of air contaminants to the atmosphere from any sources." Philadelphia Code Section 3-302(1). A proposed regulation, once approved by the APCB and reviewed by the City Law Department, must be filed with the City's Department of Records and be made available for public inspection for 30 days. Notice of this filing must be published in the City and County of Philadelphia. Upon written request during the inspection period, the APCB must hold a hearing on the proposed regulation to allow for public comment. Following the hearing, the APCB must file a report either modifying or affirming the proposed regulation. The proposed regulation, as modified or affirmed, becomes effective ten days after the report is filed. See Philadelphia Charter Section 8-407(a)-(c). Aside from the publishing requirement, the City is not legally required to provide any additional notice regarding a proposed regulation. Nor is the City or the APCB legally obligated to consider public comments on a proposed regulation made outside of a requested public hearing. Id.

The City and APCB met and in fact exceeded their legal obligations to provide the public with notice of, and the opportunity to comment on, the proposed Dry Cleaning Regulation provisions. The Dry Cleaning Regulation was first proposed in August of 2008 and discussed in subsequent meetings of the APCB in 2009 and 2010 that were open to the public. See APCB Meeting Minutes, dated August 5, 2008; November 5, 2008; March 5, 2009; October 21, 2009; January 20, 2010; February 16, 2010; and June 24, 2010 (http://www.phila.gov/health/AirManagement/AirManageBoards.html). Following the approval of the proposed Dry Cleaning Regulation on June 24, 2010, notice of the approval was published in the *Philadelphia Daily News*, the *Philadelphia Inquirer*, and the *Legal Intelligencer* on July 6, 2010, and a copy of the entire Regulation was made publicly available.

Notice of the public hearing was published in the *Philadelphia Daily News* on July 31, 2010 and was provided directly to known interested parties. The public hearing on the regulation, as requested, was held on August 12, 2010 and attended by representatives of dry cleaners, dry cleaning solvent producers (including but not limited to n-Propyl Bromide (n-PB) solvent manufacturers), environmental groups, and other private citizens. It is important to note that despite considerable effort and expense expended before and after the proposed Dry Cleaning Regulation was approved; the City has not located any Dry Cleaning Facilities in Philadelphia

that use n-PB. Nevertheless, the APCB also met separately, and took further comment from, n-Propyl Bromide dry cleaning solvent producers Enviro Tech International Inc. and Poly Systems USA, on October 7, 2010.

Despite having no formal legal obligation to do so, the APCB commissioned scientific reports evaluating the health risks and dangers posed by Perchloroethylene (Perc) and n-Propyl Bromide (n-PB) dry cleaning solvents, discussed the reports at the public APCB meetings, and made them available to the public via the APCB's website. See, e.g., Preliminary Evaluation of Perchloroethylene Risks and the Philadelphia Dry-Cleaning Proposal Presentation, (October 21, 2009) (discussing health risks posed by Perc and n-PB substitution); Evaluation of Perchloroethylene Risks and the Philadelphia Dry Cleaning Proposal, Pages 6-37 (January 13, 2010) (discussing health risks posed by Perc and n-PB); and Increased Toxicity and Carcinogenicity of n-Propyl Bromide (1-Bromopropane) Relative to Perchloroethylene, Dated June 2010. Oral and written comments made outside of the required August 12, 2010 public hearing were also considered. See Appendix; Comment / Response Document – Dr. Finkel's APCB Perc Presentation, Dated October 21, 2009. See also APCB Meeting Minutes, Dated November 5, 2008; March 5, 2009; October 21, 2009; January 20, 2010; and June 24, 2010 (http://www.phila.gov/health/AirManagement/AirManageBoards.html). The title of AMR XIV has been changed to reflect its application to Perc and n-PB Dry Cleaning in Philadelphia. Accordingly, the APCB has gone beyond its legal obligations to engage the public in promulgating the Dry Cleaning Regulation.

COMMENT #19:

Ban on n-PB

Rich Morford from Enviro Tech International, Inc. (manufacturer of DrySolv dry cleaning solvent) - Letter received July 30, 2010 by Department of Records and Hearing Testimony
Joseph Iannarelli from Enviro Tech - Hearing Testimony
Dr. Mark Stelljes from SLR International Corp. - Hearing Testimony and E-mail received on August 20, 2010 by AMS on the "White Paper On The Toxicity Of 1-Bromopropane"
Dov Shellef from Poly Systems USA - Hearing Testimony
Dr. Mark Stelljes from SLR International Corp. - Presentation to AMS and the APCB Ad Hoc Committee on October 7, 2010 on the "Carcinogenic Potential of 1-Bromopropane (nPB)"
Scott Mondi and Dov Shellef from Poly Systems USA, Kevin Andrews, Joseph Iannarelli, Ray Roccon, and Richard Morford from Enviro Tech International, Inc., and Dr. Mark Stelljes from SLR International Corp. – Meeting Minutes with AMS and the APCB Ad Hoc Committee on October 7, 2010

"The Department has been clear that the proposed nPB ban is based solely on one report from Mr. Finkel dated June, 2010. Mr. Finkel cites less than ten toxicological reports regarding nPB. In fact, there are over 150 published toxicological studies of nPB which are easily available. Many of these peer reviewed and published reports do not support and actually question the assumptions made by Mr. Finkel. The Department should be aware that the USEPA has approved of the use of nPB based compounds under its SNAP program in May, 2007. …the

USEPA had taken thirteen years to do the most exhaustive toxicology, health and safety investigation into n-PB. …In 2007, the USEPA said that they were not going to propose any workplace exposure level. Because the industry users have shown that they were far under twenty-five part per million in normal operations with regular good work practices. We have shown, we have the data that operating enclosed loop dry cleaning machines, the exposures to n-PB from Dry-Solv are well under ten part per million. Generally in the four part per million range for the actual operator of the machine and either one part per million or below for those other people who happen to be in the dry clean establishment itself. …Over a hundred and sixty-five pier reviewed published articles in scientific journals. I really don't think again to the Board that the Board has had even the time to find them all because they did not call me. I've got them and certainly if they can't find them all, they have not considered them all.…The report Toxicological Assessment of Industrial Solvents, a peer reviewed and published scientific report, concludes that based on bioassays using human live cells, nPB is one of the least toxic solvents in use today. …Mr. Finkel's assumptions, unsupported by actual data, are erroneous. …published reports conclude that neurological effects are not found until headaches start at exposures of about 180 ppm. …We request that the proposed ban on the use of nPB be stricken from the proposed rule at this time. …see if there is an opportunity to exchange information on a technical level in order to better understand the situation in Philadelphia as it relates to nPB. …n-PB as a safe and useful solvent. …evaluation from the CDC from NIOSH which is an evaluation of one Bromylpropane use in four New Jersey commercial dry cleaning facilities. …they found no human health hazard in the four cleaners and that when you use good work practices and have your machine professionally altered to run Dry-Solv, your exposure levels to yourself in the workplace are going to be well under the very conservative of ten part per million, and that your exposure outdoors to the public is going to be well under the proposed reference concentration of one part per million that the EPA has proposed. …there is a range in the published literature from three different authors ranging from sixty to a hundred and fifty parts per million. From the regulatory standpoint, we have the twenty-five parts per million from EPA. We have the one part per million from Cal EPA. We have the ten parts per million TLB that was actually calculated incorrectly. …If it were regulated today, n-Propyl Bromide would be regulated as a non-carcinogen as opposed to PERC which is regulated as a carcinogen. If you look on the Prop-65 List For California, PERC is on there as a carcinogen. …This little ring is what causes the cancer. When you look at the metabolism of one Propopropane and compare it to two Bromopropane and compare it to DBCP, that does not form in one Bromopropane. ...A reference concentration is a concentration to which somebody can be exposed on a daily basis over the course of their lifetime without any adverse affects. I look at Perchloroethylene in probably fifty of the sites that I've done over the last twenty years, and the value for PERC is 0.0003 parts per million. n-PB is one. I think the decision as to which one is safer has just been answered. …under certain and good condition, practically every cycle dry cleaner would lose about two ounce of solvent into the air. ....and we made this calculation and we monitored the air around, we never got into a situation where the concentration was too high. Meaning too high for us too high is about twenty ppm. …although Fabrisolv costs about three to four times as much as PERC, practically the cost for the dry cleaner in the machine, to use Fabrisolv in the machine will be the cost like they are using PERC. Because as you heard before, the consumption of the energy is much less with Fabrisolv. And by the time that the PERC machine brings out fifty pounds of dry cleaning, the Fabrisolv when it runs in the machine brings twice as much poundage because the cycle is half the time of the PERC. …Regarding the environment, you

have no issue with Fabrisolv or n-PB because in eleven days whatever you release from your dry cleaning or any operation, the Fabrisolv, the n-PB will break in the air and disappear in eleven days. Gone. Now, if you have some n-PB, some Fabrisolv and around six hundred ppm goes into the water in the water separator and it's going to the waste stream in between sixty to a hundred and twenty days, it's gone. Disappeared. Any n-PB, any Fabrisolv that is dissolved in water and goes to the drain, it's disappearing from the face of the earth in sixty to a hundred and twenty days. …some of the people who are using n-PB based solvents in the United States today. Boeing Aircraft Company. The Department of Defense. A number of Air Force bases use it. Aniston Army Depot uses it. Corpus Cristi Army Depot uses it for M1 tanks. Lockheed Martin. Martin Marietta. Honeywell. Goodrich. MacDonald Douglas. They are all using n-PB safely. Have been using it from my company, Dov's company and others for the past fifteen years with one reported inhalation problem from a person, from a user on a vapor degreaser who not using it properly. In the literature where you will find problems with n-PB is in the adhesives coatings and inks where they use it to melt glue and then they spray it all over the place coming up with doses up to three hundred, four hundred parts per million which is a criminal dose in my book. That will not happen in closed roof dry cleaning machines. … we will not put it in anything older than a 4th generation machine. …NTP Draft Conclusions from Study: “No evidence” of carcinogenic evidence potential – Male mice, “Some evidence” of carcinogenic potential – Male rats (skin tumors), “Clear evidence” of carcinogenicity – Female rats (colon tumors) – Female mice (lung/bronchiole tumors)”, Weight of Evidence Summary: Negative in genotoxicity tests, Negative in mutagenicity tests, Negative in in vitro bioassays DNA damage), No evidence of tumors associated with sites of action of nPB – No reproducible tumors across sex or species, Not on any EPA list of potential carcinogens.”
(See Appendix)

APCB RESPONSE TO COMMENT #19:

Please see response to Comment #18 above. While it has carefully reviewed and considered the n-PB industry comments and related presentations, the APCB continues to believe that n-PB is a more potent neurotoxin and carcinogen than Perc. See Finkel, A., “Increased Toxicity and Carcinogenicity of n-Propyl Bromide (1-Bromopropane) Relative to Perchloroethylene,” (June 2010). See also Ichihara, G., et al.: "Neurologic abnormalities in workers of a 1-bromopropane factory." Environ. Health Perspect. 112(13): 1319-1325, 2004; NTP/CERHR Monograph on the Potential Human Reproductive and Developmental Effects of 1-Bromopropane, National Institutes of Health Publication No. 04-4479 (October 2003); "Technical Report on the Toxicology and Carcinogenesis of Studies of 1-Bromopropane in F344/N Rats and B6C3F1 Mice." National Toxicology Program TR-564, (November 2009). In particular, the APCB notes the in vitro n-PB bioassays cited by the n-PB industry do not adequately demonstrate n-PB's health effects on complex, multi-cellar organisms with separate respiratory, neurological, and reproductive systems. Similarly, the APCB has also determined that reliance on the Environmental Protection Agency’s (EPA) Significant New Alternatives Policy (SNAP) n-PB Rule would be inappropriate. The SNAP n-PB Rule only determined that n-PB could be safely used as an alternative to ozone depleting solvents in metals, electronics, and industrial precision cleaning processes. See 72 F.R. 30142, 30151 (May 30, 2007) (n-PB use acceptable “only in those end uses where it has been shown to be used safely, as compared with other substitutes that are currently or potentially available. We find this to be the case for metals cleaning, electronics

cleaning, and precision cleaning.”). The SNAP n-PB Rule did not address the use of n-PB in Dry Cleaning equipment that is typically operated at higher temperatures, with different emissions controls, than corresponding industrial degreasing or cleaning equipment.

The APCB is especially concerned that n-PB’s volatility and tendency to form caustic Bromic acid, when combined with poor work practices, may exacerbate fugitive emissions from n-PB Dry Cleaning Facilities well in excess of the 10 ppm n-PB per 8 hour period Threshold Limit Value safety standard established by the American Conference of Governmental Industrial Hygienists. See e.g. Preliminary Study of Propyl Bromide Exposure among New Jersey Dry Cleaners as a Result of a Pending Ban on Perchloroethylene,” Blando, James, D., Donald P. Schill, Mary P. De La Cruz, Lin Zhang, and Junfeng Zhang in the Journal of the Air and Waste Management Association (August 2010).

Nevertheless, the APCB has determined that n-PB may be safely used in dry cleaning operations in certain circumstances. See e.g. Ambient Air Sampling at Sacramento Dry Cleaner Memorandum, from Dr. Mark Stelljes to Rich Morford (worst case scenario of 16 ppb n-PB immediately outside a Dry Cleaning Facility running converted, 3rd generation Dry Cleaning Machines). Accordingly, AMR XIV has been revised to allow the use of n-PB in Stand-alone and Co-commercial facilities. The owners and operators of n-PB Dry Cleaning Facilities will be expected to comply with all provisions of AMR XIV, as modified by Section IX. Section IX, in part, requires the owners or operators of Co-commercial n-PB Facilities to obtain an Air Management permit prior to any installation or modification of existing Dry Cleaning Equipment using n-PB and an operating license, that Co-commercial n-PB Facilities demonstrate that the airborne concentration of n-PB in adjoining commercial or industrial sites is at or below 40 ppb, and establishes an acute 225 ppb n-PB exposure limit and 10 ppm n-PB fugitive emission level for all n-PB Dry Cleaning Facilities. See Section IX. For further discussion on n-PB, and the derivation of the 40 ppb, 225 ppb, and 10 ppm limits, please see the memo “Rationale for, and Derivation of, Performance Standards for n-propyl bromide (n-PB) in Co-commercial Dry Cleaners” from Dr. Finkel, November 2010. The APCB is confident that n-PB Dry Cleaning Machines, appropriately operated and maintained, can meet these requirements.

COMMENT #20:

Consider all alternatives

Patton Boggs LLP (on behalf of Halogenated Solvents Industry Alliance, Inc. (HSIA) - Letter sent by e-mail on August 10, 2010 to Air Management Services by W. Caffey Norman

“We urge the Philadelphia Department of Public Health to consider fully the potential implications for public health of any alternative that would be used as a result of restrictions it imposes on the use of perc.” (See Appendix)

APCB RESPONSE TO COMMENT #20:

The APCB has, after a scientific review, determined that Perc and n-PB exposure is linked to a variety of negative health effects. See, e.g. "Evaluation of Perchloroethylene Risks and Philadelphia Dry-Cleaning Proposal Report", Dated January 13, 2010 (http://www.phila.gov/health/pdfs/Finkel_Perc_Report.pdf), "Increased Toxicity and Carcinogenicity of n-Propyl Bromide (1-Bromopropane) Relative to Perchloroethylene", Dated June 2010 (http://www.phila.gov/health/pdfs/Finkel Perc & nPB.pdf). AMR XIV mitigates these risks by regulating use of Perc and n-PB in dry cleaning operations. Pursuant to the City Code, the APCB may in the future regulate the emissions of other dry cleaning chemicals that pose a demonstrable danger to public health and air quality. See Philadelphia Code Section 3-302.

The APCB is also aware that the use of other dry cleaning solvent alternatives, namely certain hydrocarbon blends, may require the owners or operators of Dry Cleaning Facilities to take additional measures to ensure that those solvents are used safely. Both the Philadelphia Fire and Water Departments have been consulted and have opined that the safety and operational challenges posed by these alternatives can be adequately addressed under the City's ordinances and regulations.

COMMENT #21:

Support of the APCB Regulation

Mark Dann – Philadelphia Resident - Hearing Testimony
Myriam Fallon – Greenpeace - Hearing Testimony
Barbara Rahke – Philaposh (Philadelphia Area Project on Occupational Safety and Health) - Hearing Testimony
Alyssa Tombler – Citizens for Pennsylvania's Future (Penn Future) - Hearing Testimony

"When the EPA banned lead in gasoline, oil companies strongly opposed the regulations. However, over time the public has greatly benefited from less lead in the environment and cars run just fine. …Chemicals such as PERC and n-PB are dangerous to public health, the environment and are not needed for dry cleaning… The Philadelphia Department of Health should be commended for addressing this now and not simply waiting for others to do so. …I know many years ago, we were part of the hearings that passed the first community Right-To-Know Act in the country. The first city in the country, and that was an historic event and I think began to set the tone for the City looking at the issue of the communities Right-To-Know, the chemicals that they were exposed to not only, you know, through facilities that were close by, et cetera. …six years ago, the City voluntarily got rid of chlorine gas at all of the six City water treatment facilities. Now, that was post 911 the City took the initiative to do that and is the only city in the State of Pennsylvania to have done that, and I take pride in that, and I feel safer as a citizen of Philadelphia that you took that action. …The proposed regulations will over time result in dry cleaners in Philadelphia switching to less toxic solvent or purchasing more modern equipment that will lower emissions of PERC. …We agree that dry cleaners should obtain a

permit before installing a dry cleaning machine that uses PERC and an operating license to use a PERC dry cleaning machine."
(See Appendix)

APCB RESPONSE TO COMMENT #21:

The APCB recognizes and appreciates the public's concern over the health risks posed by Perc and n-PB exposure. AMR XIV was drafted specifically to address these concerns.

COMMENT #22:

Hearing Request

Jason Kim from The Korean Dry Cleaners Association - Letter dated July 20, 2010 and received July 27, 2010 by Department of Records
Jon Meijer from the Drycleaning & Laundry Institute, Nora Nealis from the National Cleaners Association, & Carol Member from the Pennsylvania and Delaware Cleaners Association - Letter dated July 22, 2007 and received July 27, 2010 Department of Records
Seung Jo Lee from Lee's Cleaners - Letter dated July 25, 2010
Kwikleen Cleaners - Letter received July 27, 2010 by Department of Records
Westbury Cleaners - Letter received July 27, 2010 by Department of Records
Soo Lee from KYL Dry Cleaners - E-mail received by AMS on July 28, 2010
Rich Morford from Enviro Tech International, Inc. (manufacturer of DrySolv dry cleaning solvent) - Letter received July 30, 2010 by Department of Records

"Requests a Public Hearing" (See Appendix)

APCB RESPONSE TO COMMENT #22:

A letter dated August 2, 2010, was sent to each Commentator that sent in comments and were received by August 2, 2010 by AMS, notifying them of the hearing date and time that took place on August 12, 2010. Notice indicating the time, date, and location of the public hearing was also published in the *Philadelphia Daily News* on July 31, 2010 and posted on AMS's website.

APPENDIX

All Comments, Hearing and Meeting Materials, and Attachments

APPENDIX A –
COMMENTS BEFORE PUBLIC HEARING

nca nca nca nca nca

NATIONAL CLEANERS ASSOCIATION 252 West 29th Street New York, NY 10001 • Phone: 212.967.3002 • www.nca-i.com

RECEIVED

JUL 27 2010

AIR MANAGEMENT SERVICES
DIRECTOR'S OFFICE

July 21, 2010

Mr. Thomas Huynh, AMS Director
Department of Public Health: Air Management Services
321 University Ave., 2nd. Floor
Philadelphia, PA 19104

Re: Comments to the Air Management Regulation XIV–Control of Perchloroethylene from Dry cleaning Facilities 06/15/2010 Recommended Proposal and the Department's Comments to Industry's Comments

Dear Mr. Huynh:

The drycleaning industry appreciates the opportunity to provide written comments to the Department of Public Health: Air Pollution Control Board's, "Air Management Regulation XIV–Control of Perchloroethylene from Dry cleaning Facilities" draft proposal dated 06/15/2010 as adopted by the APCD at its most recent meeting.

Regulation:

II. Prohibitions (a)(3) – Use of any Perc Dry Cleaning Equipment as a Transfer Machine, III. Work Practice Standards (b) (1) (i) and IV. Leak Detection & Repair: (a) (2) (iii)

Given that the City will be prohibiting the use of transfer equipment, industry repeats its opposition to the use of the 20°F temperature differential set forth in the Federal NESHAP that refers to a refrigerated vapor condenser controlling emissions from cold washer in a transfer (first generation) system. This parameter is outlined in your draft proposal in III. Work Practice Standards" (b) (1) (i): '...the air-perc gas vapor stream entering and exiting the Refrigerated Condenser must be greater than or equal to 20°F", and requires cleaners to check for same weekly.

The requirement re: the proper operation of the refrigerated condenser should be limited to the exit air temperature check of 45°F or less.

Similarly, requiring the cleaner to check for a temperature differential when the standard does not apply to the generation of equipment in service will undoubtedly prove

confusing for both the regulated community and the inspectors. The requirement to inspect weekly for the 45°F exit air temperature should suffice.

I tried to make this point during the recent Board meeting and was told it was a 'technical' issue that I needed to put in writing. I cannot state strongly enough that the 20°F temperature differential does not apply to 3rd or 4th generation equipment and MUST not be cited as a performance standard in the rule. If you wish to have EPA confirmation of my information, I urge you to contact Kim Teal at EPA, Research Triangle Park, NC.

II. Prohibitions (a) (7) and III. Work Practice Standards (b) (3)

While cleaners are prohibited from evaporating untreated separator water, no work place standard has been established for vaporizing treated water or treating vaporized water that meets the 20 ppb standard set forth for sewered water. Industry would like to suggest that vaporization of such water be added as an option in III. (b) (3) ii. Due to the development of new technologies currently underway in the industry, vaporize, treat and emit may prove to be most environmentally friendly option.

IV. Leak Detection and Repairs (b) Repair of detected leaks:
Industry suggests that the stated exception to 'short term maintenance' should be expanded to include the loading and unloading of the clothing/textiles into the machine.

V. Monitoring (a) (1)
The cleaner's ability to monitor rests on his ability to gain access to the space in question. This is likely to be an area he has neither control nor custody over. Some provision must be made or some remedy offered if a cleaner is prohibited from conducting the required monitoring through no fault of his own.

In addition, industry would like to suggest that the Board consider modifying their 24 hour standard to the two hour passive monitoring badge protocol employed by both the NYS and NYC Departments of Health. We would be happy to provide contact information at both agencies. Prior to adopting this protocol, NYS DOH conducted several tests to satisfy themselves that the two hour sampling with a passive monitoring badge was sufficient to protect public health and the environment.

We would also like to express our concern about the need for a protocol on the testing of adjacent spaces to ensure that (1) no products are being stored or used that contain perc on those premises. As we all know, perc can be found in any number of consumer products and it is important that the cleaner be protected against the possibility that these products are in use by neighbors and are therefore tainting the test results; (2) that the monitoring equipment is not tampered with during the testing period (this is another reason for the two hour sampling, which would make the testing far more affordable)

In all appropriate places, industry would suggest the language 'or equivalent control technology' be used to allow for the possibility of technology advances that are not currently available and therefore not addressed in the current proposal.

Lastly, we repeat our objections regarding the use of a perchloroethylene drycleaner rule to prohibit the use of an alternative solvent.

The fact is that while the industry outreach concerning this rule was considerable, at no point prior to the draft dissemination in June was anyone in industry led to believe that the prohibitions and restrictions imposed by this proposal would extend beyond the proper use and permitting of perc drycleaners. Even your published Public Notice after the APCD meeting identified the regulation as one **governing PERC drycleaners**.

It seems to us to be blatantly unfair to impose a prohibition on any solvent without first meeting with those who make it available to the industry and are most intimately aware of whatever health concerns or risk assessments its use may portend. While it is extremely proactive of Philadelphia to be concerned with what solvents the industry may turn to as a replacement (a position we believe all regulators should be attuned to), such drastic action should be based on more thought, research and study than it appears was given in this case. As members of the Board suggested when we raised these concerns during the last meeting, we have taken the initiative and notified those who we view as stakeholders in this issue. Needless to say, your actions came as a complete surprise to them. We are sure you will hear from them. In the meantime, we want you to know that should such a prohibition remain in the finally adopted rule, it is the NCA's position that the need for a public hearing regarding this rule is imperative if due process is to be served.

We thank you for the opportunity to comment, and remain available to answer whatever questions you may have.

Respectfully Submitted,

Nora Nealis
National Cleaners Association

Dear sir or Madam:

I am a 68 years old man who has been doing a small dry cleaning business for 31 years. I had purchased a dry cleaning machine 4 years ago and using it now. I am so frustrated and scared since I heard the news that the City of Philadelphia will prohibit using Perc machines. As a small business owner, we can't even afford to buy new machines because of struggling through the bad economy. Therefore, we, small business owners, worry about the new regulation.

There are no buyers for businesses because of this new regulation. The price for Perc has been sky rocketing. It is almost precious as gold so we are using it very carefully. It is true that Perc is harmful to human body if you are exposed for long period of time. In my opinion, it is almost safe since Perc is fully dried inside the machine. Sometimes, you can smell polluting gas from big trucks. In comparison to truck polluting, Perc merely affects not even 0.001% to air pollution.

I really wish to the people who are in charge of environmental issues to make appropriate judgment, and lead to good solutions. If the city of Philadelphia can create special budge for providing 10 year interest free loan to the owners of small dryeleaners, that would be one of great solution for keeping our businesses. Lastly, I hope that the city of Philadelphia consider many ways to help small businesses for the better future.

Please be well in this severe hot weather.

Thank You.

Sincerely

Seung Jo Lee, Owner of Lee's Cleaners [redacted]

7/25/2010

*Also, I would like to request for a public hearing in regards to this matter. Thank you again.

Memorandum

City of Philadelelphia

Date: 7/27/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

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The enclosed letter from Jason Kim, on behalf of The Korean Dry Cleaners Association of Philadelphia, P.O. Box 26726, Elkins Park, PA.19027 requests a hearing on the above Regulation.

Please notify interested parties of the date and time of the scheduled hearing.

Cc: Thomas Huynh, AMS Director

The Korean Dry Cleaners Association of Philadelphia

필라 한인 세탁인 협회

P. O. Box 26726, Elkins Park, PA 19027 Tel 215-519-8887, Fax 215-635-1809

July 20, 2010

Dear Air management Services,

In regards to the regulation XIV – Control of Perchloroethylene from Dry Cleaning facilities in which you have recently approved thru Philadelphia Air Pollution Control Board, Our association would like to formally request a Public hearing on this matter.

Thru our membership meetings, our members have more questions and comments.

Sincerely,

Jason Kim
President

336606

DEPARTMENT OF HEALTH
2010 JUL 27 AM 8:39

Memorandum

City of Philadelelphia

Date: 7/27/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

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The enclosed letter from Kwikleen Cleaners, 6125 Woodland Ave., Philadelphia, PA.19142 requests a hearing on the above Regulation.

Please notify interested parties of the date and time of the scheduled hearing.

Cc: Thomas Huynh, AMS Director

To whom it may concern,

As one of the owners of an operating dry cleaning facility in the Philadelphia area, I felt it necessary to discuss the new regulations concerning the perc machines.

First, it should be in the best interest of everyone to consider the many factors connected in the rules and regulations before making any major changes.

For example,

1. The deteriorating economy
2. Allowing the usage of advanced perc machines (4th and 5th generation)
3. The need for financial assistance for the new machines

And more to be discussed.

Therefore, it seems important to hold a public hearing for more proper, effective, new regulations.

Thank you,
Sincerely,

33660
DEPARTMENT OF ENVIRONMENTAL PROTECTION
2010 JUL 27 AM 8:39

Memorandum

City of Philadelelphia

Date: 7/27/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

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The enclosed letter from Westbury Cleaners, 269 S. 15th Street, Philadelphia, PA.19102 requests a hearing on the above Regulation.

Please notify interested parties of the date and time of the scheduled hearing.

Cc: Thomas Huynh, AMS Director

To whom it may concern,

As one of the owners of an operating dry cleaning facility in the Philadelphia area, I felt it necessary to discuss the new regulations concerning the perc machines.

First, it should be in the best interest of everyone to consider the many factors connected in the rules and regulations before making any major changes.

For example,

1. The deteriorating economy
2. Allowing the usage of advanced perc machines (4th and 5th generation)
3. The need for financial assistance for the new machines

And more to be discussed.

Therefore, it seems important to hold a public hearing for more proper, effective, new regulations.

Thank you,
Sincerely,

336607
DEPARTMENT OF ENVIRONMENTAL
2010 JUL 27 AM 8:39

Memorandum

City of Philadelelphia

Date: 7/27/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

---

The enclosed letter from Jon Meijer, on behalf of Drycleaning & Laundry Institute, Nora Nealis, on behalf of National Cleaners Association, and Carol Memberg on behalf of Pennsylvania and Delaware Cleaners Association, 14700 Sweitzer Lane, Laurel, Maryland 20707 requests a hearing on the above Regulation.

Please notify interested parties of the date and time of the scheduled hearing.

Cc: Thomas Huynh, AMS Director

Drycleaning & Laundry Institute
international

Joan T. Decker, Commission of Records
Department of Records
Room 158, City Hall
Philadelphia, PA 19107 - 3298

July 22, 2007

Re: Request for a public hearing with the Department of Records - Air Management Regulation X14–Control of Perchloroethylene from Dry Cleaning Facilities

Joan T. Decker:

The Drycleaning and Laundry Institute (DLI), National Cleaners Association (NCA), and Pennsylvania and Delaware Cleaners Association (PDCA) are national and international trade associations representing retail dry cleaners, launderers, and wet cleaners in the United States. On behalf of its members in Philadelphia, DLI, NCA and PDCA submits the following request for a public hearing to address specific concerns regarding the *Air Management Regulation X14–Control of Perchloroethylene from Dry cleaning Facilities*, promulgated on July 1, 2010.

Respectfully Submitted,

Jon Meijer
Drycleaning & Laundry Institute

Nora Nealis
National Cleaners Association

Carol Memberg
Pennsylvania and Delaware Cleaners Association

336609

DEPARTMENT OF RECORDS
2010 JUL 27 AM 10:48

14700 Sweitzer Lane ◆ Laurel, Maryland 20707 ◆ Tel. 800-638-2627 Fax 240-295-0685 ◆ www.dli.org

Soo Lee
<soo.lee76@gmail.com>
07/28/2010 11:29 AM

To dphams_service_requests@phila.gov
cc
Subject In Regards to Proposed Air Management Regulation XIV

To Thomas Huynh,

I am requesting a public hearing and the opportunity to comment on the proposed regulatory process to phase down of Perc and use its substitute nBP. ATtached is a word doc.

Sincerely,

Soo H Lee
KYL Dry Cleaners

To: See Distribution List

Date: July 28, 2010

From: KYL Dry Cleaners

Ref: Proposed Air Management Regulation XIV

CC: Thomas Huynh
Air Management Services

Proposed Air Management Regulation XIV

I am requesting a public hearing and the opportunity to comment on the proposed regulatory process to phase down of Perc and use its substitute nBP.

Based on Dr Finkel's research (enc.) nBP is a NEUROTOXIN which poses more health risks and hazards than Perc. As indicated in the excerpt below.

"As this report will summarize, in my expert opinion, far from being "non hazardous," nPB is a potent neurotoxin, and has recently been shown to be a potent animal carcinogen. To a reasonable degree of scientific certainty, equal exposures to nPB will harm more residents and workers than would exposures to Perc: both are harmful substances, but nPB is the more harmful of the two." (Adam M. Finkel, JUNE 2010)

Based on the Environmental Protection Agency's Chemical Fact Sheet on Perc also noted below,

"Perchloroethylene by itself is not likely to cause environmental harm at levels normally found in the environment." (749-F-94-020, August 1994)

In addition, based on the United States of National Library of Medicine, TOXMAP, National Priorities List (NPL) release of the Perc chemical is minimal in Philadelphia. Additionally, the Hazardous Substances Data Bank (HSDB) (enc.) Human Health Effects study indicates that

"Although tetrachloroethylene is known to induce peroxisome proliferation in mouse liver, a poor quantitative correlation was seen between peroxisome proliferation and tumor formation in the liver after administration of tetrachloroethylene by inhalation." ((1995))

In light of this information data available as above, we would like to request a ***public hearing*** with regards to this regulation to evaluate the information the City has for the people, in addition to what recourse and assistance will the City of Philadelphia be providing to the Dry Cleaners in support of this regulation.

Sincerely,

Soo Hwan Lee

Distribution list:

Donald F. Schwarz
Department of Public Health
City of Philadelphia

Nan Feyler
Chief of Staff
Department of Public Health

KYL Org Cleaners
2625 Germantown Avenue
Philadelphia, PA 19133

Enclosures:

1. Proposed Regulation XIV - Control of Perchloroethylene (Perc) from Dry Cleaning Facilities CHEMICALS IN THE ENVIRONMENT: PERCHLOROETHYLENE (CAS NO. 127-18-4) prepared by OFFICE OF POLLUTION PREVENTION AND TOXICS U.S. ENVIRONMENTAL PROTECTION AGENCY August 1994
2. SUPPLEMENTAL REPORT TO THE CITY OF PHILADELPHIA, DEPARTMENT OF PUBLIC HEALTH/ AIR MANAGEMENT SERVICES, INCREASED TOXICITY and CARCINOGENICITY OF n-PROPYL BROMIDE (1-BROMOPROPANE) RELATIVE TO PERCHLOROETHYLENE June 2010

Memorandum

City of Philadelelphia

Date: 8/2/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

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The enclosed letter from Royal Cleaners, 6391 Oxford Ave. Philadelphia, PA 19111 has comments on the above Regulation.

Cc: Thomas Huynh, AMS Director

City of Philadelphia
The Department of Records
Room 158, City Hall
Philadelphia, PA 19102

RE: Air Management Regulation XIV-Control of Perchloroethylene (Perc) from Dry Cleaning Facilities

To Whom It May Concern,

We would like to comment on the proposed Air Management Regulation XIV. We own Royal Cleaners in the city of Philadelphia.

We own a small business and for the past couple of years, business has been very slow due to economic conditions. Therefore, changing new equipments for our business in such a short period of time will be very difficult for us.

We would like to propose that the city of Philadelphia grant us a small business loan at a very low interest rate, and/or extend the time period for us to pass these regulations.

Thank you for reading our comments.

Sincerely,

Royal Cleaners
6391 Oxford Ave.
Philadelphia, PA 19111

33669
2010 AUG -2 AM 9:49
DEPARTMENT OF RECORDS

Royal Cleaners
6391 Oxford Ave
Phila PA 19111

To: City of Philadelphia
The Department of Records
Room 158, City Hall
Philadelphia, PA 19102

19107\3242

Memorandum

City of Philadelelphia

Date: 7/30/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

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The enclosed Petition with comments from Enviro Tech International, Inc, requests a hearing on the above Regulation.

Please notify interested parties of the date and time of the scheduled hearing.

Cc: Thomas Huynh, AMS Director

PETITION FOR PUBLIC HEARING CONCERNING AIR MANAGEMENT REGULATION XIV - CONTROL OF PERCHLOROETHYLENE (PERC) FROM DRY CLEANING FACILITIES

I represent Enviro Tech International, Inc., the manufacturer of DrySolv dry cleaning solvent. Enviro Tech International, Inc. Does business within the State of Pennsylvania and the city of Philadelphia, has employees in the State of Pennsylvania, is contracted with independent consultants in Pennsylvania and pays taxes to the State of Pennsylvania. Pursuant to the Notice published in local Philadelphia media, I respectfully request a public hearing regarding Air Management Regulation XIV - Control of Perchloroethylene (PERC) from Dry Cleaning Facilities. As the manufacturer of DrySolv dry cleaning solvent, which is referred to by name in Mr. Finkel's report, we are an adversely effected party as the regulation proposes to ban the use of nPB based dry cleaning solvents within the city effects.

Our comments regarding the proposed regulation are below.

1. (a) Enviro Tech, along with its product, DrySolv, which is mentioned prominently on the first page of Mr. Finkel's report, was clearly known to the Department of Health/Air Management Services prior to passing the proposed Rule. Further, it is reasonable to assume that the Department was fully aware that a complete ban on the use of nPB in dry cleaning facilities would be detrimental to Enviro Tech. However, Enviro Tech was never contacted in any form by any representative from the Department regarding health and safety matters or the use of DrySolv in dry cleaning establishments. No notice of the proposed rule itself and no notice of the one meeting held which discussed Mr. Finkel's report regarding the proposed rule were sent to Enviro Tech, nor were they published in a form which could be reasonably expected to adequately inform Enviro Tech, or anyone else, of the proposed ban. Further, the letter of July 13, 2010 sent to Dry Cleaning Professionals by the Department clearly mentions the rule as Control of Perchloroethylene (PERC) from Dry Cleaning Facilities" but again, does not mention the ban on nPB based dry cleaning solvents. Enviro Tech and users of DrySolv within Philadelphia had no reason to know or even assume that nPB would be included in a rule specifically aimed at PERC.

(b) The Department states the proposed ban on nPB was based solely on the report from Mr. Finkel. Mr. Finkel's report is dated June , 2010. It is obvious from the documentation available that the PERC rule was discussed for well over six months. However, since Mr. Finkel's report was not presented until June, 2010. Therefore, less than one month was given to the consideration of the proposed ban on nPB whereas well over six months were given to discussing mere regulation of PERC. So, no real attempt was made by the Department to do a thorough investigation of the use of nPB.

(c) Notices from the Department regarding discussions, agendas and public meetings concerning the proposed rule were identified by the Department as concerning "Control of Perchloroethylene (PERC) from Dry Cleaning Facilities". We find no notice of any kind that mentioned any regulation of nPB as a dry cleaning solvent. Even if Enviro Tech had the opportunity to see the Notices actually published by the Department, there was no reasonable expectation that a proposed rule aimed at the "Control of Perchloroethylene (PERC) from Dry

2010 JUL 30 PM 2:14
DEPARTMENT OF HEALTH

Cleaning Facilities" would include just one sentence that completely banned nPB from use in the city. Further, the letter of July 13, 2010, sent to Dry Cleaning Professionals by the Department (but not to Enviro Tech) clearly mentions the rule as Control of Perchloroethylene (PERC) from Dry Cleaning Facilities" but yet again, does not mention the ban on nPB based dry cleaning solvents. On their face, each Notice and letter published by the Department were deficient as they did not adequately inform the public as to the contents of the proposed rule and the intent of the Department.

(d) The Department has stated that Notice of the proposed nPB ban was given to various dry cleaning trade groups and therefore was sufficient Notice as to Enviro Tech. A very brief investigation by the Department would have shown that Enviro Tech was never and is not now a member of any of the dry cleaning trade groups contacted by the Department. In fact, since Enviro Tech is a new competitor to the established dry cleaning companies, Enviro Tech has been, on different occasions, invited *not* to join these trade groups. Further, none of these trade groups have the information or expertise necessary for a truly informed discussion regarding the use of nPB in the dry cleaning industry.

Therefore, due to the total lack of notice and the deficiency of the Notices actually published, we are seriously concerned about the lack of due process afforded by the Department to a company with employees in and paying taxes to the State of Pennsylvania. On this basis alone, the proposed ban on nPB should be stricken from the proposed rule.

2. The Department has been clear that the proposed ban is based solely on one report from Mr. Finkel dated June, 2010. First, Mr. Finkel cites less than ten toxicological reports regarding nPB.
In fact, there are over 150 published toxicological studies of nPB which are easily available. Many of these peer reviewed and published reports do not support and actually question the assumptions made by Mr. Finkel. The Department should be aware that USEPA has approved of the use of nPB based compounds under its SNAP program in May, 2007. The Federal Register publication is attached. Simply, the position of USEPA is that nPB solvents are safe to use when exposures are under or in the range of 18 ppm to 30 ppm. As actual data attached hereto shows, exposures in a dry cleaning establishment using recommended work practices are below 10 ppm and are usually in the area of 4 ppm.

Discussed is a short discussion of six of the many issues we have with Mr. Finkel's flawed analysis.

(a) the overall conclusion of Mr. Finkel is that nPB is "more harmful" than PERC to human health and safety. The report *Toxicological Assessment of Industrial Solvents*, a peer reviewed and published scientific report, concludes that based on bioassays using *human* liver cells, nPB is one of the least toxic solvents in use today. This report is easily found on a web search of studies regarding nPB and is attached hereto.

(b) Finkel assumes that exposure to nPB would be greater than PERC to the general public, based only on a comparison of vapor pressure. Years ago, USEPA did computer modeling of exposures to the general public based on the most emissive application then in use.

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DEPARTMENT OF ECONOMIC

spraying glue on foam cushions. In even the most egregious situations at much higher emission rates, the exposure of the general public to nPB was in all cases below the proposed Reference Concentration (Rfc) of 1 ppm. The USEPA report is attached. Further, in tests done in California, actual real world data shows that worker exposure to nPb in a dry cleaning facility is, even in the worst case, below the ACGIH recommended workplace exposure level of 10 ppm. The test results are attached. Clearly, Mr. Finkel's assumptions, unsupported by actual data, are erroneous.

(c) Finkel argues that nPB causes sever neurological damage at only 50 ppm. This statement's only support is an report published in 2004 entitled *Neurological Abnormalities in Workers of a 1-Bromopropane Factory* (attached). This report does show neurological effects on workers. However, it has been shown as is now well known that the effected workers were in fact exposed to many different chemical compounds since the factory was a large brominated chemical manufacturing plant producing a wide variety of chemicals. In fact, a "factory" producing *only* nPB doe not exist in the world. A small factory dedicated solely to nPB production would produce the entire world's production of nPB within 60 days. Attached are peer reviewed and published reports which conclude that neurological effects are not found until headaches start at exposures of about 180 ppm.

(d) Finkel also discusses workers showing neurological symptoms based on very emissive adhesive uses in the US, but misstates the exposures and omits very important information regarding the incidents. Many of these workers were inexcusably exposed to up to 400 ppm of nPB for at least one year. These extremely high exposures would have caused adverse effects from most chemical compounds on the market today. Also, Mr. Finkel does not adequately discuss the fact that high levels of arsenic were also found in the blood of all of the effected workers. This was likely due to the fact that traditionally in the foam cushion industry in North Carolina, arsenic was added to the glue to reduce mold buildup. The presence of arsenic in the blood of the effected workers raises questions as to what compound caused the effects which were seen. I have attached the report *Arsenic as a Potential Confounding Factor in Human occupational Exposure to nPB* which discusses the questions of arsenic contamination.

(e) Finkel uses what is known as structural activity relationship analysis to assume nPB is toxicologically related to other compounds which are known to be hazardous, such as 1, 2 dibromochlroopropane. This analysis, as it relates to nPB, has been shown to be wrong for quite some time now. Scientific testing has shown that the mechanism of action and metabolic pathways of nPB and the other compounds mentioned by Finkel are entirely different, and that nPb is less toxic than all of the compounds mentioned by Finkel. A detailed discussion of this matter is well beyond the scope of this Petition, but Enviro Tech would like the opportunity to discuss this matter in depth with the Department's toxicologists, so that they have a better understanding of nPB. Enviro Tech is prepared to discuss this matter, and all others, in depth at the Public Hearing. I have attached the report *Mechanistic Hypothesis for n Propyl Bromide and Ramifications for Occupational Exposure in the United States*, which, inter alia, discusses the structural activity relationship theory.

(f) Finkel *assumes* that benign and malignant tumors found in mice and rats in the NTP cancer bioassays must result in a finding nPB a human carcinogen. Attached to this Petition is a

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2010 JUL 30 PM 2:14
DEPARTMENT OF REGULATORY

paper authored by Dr. Harvey Clewell, Ph. D., a well known and respected expert who was intimately involved in the OSHA PEL for methylene chloride. The report shows that the effects seen in the test animals are inconclusive on their face and that much more study needs to be done before a finding can be made that any of the effects are relatable to humans. It is also important to note that all but one of the standard bioassays used to predict carcinogenicity have been negative, including all those done by the National Toxicology Program. These bioassay test results are available upon request.

Finally, Enviro Tech has been on record for the last fifteen years that emissive uses, such as in the adhesive sector, should not use nPB based products. Modern dry cleaning machines are better emission control devices than vapor degreasers, which are approved for use by USEPA. Therefore, in a properly rum establishment, exposure of nPB to the workers is at a safe level and exposure to the general population is at a level so low as to be almost non-existent.

Therefore, we respectfully request that the proposed ban on the use of nPB, namely paragraph II(a)(9) be stricken from the proposed rule at this time and that a public hearing be held so that the Department may be fully advised of the scientific facts regarding the safety of our nPB based DrySolv product.

Enviro Tech will attend, along with its expert toxicologists, a Public hearing schedule pursuant to this Petition and the Departments Notice. Enviro Tech is also ready to meet with Department personal before the meeting to discuss any questions the staff may have and will make available to the Department any of the toxicological, health and safety information Enviro Tech has upon request, at no cost to the Department.

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DEPARTMENT OF ENVIRONMENTAL
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Federal Register

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May 30, 2007

Part III

Environmental Protection Agency

40 CFR Part 82

Protection of Stratospheric Ozone: Listing of Substitutes for Ozone-Depleting Substances-n-Propyl Bromide in Solvent Cleaning; Protection of Stratospheric Ozone: Listing of Substitutes for Ozone-DepletingSubstances-n-Propyl Bromide in Adhesives, Coatings, and Aerosols; Final Rule and Proposed Rule

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 82

[EPA–HQ–OAR–2002–0064; FRL–8316–8]

RIN 2060–AO10

Protection of Stratospheric Ozone: Listing of Substitutes for Ozone-Depleting Substances-n-Propyl Bromide in Solvent Cleaning

AGENCY: Environmental Protection Agency.

ACTION: Final Rule.

SUMMARY: The Environmental Protection Agency (EPA) determines that n-propyl bromide (nPB) is an acceptable substitute for methyl chloroform and chlorofluorocarbon (CFC)–113 in the solvent cleaning sector under the Significant New Alternatives Policy (SNAP) program under section 612 of the Clean Air Act. The SNAP program reviews alternatives to Class I and Class II ozone depleting substances and approves use of alternatives which do not present a substantially greater risk to public health and the environment than the substance they replace or than other available substitutes.

DATES: This final rule is effective on July 30, 2007.

ADDRESSES: EPA has established a docket for this action under Docket ID No. EPA–HQ–OAR–2002–0064. All documents in the docket are listed on the *http://www.regulations.gov* Web site. Although listed in the index, some information is not publicly available, *i.e.*, Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either electronically in *http://www.regulations.gov* or in hard copy at the Air and Radiation Docket, EPA/DC, EPA West, Room 3334, 1301 Constitution Ave., NW., Washington, DC. This docket facility is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the Air and Radiation Docket is (202) 566–1742.

FOR FURTHER INFORMATION CONTACT: Margaret Sheppard, Stratospheric Protection Division, Office of Atmospheric Programs, Mail Code 6205J, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number (202) 343–9163; fax number (202) 343–2362, *e-mail address: sheppard.margaret@epa.gov.* Notices and rulemakings under the SNAP program are available on EPA's Stratospheric Ozone World Wide Web site at *http://www.epa.gov/ozone/snap/regs.*

SUPPLEMENTARY INFORMATION: Table of Contents: This action is divided into eight sections:

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I. General Information

A. Does this action apply to me?

This final rule lists n-propyl bromide (nPB) as an acceptable substitute when used as a solvent in industrial equipment for metals cleaning, electronics cleaning, or precision cleaning. General metals, precision, and electronics cleaning includes cleaning with industrial cleaning equipment such as vapor degreasers, in-line cleaning systems, or automated equipment used for cleaning below the boiling point. We understand that nPB is used primarily for cleaning in vapor degreasers. Manual cleaning, such as pail-and-brush, hand wipe, recirculating over-spray (''sink-on-a-drum'') parts washers, immersion cleaning into dip tanks with manual parts handling, and use of squirt bottles, is not currently regulated under the SNAP program. EPA also does not regulate the use of solvents as carriers for flame retardants, dry cleaning, or paint stripping under the SNAP program.

This final action does not address the use of n-propyl bromide as an aerosol solvent or as a carrier solvent in adhesives or coatings. We are issuing a proposed rule addressing these end uses in a separate **Federal Register** action. Neither this final nor the proposed rule issue a decision on other end uses in which nPB was submitted as an ozone-depleting substance (ODS) substitute, such as fire suppression or foam blowing, because of insufficient information.

Affected users under this final rule could include:

- Businesses that clean metal parts, such as automotive manufacturers, machine shops, machinery manufacturers, and electroplaters.
- Businesses that manufacture electronics or computer equipment.
- Businesses that require a high level of cleanliness in removing oil, grease, or wax, such as for aerospace applications or for manufacture of optical equipment.

TABLE 1.—POTENTIALLY REGULATED ENTITIES, BY NORTH AMERICAN INDUSTRIAL CLASSIFICATION SYSTEM (NAICS) CODE OR SUBSECTOR

Category	NAICS code or subsector	Description of regulated entities
Industry	331	Primary Metal Manufacturing.
Industry	332	Fabricated Metal Product Manufacturing.
Industry	333	Machinery Manufacturing.
Industry	334	Computer and Electronic Product Manufacturing.
Industry	335	Equipment Appliance, and Component Manufacturing.
Industry	336	Transportation Equipment Manufacturing.
Industry	337	Furniture and Related Product Manufacturing.
Industry	339	Miscellaneous Manufacturing.

This table is not intended to be exhaustive, but rather a guide regarding entities likely to be regulated by this action. If you have any questions about whether this action applies to a particular entity, consult the person listed in the preceding section, **FOR FURTHER INFORMATION CONTACT.**

B. What is n-propyl bromide?

n-propyl bromide (nPB), also called 1-bromopropane, is a non-flammable organic solvent with a strong odor. Its chemical formula is C_3H_7Br. Its identification number in Chemical Abstracts Service's registry (CAS Reg. No.) is 106–94–5. nPB is used to remove wax, oil, and grease from electronics, metal, and other materials. It also is used as a carrier solvent in adhesives. Some brand names of products using nPB are: Abzol®, EnSolv®, and Solvon® cleaners; Pow-R-Wash® NR Contact Cleaner, Superkleen Flux Remover 2311 and LPS NoFlash NU Electro Contact Cleaner aerosols; and Whisper Spray and Fire Retardant Soft Seam 6460 adhesives.

C. What acronyms and abbreviations are used in the preamble?

Below is a list of acronyms and abbreviations used in this document.

8-hr—eight hour
ACGIH—American Conference of Governmental Industrial Hygienists
AEL—acceptable exposure limit
ASTM—American Society for Testing and Materials
BMD—benchmark dose
BMDL—benchmark dose lowerbound, the lower 95%-confidence level bound on the dose/exposure associated with the benchmark response
BSOC—Brominated Solvents Consortium
CAA—Clean Air Act
CAS Reg. No.—Chemical Abstracts Service Registry Identification Number
CBI—Confidential Business Information
CEG—community exposure guideline
CERHR—Center for the Evaluation of Risks to Human Reproduction
CFC-113—the ozone-depleting chemical 1,1,2-trifluoro-1,2,2-trichloroethane, $C_2Cl_3F_3$, CAS Reg. No. 76–13–1
CFC—chlorofluorocarbon
cfm—cubic feet per minute
CFR—Code of Federal Regulations
CNS—central nervous system
DNA—deoxyribonucleic acid
EDSTAC—The Endocrine Disruptor Screening and Testing Advisory Committee
EPA—the United States Environmental Protection Agency
FR—**Federal Register**
GWP—global warming potential
HCFC-123—the ozone-depleting chemical 1,2-dichloro-1,1,2-trifluoroethane, CAS Reg. No. 306–83–2
HCFC-141b—the ozone-depleting chemical 1,1-dichloro-1-fluoroethane, CAS Reg. No. 1717–00–6
HCFC-225ca/cb—the commercial mixture of the two ozone-depleting chemicals 3,3-dichloro-1,1,1,2,2-pentafluoropropane, CAS Reg. No. 422–56–0 and 1,3-dichloro-1,1,2,2,3-pentafluoropropane, CAS Reg. No. 507–55–1
HCFC—hydrochlorofluorocarbon
HEC—human equivalent concentration
HFC-245fa—the chemical 1,1,3,3,3-pentafluoropropane, CAS Reg. No. 460–73–1
HFC-365mfc—the chemical 1,1,1,3,3-pentafluorobutane, CAS Reg. No. 405–58–6
HFC-4310mee—the chemical 1,1,1,2,3,4,4,5,5,5-decafluoropentane, CAS Reg. No. 138495–42–8
HFC—hydrofluorocarbon
HFE—hydrofluoroether
HHE—health hazard evaluation
ICF—ICF Consulting
ICR—Information Collection Request
iPB—isopropyl bromide, C_3H_7Br, CAS Reg. No. 75–26–3, an isomer of n-propyl bromide; also called 2-bromopropane or 2-BP
K_{oc}—organic carbon partition coefficient, for determining the tendency of a chemical to bind to organic carbon in soil
LC_{50}—the concentration at which 50% of test animals die
LOAEL—Lowest Observed Adverse Effect Level
Log K_{ow}—logarithm of the octanol-water partition coefficient, for determining the tendency of a chemical to accumulate in lipids or fats instead of remaining dissolved in water
mg/l—milligrams per liter
MSDS—Material Safety Data Sheet
NAICS—North American Industrial Classification System
NESHAP—National Emission Standard for Hazardous Air Pollutants
NIOSH—National Institute for Occupational Safety and Health
NOAEL—No Observed Adverse Effect Level
NOEL—No Observed Effect Level
nPB-n-propyl bromide, C_3H_7Br, CAS Reg. No. 106–94–5; also called 1-bromopropane or 1-BP
NPRM—Notice of Proposed Rulemaking
NTP—National Toxicology Program
NTTAA—National Technology Transfer and Advancement Act
ODP—ozone depletion potential
ODS—ozone-depleting substance
OEHHA—Office of Environmental Health Hazard Assessment of the California Environmental Protection Agency
OMB—U.S. Office of Management and Budget
OSHA—the United States Occupational Safety and Health Administration
PCBTF—parachlorobenzotrifluoride, CAS Reg. No. 98–56–6
PEL—Permissible Exposure Limit
ppm—parts per million
RCRA—Resource Conservation and Recovery Act
RFA—Regulatory Flexibility Act
RfC—reference concentration
SIP—state implementation plan
SNAP—Significant New Alternatives Policy
STEL—Short term exposure limit
TCA—the ozone-depleting chemical 1,1,1-trichloroethane, CAS Reg. No. 71–55–6; also called methyl chloroform, MCF, or 1,1,1
TCE—the chemical 1,1,2-trichloroethene, CAS Reg. No. 79–01–6, C_2Cl_3H; also call trichloroethylene
TERA—Toxicological Excellence for Risk Assessment
TLV—Threshold Limit Value™
TSCA—Toxic Substances Control Act
TWA—time-weighted average
UMRA—Unfunded Mandates Reform Act
U.S.C.—United States Code
VMSs—volatile methyl siloxanes
VOC—volatile organic compound
WEL—workplace exposure limit

II. How does the Significant New Alternatives Policy (SNAP) program work?

A. What are the statutory requirements and authority for the SNAP program?

Section 612 of the Clean Air Act (CAA) authorizes EPA to develop a

program for evaluating alternatives to ozone-depleting substances, referred to as the Significant New Alternatives Policy (SNAP) program. The major provisions of section 612 are:

• *Rulemaking*—Section 612(c) requires EPA to promulgate rules making it unlawful to replace any class I (chlorofluorocarbon, halon, carbon tetrachloride, methyl chloroform, and hydrobromofluorocarbon) or class II (hydrochlorofluorocarbon) substance with any substitute that the Administrator determines may present adverse effects to human health or the environment where the Administrator has identified an alternative that (1) reduces the overall risk to human health and the environment, and (2) is currently or potentially available.

• *Listing of Unacceptable/Acceptable Substitutes*—Section 612(c) also requires EPA to publish a list of the substitutes unacceptable for specific uses. We must publish a corresponding list of acceptable alternatives for specific uses.

• *Petition Process*—Section 612(d) grants the right to any person to petition EPA to add a substitute to or delete a substitute from the lists published in accordance with section 612(c). EPA has 90 days to grant or deny a petition. Where the Agency grants the petition, we must publish the revised lists within an additional six months.

• *90-day Notification*—Section 612(e) requires EPA to require any person who produces a chemical substitute for a class I substance to notify the Agency not less than 90 days before new or existing chemicals are introduced into interstate commerce for significant new uses as substitutes for a class I substance. The producer must also provide the Agency with the producer's health and safety studies on such substitutes.

• *Outreach*—Section 612(b)(1) states that the Administrator shall seek to maximize the use of federal research facilities and resources to assist users of class I and II substances in identifying and developing alternatives to the use of such substances in key commercial applications.

• *Clearinghouse*—Section 612(b)(4) requires the Agency to set up a public clearinghouse of alternative chemicals, product substitutes, and alternative manufacturing processes that are available for products and manufacturing processes which use class I and II substances.

B. How do the regulations for the SNAP program work?

On March 18, 1994, EPA published the original rulemaking (59 FR 13044) that described the process for administering the SNAP program and issued the first acceptability lists for substitutes in the major industrial use sectors. These sectors include: Refrigeration and air conditioning; foam blowing; solvents cleaning; fire suppression and explosion protection; sterilants; aerosols; adhesives, coatings and inks; and tobacco expansion. These sectors comprise the principal industrial sectors that historically consumed large volumes of ozone-depleting substances.

Anyone who plans to market or produce a substitute for an ODS in one of the eight major industrial use sectors must provide the Agency with health and safety studies on the substitute at least 90 days before introducing it into interstate commerce for significant new use as an alternative. This requirement applies to the person planning to introduce the substitute into interstate commerce, typically chemical manufacturers, but may also include importers, formulators or end-users when they are responsible for introducing a substitute into commerce.

C. How does the SNAP program list our decisions?

The Agency has identified four possible decision categories for substitutes: Acceptable; acceptable subject to use conditions; acceptable subject to narrowed use limits; and unacceptable. Use conditions and narrowed use limits are both considered ''use restrictions'' and are explained below. Substitutes that are deemed acceptable with no use restrictions (no use conditions or narrowed use limits) can be used for all applications within the relevant sector end-use. Substitutes that are acceptable subject to use restrictions may be used only in accordance with those restrictions. It is illegal to replace an ODS with a substitute listed as unacceptable.

After reviewing a substitute, the Agency may make a determination that a substitute is acceptable only if certain conditions of use are met to minimize risks to human health and the environment. We describe such substitutes as ''acceptable subject to use conditions.'' If you use these substitutes without meeting the associated use conditions, you use these substitutes in an unacceptable manner and you could be subject to enforcement for violation of section 612 of the Clean Air Act.

For some substitutes, the Agency may permit a narrowed range of use within a sector. For example, we may limit the use of a substitute to certain end-uses or specific applications within an industry sector or may require a user to demonstrate that no other acceptable end uses are available for their specific application. We describe these substitutes as ''acceptable subject to narrowed use limits.'' If you use a substitute that is acceptable subject to narrowed use limits, but use it in applications and end-uses which are not consistent with the narrowed use limit, you are using these substitutes in an unacceptable manner and you could be subject to enforcement for violation of section 612 of the Clean Air Act.

The Agency publishes its SNAP program decisions in the **Federal Register**. For those substitutes that are deemed acceptable subject to use restrictions (use conditions and/or narrowed use limits), or for substitutes deemed unacceptable, we first publish these decisions as proposals to allow the public opportunity to comment, and we publish final decisions as final rulemakings. In contrast, we publish substitutes that are deemed acceptable with no restrictions in ''notices of acceptability,'' rather than as proposed and final rules. As described in the rule implementing the SNAP program (59 FR 13044), we do not believe that rulemaking procedures are necessary to list alternatives that are acceptable without restrictions because such listings neither impose any sanction nor prevent anyone from using a substitute.

Many SNAP listings include ''comments'' or ''further information.'' These statements provide additional information on substitutes that we determine are either unacceptable, acceptable subject to narrowed use limits, or acceptable subject to use conditions. Since this additional information is not part of the regulatory decision, these statements are not binding for use of the substitute under the SNAP program. However, regulatory requirements listed in this column are binding under other programs. The further information does not necessarily include all other legal obligations pertaining to the use of the substitute. However, we encourage users of substitutes to apply all statements in the **FURTHER INFORMATION** column in their use of these substitutes. In many instances, the information simply refers to sound operating practices that have already been identified in existing industry and/or building-code standards. Thus, many of the comments, if adopted, would not require the affected industry to make significant changes in existing operating practices.

D. Where can I get additional information about the SNAP program?

For copies of the comprehensive SNAP lists of substitutes or additional information on SNAP, look at EPA's

Ozone Depletion World Wide Web site at *http://www.epa.gov/ozone/snap/lists/index.html*. For more information on the Agency's process for administering the SNAP program or criteria for evaluation of substitutes, refer to the SNAP final rulemaking published in the **Federal Register** on March 18, 1994 (59 FR 13044), codified at Code of Federal Regulations at 40 CFR part 82, subpart G. You can find a complete chronology of SNAP decisions and the appropriate **Federal Register** citations at *http://www.epa.gov/ozone/snap/chron.html*.

III. What is EPA's final listing decision on nPB in solvent cleaning?

The Agency is listing nPB as an acceptable substitute in metals, precision and electronics cleaning end uses. Based on the available information, we find that nPB can be used with no substantial increase in overall risks to human health and the environment, compared to other available or potentially available substitutes for ozone-depleting substances in these end uses.

EPA is issuing today's listing in the form of a final rule, rather than in a notice of acceptability, in order to respond to the public comments received on a Notice of Proposed Rulemaking (NPRM) that we issued on June 3, 2003 (68 FR 33284). In that rule, we proposed listing n-propyl bromide (nPB) as an acceptable substitute for use in metals, precision, and electronics cleaning, and in aerosols and adhesives end-uses, subject to the use condition that nPB used in these applications contains no more than 0.05% by weight of isopropyl bromide. In addition, in that proposed rule, EPA indicated that we also would recommend that users adhere to a voluntary acceptable exposure limit (AEL) of 25 parts per million averaged over an eight-hour time-weighted average (TWA). Based on new information received after the close of the comment period on the June 2003 NPRM relevant to our proposed determinations for adhesive and aerosol solvent end uses in that same proposal, the Agency is issuing a new proposal for those end uses in a separate **Federal Register** action. The Agency is not including a recommended AEL in this final rule.

Table 2 contains the text pertaining to nPB use in solvent cleaning end-uses that will be added to EPA's list of acceptable substitutes located on the SNAP Web site at *http://www.epa.gov/ozone/snap/lists/index.html*. This and other listings for substitutes that are acceptable without restriction are not included in the Code of Federal Regulations because they are not regulatory requirements. The information contained in the ''Further Information'' column of those tables are non-binding recommendations on the safe use of substitutes.

TABLE 2.—SOLVENT CLEANING ACCEPTABLE SUBSTITUTE

End use	Substitute	Decision	Further information
Metals cleaning, electronics cleaning, and precision cleaning.	n-propyl bromide (nPB) as a substitute for CFC–113 and methyl chloroform.	Acceptable	EPA recommends the use of personal protective equipment, including chemical goggles, flexible laminate protective gloves and chemical-resistant clothing. EPA expects that all users of nPB would comply with any final Permissible Exposure Limit that the Occupational Safety and Health Administration issues in the future under 42 U.S.C. 7610(a). nPB, also known as 1-bromopropane, is Number 106–94–5 in the Chemical Abstracts Service (CAS) Registry.

IV. What criteria did EPA consider in making this final determination?

In the original rule implementing the SNAP program (March 18, 1994; 59 FR 13044, at 40 CFR 82.180(a)(7)), the Agency identified the criteria we use in determining whether a substitute is acceptable or unacceptable as a replacement for class I or II compounds:

(i) Atmospheric effects and related health and environmental impacts; [e.g., ozone depletion potential]

(ii) General population risks from ambient exposure to compounds with direct toxicity and to increased ground-level ozone;

(iii) Ecosystem risks [e.g., bioaccumulation, impacts on surface and groundwater];

(iv) Occupational risks;

(v) Consumer risks;

(vi) Flammability; and

(vii) Cost and availability of the substitute.

In this review, EPA considered all the criteria above. However, n-propyl bromide is used in industrial applications such as electronics cleaning. In those consumer products made using nPB, such as a computer, the nPB would have evaporated long before a consumer would purchase the item. Therefore, we believe there is no consumer exposure risk in the end uses we evaluated for this rule.

Section 612(c) of the Clean Air Act directs EPA to publish a list of replacement substances (''substitutes'') for class I and class II ozone depleting substances based on whether the Administrator determines they are safe (when compared with other currently or potentially available substitutes) for specific uses or are to be prohibited for specific uses. EPA must compare the risks to human health and the environment of a substitute to the risks associated with other substitutes that are currently or potentially available. In addition, EPA also considers whether the substitute for class I and class II ODSs ''reduces the overall risk to human health and the environment'' compared to the ODSs being replaced. Our evaluation is based on the end use; for example, we compared nPB as a metal cleaning solvent against other available or potentially available metal cleaning alternatives.

Although EPA does not judge the effectiveness of an alternative for purposes of determining whether it is acceptable, we consider effectiveness when determining whether alternatives that pose less risk are available in a particular application within an end use. There are a wide variety of acceptable alternatives listed for solvent cleaning, but not all are appropriate for a specific application because of differences in soils, materials compatibility, degree of cleanliness required, local environmental requirements, and other factors. For example, aqueous cleaners are effective cleaners in many situations and are the substitute of choice for many in the metal cleaning end use. However, in some specific precision cleaning applications that require a high degree of cleanliness and that have narrow

spaces that may trap water used in rinsing, aqueous cleaners may not be appropriate and thus are not available in those specific applications.

EPA evaluated each of the criteria separately and then considered overall risk to human health and the environment in comparison to other available or potentially available alternatives. We concluded that overall, while there are a number of alternatives that reduce the risks from ozone depletion or from smog production [1] slightly more than nPB when used in industrial solvent cleaning equipment, we found no single alternative that could work in all applications that clearly would reduce overall risks to human health and the environment in metals cleaning, electronics cleaning, and precision cleaning. Balancing the different criteria discussed below, nPB used in solvent cleaning end-uses does not pose a significantly greater risk than other substitutes or than the ODS it is replacing in these end uses. Thus, we are listing nPB as acceptable in metals cleaning, electronics cleaning, and precision cleaning.

A. Availability of Alternatives to Ozone-Depleting Substances

Other alternatives to methyl chloroform and CFC–113 are available for metals, electronics, and precision cleaning that have already been found acceptable or acceptable subject to use conditions under the SNAP program including: Aqueous cleaners, semi-aqueous cleaners, alcohols, ketones, esters, ethers, terpenes, HCFC–225ca/cb, hydrofluoroethers (HFEs), hydrofluorocarbon (HFC)–4310mee, HFC–365mfc, heptafluorocyclopentane, hydrocarbons, volatile methyl siloxanes (VMSs), trans-1,2-dichloroethylene, methylene chloride, trichloroethylene [2] (TCE), perchloroethylene,[3] parachlorobenzotrifluoride (PCBTF), and alternative technologies like supercritical fluids, plasma cleaning, and ultraviolet/ozone cleaning. Some alternatives are unlikely to be used in particular end uses because of constraints such as cleaning performance, materials compatibility, cost, workplace exposure requirements, or flammability. For example, no-clean technology is used in electronics cleaning and not in precision cleaning because of the need for a high degree of cleanliness in precision cleaning. Of the available substitutes, aqueous cleaners or solvents for vapor degreasing such as TCE, blends of alcohols or trans-1,2-dichloroethylene and HFCs or HFEs, and HCFC–225ca/cb are most likely to be used in the same applications as nPB. nPB is already commercially available in solvent cleaning, and is used mostly for vapor degreasing in the electronics and precision cleaning end uses (IBSA, 2002).

B. Impacts on the Atmosphere and Local Air Quality

As discussed in the June 2003 proposal, nPB emissions from the continental United States are estimated to have an ozone depletion potential (ODP) of approximately 0.013–0.018, (Wuebbles, 2002) [4], lower than that of the ozone depletion potential of the substances that nPB would replace—CFC–113 (ODP=1.0), and methyl chloroform and HCFC–141b (ODPs = 0.12) (WMO, 2002). Some other acceptable alternatives for these ODSs also have low ODPs. For example, HCFC–225ca/cb has an ODP of 0.02–0.03 (WMO, 2002) and is acceptable in metals cleaning and aerosol solvents, and acceptable subject to use conditions in precision cleaning and electronics cleaning. HCFC–123 has an ODP of 0.02 (WMO, 2002), and is an acceptable substitute in precision cleaning. There are other acceptable cleaners that essentially have no ODP—aqueous cleaners, HFEs, HFC–4310mee, HFC–365mfc, HFC–245fa, hydrocarbons, VMSs, methylene chloride, TCE, perchloroethylene, and PCBTF.

The global warming potential (GWP) index is a means of quantifying the potential integrated climate forcing of various greenhouse gases relative to carbon dioxide. Earlier data found a direct 100-year integrated GWP (100yr GWP) for nPB of 0.31 (Atmospheric and Environmental Research, Inc., 1995). More recent analysis that considers both the direct and the indirect GWP of nPB found a 100-yr GWP of 1.57 (ICF, 2003a; ICF, 2006a). In either case, the GWP for nPB is comparable to or below that of previously approved substitutes in these end uses.

Use of nPB may be controlled as a volatile organic compound (VOC) under state implementation plans (SIPs) developed to attain the National Ambient Air Quality Standards for ground-level ozone, which is a respiratory irritant. Users located in ozone non-attainment areas may need to consider using a substitute for cleaning that is not a VOC or if they choose to use a substitute that is a VOC, they may need to control emissions in accordance with the SIP. Companies have petitioned EPA, requesting that we exempt nPB from regulation as a VOC. However, unless and until EPA issues a final rulemaking exempting a compound from the definition of VOC and states change their SIPs to exclude such a compound from regulation, that compound is still regulated as a VOC. Other acceptable ODS-substitute solvents that are VOCs for state air quality planning purposes include most oxygenated solvents such as alcohols, ketones, esters, and ethers; hydrocarbons and terpenes; trichloroethylene; trans-1,2-dichloroethylene; monochlorotoluenes; and benzotrifluoride. Some VOC-exempt solvents that are acceptable ODS substitutes include HFC–245fa for aerosol solvents; HCFC–225ca/cb, HFC–365mfc and HFC–4310mee for metals electronics, and precision cleaning and aerosol solvents; and methylene chloride, perchloroethylene, HFE–7100, HFE–7200, PCBTF, acetone, and methyl acetate for metals, electronics, and precision cleaning, aerosol solvents, adhesives, and coatings.

C. Ecosystem and Other Environmental Impacts

EPA considered the possible impacts of nPB if it were to pollute soil or water as a waste and compared these impacts to screening criteria developed by the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC, 1998) (see Table 3). Available data on the organic carbon partition coefficient (K_{oc}), the breakdown processes in water and hydrolysis half-life, and the volatilization half-life indicate that nPB is less persistent in the environment than many solvents and would be of low to moderate concern for movement in soil. Based on the LC_{50}, the acute concentration at which 50% of tested animals die, nPB's toxicity to aquatic life is moderate, being less than that for some acceptable cleaners (for example, trichloroethylene, hexane, *d*-limonene, and possibly some aqueous cleaners) and greater than that for some others (methylene chloride, acetone, isopropyl alcohol, and some other aqueous cleaners). The LC_{50} for nPB is 67 mg/l, which is greater than 10 mg/l. Based on EPA's criteria for listing under the Toxics Release Inventory (U.S. EPA,

[1] Smog, also known as ground-level ozone, is produced from emissions of volatile organic compounds that react under certain conditions of temperature and light.

[2] Also called trichlorethene or TCE, C_2Cl_3H, CAS Reg. No. 79–01–6.

[3] Also called PERC, tetrachloroethylene, or tetrachloroethene, C_2Cl_4, CAS Reg. No. 172–18–4.

[4] nPB emissions in the tropics have an ODP of 0.071 to 0.100; the portions of the U.S. outside the continental U.S., such as Alaska, Hawaii, Guam, and the U.S. Virgin Islands, contain less than 1 percent of the U.S.'s businesses in industries that could use nPB. Thus, their potential impact on the ozone layer must be significantly less than that of the already low impact from nPB emissions in the continental U.S. (U.S. Economic Census, 2002a through f).

1992), we believe that nPB would not be sufficiently toxic to aquatic life to warrant listing under the Toxics Release Inventory. Based on its relatively low bioconcentration factor and log K_{ow} value, nPB is not prone to bioaccumulation. Table 3 summarizes information on environmental impacts of nPB; trans-1,2-dichloroethylene, a commonly-used solvent in blends for aerosol solvents, precision cleaning, and electronics cleaning; trichloroethylene, a solvent used for metals, electronics, and precision cleaning; and methyl chloroform, an ODS that nPB would replace.

TABLE 3.—ECOSYSTEM AND OTHER ENVIRONMENTAL PROPERTIES OF nPB AND OTHER SOLVENTS

Property	Description of environmental property	Value for nPB	Value for trans-1,2-dichloro-ethylene	Value for trichloro-ethylene	Value for methyl chloroform
K_{oc}, organic-carbon partition coefficient.	Degree to which a substance tends to stick to soil or move in soil. Lower values (< 300)* indicate great soil mobility; values of 300 to 500 indicate moderate mobility in soil.	330 (Source: ICF, 2004a).	32 to 49 (Source: ATSDR, 1996).	106 to 460 (Source: ATSDR, 1997).	152 (Source: U.S. EPA, 1994a).
Break down in water.	Mechanism and speed with which a compound breaks down in the environment. (Hydrolysis half-life values > 25 weeks* are of concern.)	Hydrolysis is significant. Hydrolysis half-life of 26 days (Source: ICF, 2004a).	Photolytic decomposition, dechlorination and biodegradation are significant; hydrolysis not significant (Source: ATSDR, 1996).	Volatilization and biodegradation most significant, with hydrolysis relatively insignificant. Hydrolysis half-life of 10.7 to 30 months (Source: ATSDR, 1997).	Volatilization most significant; biodegradation and hydrolysis also occur (Source: ATSDR, 2004).
Volatilization half-life from surface waters.	Tendency to volatilize and pass from water into the air.	3.4 hours-4.4 days (Source: ICF, 2004a).	3 to 6.2 hours (Source: ATSDR, 1996).	3.4 hours to 18 days (Source: ATSDR, 1997).	Hours to weeks (Source: U.S. EPA, 1994a).
LC_{50} (96 hours) for fathead minnows.	Concentration at which 50% of animals die from toxicity after exposure for 4 days.	67 mg/L (Source: Geiger, 1988).	108 mg/L (Source: U.S. EPA, 1980).	40.7 to 66.8 mg/L (Source: NPS, 1997).	52.8 to 105 mg/L (Source: U.S. EPA, 1994a).
log K_{ow}	Logarithm of the octanol/water partition coefficient, a measure of tendency to accumulate in fat. Log K_{ow} values >3* indicate high tendency to accumulate.	2.10 (Source: ICF, 2004a).	−0.48 (Source: LaGrega *et al.*, 2001, p. 1119).	2.38 (Source: LaGrega *et al.*, 2001, p. 1127).	2.50 (Source: LaGrega *et al.*, 2001, p. 1127).
Bioconcentration factor.	High factors (>1000)* indicate strong tendency for fish to absorb the chemical from water into body tissues.	23 (Source: HSDB, 2004).	5 to 23 (Source: ATSDR, 1996).	10 to 100 (Source: ATSDR, 1997).	<9 (Source: U.S. EPA, 1994a).

*Criteria from EDSTAC, 1998.

nPB is not currently regulated as a hazardous air pollutant and is not listed as a hazardous waste under the Resource Conservation and Recovery Act (RCRA). nPB is not required to be reported as part of the Toxic Release Inventory under Title III of the Superfund Amendments and Reauthorization Act. Despite this, large amounts of nPB might be harmful if disposed of in water. We recommend that users dispose of nPB as they would dispose of any spent halogenated solvent (F001 waste under RCRA). Users should not dump nPB into water, and should dispose of it by incineration.

D. Flammability and Fire Safety

A number of commenters on the June 2003 proposal provided additional information on the flammability of nPB using standard test methods for determining flash point, such as the American Society for Testing and Materials (ASTM) D 92 open cup, ASTM D56 Tag closed cup, and ASTM D93 Pensky-Martens closed cup methods (BSOC, 2000; Miller, 2003; Morford, 2003a, b and c; Shubkin, 2003; Weiss Cohen, 2003). We agree with the commenters that by these standard test methods, nPB displayed no flash point. Thus under standard test conditions, nPB is not flammable, and it should not be flammable under normal use conditions. With its low potential for flammability, nPB is comparable to chlorinated solvents, HCFCs, HFEs, HFC–245fa, HFC–4310mee, and aqueous cleaners, and is less flammable than many acceptable substitutes, such as ketones, alcohols, terpenes, and hydrocarbons. nPB exhibits lower and upper flammability limits of approximately 3% to 8% (BSOC, 2000). A number of other solvents that are typically considered to be non-flammable also have flammability limits (for example, methylene chloride, HCFC–141b, and methyl chloroform). If the concentration of vapor of such a solvent falls between the upper and lower flammability limits, it could catch fire in presence of a flame. Such a situation is unusual, but users should take appropriate precautions in cases where the concentration of vapor could fall between the flammability limits.

E. Impact on Human Health

In evaluating potential human health impacts of nPB, EPA considered impacts on both exposed workers and on the general population because we identified these groups of people as the ones likely to be exposed to nPB when it is used as a substitute for ozone-depleting substances. EPA evaluated the available toxicity data using EPA guidelines to develop health-based criteria to characterize human health risks (U.S. EPA, 1994b. RfC Guidelines; U.S. EPA, 1991. Guidelines for Developmental Toxicity Risk Assessment; U.S. EPA, 1995b. Benchmark Dose guidelines; U.S. EPA, 1996. Guidelines for Reproductive Toxicity Risk Assessment).

In the June 2003 NPRM, EPA proposed that an exposure limit of 25 ppm would be protective of a range of effects observed in animal and human studies, including reproductive and developmental toxicity, neurotoxicity, and hepatotoxicity. Reduction of sperm motility in rats, noted across multiple studies at relatively low exposures, was determined to be the most sensitive effect. The Agency derived an exposure limit of 18 ppm from a dose response relationship in male rat offspring (''F1 generation'') whose parents were exposed to nPB from prior to mating through birth and weaning of the litters (WIL Research Laboratories, 2001). We then proposed to adjust this value upwards to 25 ppm based on principles of risk management consistent with one of the original ''Guiding Principles'' of the SNAP program (59 FR 13046, March 18, 1994). As we discussed in the June 2003 NPRM, EPA noted that adhesives users should be able to achieve an AEL of 25 ppm and that 25 ppm was between the level based on the most sensitive endpoint (sperm motility in the F1 offspring generation) and the second most sensitive endpoint (sperm motility in the F0 parental generation). Following SNAP program principles, we noted that ''a slight adjustment of the AEL may be warranted after applying judgment based on the available data and after considering alternative derivations'' (69 FR 33295). We stated further that ''18 ppm is a reasonable but possibly conservative starting point, and that exposure to 25 ppm would not pose substantially greater risks, while still falling below an upper bound on the occupation[al] exposure limit.''

As part of this final rulemaking, the Agency has reviewed both information available at the time of the 2003 NPRM related to the health risks associated with nPB use, as well as more recent case studies of nPB exposures and effects in the workplace, newly published toxicological studies, comments to the NPRM, new risk assessments on nPB, and a new threshold limit value (TLV) issued by the American Council of Government and Industrial Hygienists (ACGIH). The new information is reviewed in greater detail in EPA's proposal specific to the use of nPB in aerosol solvents, adhesives, and coatings.

Some general conclusions we draw from the new studies include:

- New data from toxicological studies on nervous system effects remain inconsistent and equivocal concerning the level at which nervous system effects occur (Fueta *et al.*, 2002; Fueta *et al.*, 2004; Honma *et al.*, 2003; Ishidao *et al.*, 2002, NTP, 2003; Sohn *et al.* 2002, Wang *et al.*, 2003).
- Case reports of nPB exposure in the workplace indicate that severe, possibly irreversible, neurological effects may occur at sustained concentrations of approximately 100 ppm or greater (Beck and Caravati, 2003; Majersik *et al.*, 2004; Majersik *et al.*, 2005; Ichihara *et al.*, 2002; Miller, 2005; Raymond and Ford, 2005). In other cases, similar or higher concentrations up to 170 ppm caused less severe nervous system effects (Nemhauser, 2005; NIOSH, 2003a; Ichihara, 2004a). Some neurological effects occurred in workers at levels of less than 50 ppm (Ichihara *et al.*, 2004b). Because of design and methodological limitations, such as small numbers of subjects and limited exposure information, these studies do not provide a sufficient quantitative basis to derive an acceptable exposure limit.
- Data on female rats indicate that nPB affects the maturation of ovarian follicles and the ovarian cycle (Yamada *et al.*, 2003), consistent with previously reviewed data (WIL, 2001; Sekiguchi *et al.*, 2002).
- Some data on occupation exposure suggest that workers exposed to nPB may have experienced menstrual disorders (Ichihara *et al.*, 2002; Ichihara *et al.*, 2004b). However, the data are not statistically significant and are not sufficient to conclude that nPB exposure caused these female reproductive effects.
- Data on DNA damage in workers exposed to nPB was not statistically significant (Toraason *et al.*, 2006).
- Metabolic data on mice and rats indicate some species differences. Metabolism of nPB appears to be primarily through cytochrome P450 enzymes, particularly in mice; glutathione conjugation also plays a role, and a bigger role for rats than for mice (RTI, 2005).

These more recent studies do not cause us to change our acceptability determination for solvent cleaning.

In addition, we considered new evaluations of the toxicity of nPB from Stelljes and Wood (2004), Toxicological Excellence in Risk Assessment (TERA, 2004), ICF (2004a, 2006a), and the TLV documentation from the ACGIH (ACGIH, 2005).

- Stelljes and Wood (2004) is similar in its results to SLR International (2001), a study by the same authors. EPA previously reviewed SLR International, 2001 in developing the June 2003 NPRM. Both these studies concluded with a recommended AEL of 156 ppm, based on male reproductive effects and uncertainty factors of 1 in driving the AEL. These documents assigned uncertainty factors in a manner inconsistent with EPA's guidance. This would result in a higher AEL than we would determine following the approach EPA has used on other chemicals, as well as an AEL that in our view would not sufficiently protect human health from nPB's effects because of multiple sources of uncertainty in available data (*i.e.*, variability within the working population and differences between animals and humans in how nPB affects the reproductive system).
- TERA (2004) reviews other AEL derivations for nPB, performs a benchmark dose (BMD) analysis, and recommends an AEL of 20 ppm based on live litter size. This document is consistent with EPA guidance for BMD modeling and for assigning uncertainty factors. A review of this document is available in the public docket (ICF, 2004b).
- ICF (2004c, 2006b) derived an AEL for nPB based upon female reproductive effects. ICF (2004c, 2006b) discussed the relevant literature (Ichihara *et al.*, 1999, 2002, 2004a, 2004b; Sekiguchi, 2002; Yamada *et al.*, 2003; WIL, 2001) and calculated mean estrous cycle length and the mean number of estrous cycles occurring during a three-week period at different exposure levels in the WIL, 2001 2-generation study. ICF (2004c, 2006a) found statistically significant reductions in the number of estrous cycles in a three-week period, both including and excluding females that had stopped their estrous cycles, at 250, 500, and 750 ppm in the F0 parental generation and at 500 and 750 ppm in the F1 generation. ICF (2004c, 2006a) conducted BMD modeling and calculated benchmark dose lowerbound (BMDL) values of the number of estrous cycles in a three-week period that varied from 102 to 208 ppm, depending upon the model used and the benchmark criteria selected. All data were calculated based on the mean reductions in estrous cycle number calculated from the WIL, 2001 study. Values were calculated for the F0 generation; the number of data for the F1 generation was too small for statistical analysis. The BMDLs that ICF calculated for the number of estrous cycles in a three-week period were 162 ppm and 208 ppm, depending on the benchmark response criteria (10% change in response vs. one standard deviation) and using a linear-heterogeneous model.
- The ACGIH issued a recommended TLV of 10 ppm (time-weighted average) for nPB (ACGIH, 2005). ACGIH summarized numerous studies showing

different effects of nPB and identified no observed effect levels (NOELs) of 200 ppm for hepatotoxicity (ClinTrials, 1997b) and less than 100 ppm for developmental toxicity, as evidenced by decreased fetal weight (Huntingdon Life Sciences, 2001).

The Occupational Safety and Health Administration (OSHA) has not developed a permissible exposure limit (PEL) for nPB that EPA could use to evaluate toxicity risks [5] from workplace exposure. In prior SNAP reviews, EPA has used ACGIH TLVs where available in assessing a chemical's risks and determining its acceptability if OSHA has not set a PEL. ACGIH is recognized as an independent, scientifically knowledgeable organization with expertise in issues of toxicity and industrial hygiene. However, in this case, EPA believes that ACGIH's TLV for nPB of 10 ppm has significant limitations as a reliable basis for an acceptable exposure limit, especially given the availability of other, more comprehensive analyses described in this preamble. First, according to the authors of the Huntingdon Life Sciences study, the decrease in fetal weight was an artifact of sampling procedure that biased the data (test animals were only sacrificed at the end of the day rather than at random). The Center for the Evaluation of Risks to Human Reproduction (CERHR) expert panel excluded ''aberrantly low'' fetal weights from one litter in this study and calculated a BMDL greater than 300 ppm for this endpoint after removing those outlier data (CERHR, 2002a, 2003a, and 2004a). TERA calculated a BMDL similar to that of the CERHR expert panel when analyzing the same data set (TERA, 2004). Further, the reference list in the documentation on the TLV indicates that ACGIH did not review and evaluate all the studies available prior to the development of the recommended exposure limit. For example, key supporting articles that reported disruption of estrous cycles (Yamada *et al.,* 2003 and Sekiguchi *et al.*, 2002) were not discussed in the TLV documentation. Further, ACGIH did not provide sufficient reasoning for the selection of the chosen endpoint over others (e.g., reproductive toxicity and/or neurotoxicity). The lack of discussion of applied uncertainty factors also prevents a determination of how ACGIH arrived at a TLV of 10 ppm. In summary, EPA is not basing its proposed acceptability determination for nPB on the ACGIH TLV because: (1) Other scientists evaluating the database for nPB did not find the reduced pup weight to be the most sensitive endpoint; (2) BMD analysis of the reduced pup weight data (CERHR, 2002a; TERA, 2004) results in a higher BMDL (roughly 300 ppm) than those for sperm effects and estrous cycle changes; and (3) ACGIH may not have reviewed the complete body of literature as several studies discussing neurotoxicity and female reproductive effects were omitted from the list of references. A number of reviews of this document are available in the public docket (ICF, 2004d; O'Malley, 2004). Despite some flaws in its derivation, the TLV of 10 ppm is less than two-fold lower than the low end of the range of acceptable exposure levels based on the most sensitive reproductive endpoints (see below). This small difference is well within the uncertainty we see when extrapolating a benchmark dose from an experimental study in rats to an occupational exposure limit in humans.

We summarize the data for a number of end points found in these analyses in Table 4 below. We examined these data to assess the acceptability of nPB use in the metals, electronics, and precision cleaning end uses reviewed in this final rule. These data indicate that, once uncertainty factors are applied consistent with EPA guidelines, the lowest levels for acceptable exposures would be derived for reproductive effects.[6] The data also indicate that a level sufficient to protect against male reproductive effects (e.g., reduced sperm motility) would be in a range from 18 to 30 ppm, in the range of 17 to 22 ppm to protect against female reproductive effects (e.g., estrous cycle length), and at approximately 20 ppm for effects related to reproductive success (live litter size).

TABLE 4.—SUMMARY OF ENDPOINTS USING BENCHMARK RESPONSE MODELING

Endpoint [a]	Study	BMDL[b] (ppm)	Human equivalent concentration (HEC)[c] (ppm)
Liver Effects [d]			
Liver vacuolation in males (F_1 offspring generation).	WIL, 2001 as analyzed in ICF, 2002	110	116
Liver vacuolation in males (F_0 parent generation).	WIL, 2001 as analyzed in ICF, 2002	143	150
Liver vacuolation	ClinTrials, 1997b as analyzed in ICF, 2002 and Stelljes & Wood, 2004	226	170
Reproductive Effects—Male			
Sperm motility (F_1 offspring generation).	WIL, 2001 as analyzed in ICF, 2002	169	177
	WIL, 2001 as analyzed in Stelljes & Wood, 2004	156	164
Sperm motility (F_0 parent generation)	WIL, 2001 as analyzed in ICF, 2002	282	296
	WIL, 2001 as analyzed in Stelljes & Wood, 2004	263	276
Prostate weight (F_0 parent generation).	WIL, 2001 as analyzed in TERA, 2004	190	200
Sperm count	Ichihara *et al.*, 2000b as analyzed in Stelljes & Wood, 2004	232	325

[5] Vendors of nPB-based products have recommended a wide range of exposure limits, from 5 ppm to 100 ppm (Albemarle, 2003; Chemtura, 2006; Docket A–2001–07, item II–D–19; Enviro Tech International, 2006; Farr, 2003; Great Lakes Chemical Company, 2001).

[6] By EPA guidelines, we would apply an uncertainty factor of √10, or approximately 3, for differences between species for all health effects. We would also apply an uncertainty factor of √10 (3) for variability within the working population for reproductive and developmental effects, because, among other reasons, these conditions would not necessarily screen out an individual from being able to work, unlike for liver or nervous system effects. Therefore, for reproductive and developmental effects, we use a composite uncertainty factor of 10. See further discussion of uncertainty factors in section V.B.3 below.

TABLE 4.—SUMMARY OF ENDPOINTS USING BENCHMARK RESPONSE MODELING—Continued

Endpoint [a]	Study	BMDL[b] (ppm)	Human equivalent concentration (HEC)[c] (ppm)
Sperm deformities (F_0 parent generation).	WIL, 2001 as analyzed in Stelljes & Wood, 2004	296	311
Reproductive Effects—Female			
Number of estrus cycles during a 3 week period (F_0 parent generation).	WIL, 2001 as analyzed in ICF, 2006a	162	170
	WIL, 2001 as analyzed in ICF, 2006a	208	218
Estrous cycle length (F_1 offspring generation) [d].	WIL, 2001 as analyzed in TERA, 2004	400	420
Estrous cycle length (F_0 parent generation) [e].	WIL, 2001 as analyzed in TERA, 2004	210	220
No estrous cycle incidence (F_1 offspring generation).	WIL, 2001 as analyzed in TERA, 2004	180	189
No estrous cycle incidence (F_0 parent generation).	WIL, 2001 as analyzed in TERA, 2004	480	504
Reproductive Effects—Reproductive Success			
Decreased live litter size (F_1 offspring generation).	WIL, 2001 as analyzed in TERA, 2004	190	200
Decreased live litter size (F_2 offspring generation).	WIL, 2001 as analyzed in TERA, 2004	170	179
Pup weight gain, post-natal days 21 to 28 (F_1 offspring generation).	WIL, 2001 as analyzed in TERA, 2004	180	189
Developmental Effects			
Fetal body weight	WIL, 2001 as analyzed in TERA, 2004	310	326
Fetal body weight	WIL, 2001 as analyzed in CERHR, 2002a	305	320
Nervous System Effects			
Hindlimb strength	Ichihara *et. al.*, 2000a as analyzed in Stelljes and Wood, 2004	214	300

[a] Unless explicitly stated, data are from a parental generation. Of the studies analyzed, only the WIL, 2001 study has multiple generations to be analyzed.
[b] The benchmark response value represents a specified level of excess risk above a control response.
[c] When considering workplace exposures, the human equivalent concentration is the BMDL, adjusted to apply to a 40-hour work week in which workers are exposed for 8 hours a day for five days per week. Animals in the WIL, 2001 study were exposed for 6 hours a day, 7 days a week. Animals in the Ichihara, 2000a and 2000b studies were exposed for 8 hours a day, 7 days a week. Animals in the ClinTrials, 1997b study were exposed for 6 hours a day, 5 days a week.
[d] After applying an uncertainty factor of 3 for animal to human extrapolation, acceptable levels of exposure to protect against liver effects would be in the range of 39 to 57 ppm.
[e] Omits data from those animals that have stopped estrous cycling altogether (TERA, 2004).

These more recent evaluations do not change EPA's acceptability determination for solvent cleaning. As discussed below, users of solvent cleaning equipment are reliably able to achieve exposure levels well below our proposed AEL of 25 ppm in the June 2003 NPRM and therefore we expect nPB users in the metals, electronics, and precision cleaning end uses to be able to achieve acceptable exposure levels. Concentrations of nPB emitted from industrial solvent cleaning equipment were found to be below 25 ppm in roughly 88% of 500 samples on an 8-hr time-weighted average, below 18 ppm in 81% of these samples, and below 10 ppm in roughly 70% of these samples (U.S. EPA, 2003).

Based on review of the previously available information and information submitted in comments to the NPRM, the Agency believes that its derivation of 18 ppm as a starting point in the development of a recommended acceptable exposure level is still valid. For purposes of assessing the acceptability of nPB use in solvent cleaning applications, the Agency evaluated whether exposure levels expected to result from solvent cleaning would approach either the 2003 proposed recommended AEL of 25 ppm, or the more conservative starting point of 18 ppm which was derived from the Agency's original risk analysis. We also evaluated any potential risks to the general population associated with nPB use as a solvent.

1. Workplace Risks

EPA believes that the great majority of users of nPB in metals cleaning, electronics cleaning, and precision cleaning have been able to attain exposure levels of well below 25 ppm, the proposed AEL in the 2003 NPRM, with their existing equipment. Recently measured exposure levels for nPB are much lower than historic exposure data from the 1970s and 1980s for metals cleaning and electronics cleaning (ICF, 2006a); this reflects both improvements in industrial hygiene practices and improvements in cleaning equipment since 1994 spurred by the National Emission Standard for Hazardous Air Pollutants for Halogenated Solvent Cleaning (59 FR 61801). Concentrations

of nPB emitted from industrial solvent cleaning equipment were found to be below 25 ppm in roughly 88% of 500 samples on an 8-hr time-weighted average, below 18 ppm in 81% of these samples, and below 10 ppm in roughly 70% of these samples (U.S. EPA, 2003).

One nPB supplier provided evidence that on the few occasions when nPB concentrations from vapor degreasers were higher than the company's recommended AEL of 25 ppm, users were able to reduce exposure easily and inexpensively by changing work practices, such as reducing drafts near the cleaning equipment (Kassem, 2003). The ability to meet the workplace exposure limit depends on: (1) The features of the cleaning equipment used, such as the presence of secondary cooling coils; and (2) the work practices, such as avoiding drafts near cleaning equipment and lifting cleaned pieces out slowly from the cleaning equipment. Workplace controls could include, but are not limited to, the use of the following: Covers on cold-cleaning and vapor degreasing equipment when not in use; devices to limit air movement over the degreaser; and/or a lip-vent exhaust system to capture vapors and vent them out of the room. Training workers in industrial hygiene practices and in the proper use of cold cleaning and vapor degreasing equipment, as well as warning workers of the symptoms that may occur from over-exposure to nPB, will also help reduce exposure. Therefore, we expect that users of nPB in the solvent cleaning sector following typical industry practices and using typical equipment for vapor degreasing will continue to meet acceptable exposure levels and to use nPB safely without regulatory requirements. This is the approach the SNAP program has taken with many other solvents where users are readily able to meet workplace exposure limit that will protect human health and there is no enforceable OSHA PEL (*e.g.*, HFC–365mfc, HFC–245fa, heptafluorocyclopentane, ketones, alcohols, esters, hydrocarbons, etc.). Based on the available exposure data and current industry practices, EPA believes that users of nPB as an industrial solvent for metals cleaning, electronics cleaning, and precision cleaning are likely to be exposed to concentrations of nPB well below the proposed AEL of 25 ppm from the 2003 NPRM.

2. General Population Risks

In the 2003 NPRM, the Agency provided analyses demonstrating that people living in the immediate vicinity of a facility using nPB in spray adhesives would have exposures below the community exposure guideline of 1 ppm (68 FR 33300–33301). The community exposure guideline was derived considering both sperm motility and liver effects in the WIL (2001) 2-generation study using EPA's reference concentrations (RfC) guidelines (U.S. EPA, 1994b). Since the general population would not be exposed in excess of the community exposure guideline from a highly emissive application, the less emissive uses such as metals, electronics, and precision cleaning would create insignificant exposures (well below 1 ppm). Thus, we believe that proper use of nPB in solvent cleaning would not pose measurable risks to the general population.

V. How is EPA responding to comments on the June 2003 NPRM?

In this section, EPA responds to comments on the major issues in the June 2003 NPRM. A complete response to comments is in docket EPA–HQ–OAR–2002–0064.

A. EPA's Acceptability Decision

There was no consensus among commenters about whether EPA should find nPB acceptable, acceptable subject to use conditions, or unacceptable in the various end uses listed in the proposal. Some commenters raised concerns about specific end uses, particularly aerosols and adhesives. Others supported finding nPB acceptable in solvents cleaning and in adhesives. We are not taking final action in this rule with respect to nPB as a substitute in aerosols or adhesives. We will respond to any comments regarding those end uses at the time we take final action for aerosols and adhesives.

Comment: Several commenters supported EPA's proposed approval of nPB under the SNAP program in various end uses. In contrast, two commenters opposed EPA's proposed acceptability determination in all end uses, including solvent cleaning, citing concerns about exposure and the toxicity of nPB. Another commenter stated that applications cited in the proposal (e.g., electronics and metals cleaning, label removal and spray cleaning) are not suitable for use of nPB. This commenter reasoned that if nPB provides unique performance characteristics, its uses should be limited to non-emissive and low-volume applications. A commenter from a company that markets nPB as a chemical intermediate but not as a solvent, noted that his company recognizes the health concerns associated with nPB, and thus his company continues to prohibit the sale of nPB to customers with dispersive uses. Another commenter stated that nPB is dangerous to the ozone layer and workers and urged EPA to find a safe substitute.

Response: EPA believes nPB may be found acceptable under the SNAP program only in those end uses where it has been shown to be used safely, as compared with other substitutes that are currently or potentially available. We find this to be the case for metals cleaning, electronics cleaning, and precision cleaning.

Comment: Several commenters agreed with EPA's proposed approval for nPB in metal cleaning, electronics cleaning, and precision cleaning end uses. One specifically reported that his company's industrial hygiene program for nPB-based solvents in metal and electronics cleaning has conducted extensive air sampling, and that the majority of the samples have shown values well below 25 ppm. This commenter also noted that, in those few workplaces where higher levels were found, adoption of recommended workplace ventilation and handling practices produced acceptable subsequent sample values. Thus, this commenter believes that exposures can be controlled to protective levels.

One commenter expressed concerns over the approval of nPB as acceptable for use in solvent cleaning, maintaining that toxicity data is insufficient to be convincing that long-term effects will not be a concern. Two other commenters did not support EPA's proposal to find nPB acceptable. One of the commenters concurred with EPA that exposures from manual wipe cleaning will not be acceptable and that nPB should not be used in such operations. Another commenter opposed EPA's proposed acceptability determination for solvent cleaning, stating that use of nPB in applications such as electronics and metals cleaning, label removal, and spray cleaning is not appropriate.

Response: EPA agrees with those commenters who said nPB should be acceptable for use in metal cleaning, electronics cleaning, and precision cleaning. By our definition of the solvent cleaning sector, such users are cleaning using industrial cleaning equipment. For an organic solvent, this means a vapor degreaser or an automated cold cleaning machine. Emissions from vapor degreasers can be controlled both through improving equipment (increasing the freeboard, adding cooling coils, or adding a lift that raises cleaned pieces slowly) and through improved work practices (leaving the vicinity of the vapor degreaser when done with work, tipping

work-pieces so they do not catch solvent, or lifting cleaned pieces out slowly).

In solvent cleaning equipment, exposure data show that nPB can meet an exposure level well below 25 ppm, even at levels of 5 ppm or less, the majority of the time (U.S. EPA 2003; ICF, 2006a). Concentrations of nPB emitted from industrial solvent cleaning equipment were measure to be below 25 ppm in roughly 88% of more than 500 samples, below 18 ppm in 81% of these samples, and at or below 5 ppm in 56% of these samples (U.S. EPA, 2003). In cases where exposure levels are higher, there are simple, cost-effective changes that can be made to reduce emissions (Kassem, 2003). We agree that manual cleaning using nPB is inappropriate, because of the difficulty of controlling emissions, but manual cleaning is currently beyond the scope of the SNAP Program. EPA plans to address spray cleaning using aerosols in a new proposal.

B. Toxicity

1. Health Endpoints

Comment: A number of commenters on the June 2003 NPRM suggested that EPA should consider neurotoxicity as the endpoint in deriving the AEL for nPB (Linnell, 2003; Werner, 2003; Rusch and Bernhard, 2003; Rusch, 2003). In particular, they requested that EPA consider the study conducted by Wang (2003) and epidemiological data on neurotoxic effects of nPB.

Response: Recent data collected from occupational settings indicate that severe, possibly irreversible, neurological effects may occur at sustained concentrations of approximately 100 ppm or greater (Beck and Caravati, 2003; Majersik, 2004; Majersik, 2005), with variability in effects observed in different studies, although in most cases exposures may have been much higher. Other studies with human data are discussed above in section IV.E. Because of design and methodological limitations, such as small numbers of subjects and limited exposure information, none of the recent studies individually provides a sufficient quantitative basis to derive an AEL.

In the study on rats by Wang *et al.* (2003), measurements found a decrease in enzymes in the spinal cord and brain at 200, 400, and 800 ppm, but the animals displayed no physical or behavioral changes. Because of the lack of physical symptoms or behavioral changes, EPA does not believe that the decrease in enzyme levels in the central nervous system are toxicologically relevant. Other studies examining neurological effects of nPB showed those effects to be transient and reversible at and above 200 ppm (Ichihara *et al.*, 2000a). Exposures of 200 ppm and above for three weeks had no effect on memory, learning function, or coordination of limbs (Honma, 2003); the effect of spontaneous locomotor activity seen in this study at 50 ppm and above was not considered adverse by the authors. In other studies, neurological effects were absent after extended periods of exposure—after 28 days of exposure at concentrations > 400 ppm (ClinTrials, 1997a) and after 90 days of exposure at concentrations up to 600 ppm (ClinTrials, 1997b). Thus, although neurological effects have been associated with nPB exposure, the data are currently insufficient to quantify and set an AEL based on this endpoint. More recent data does not change EPA's acceptability determination for solvent cleaning.

Comment: One commenter on the June 2003 NPRM requested that EPA evaluate a study by Yamada et al (2003), a study published just prior to the June 2003 NPRM.

Response: EPA reexamined Yamada *et al.*, 2003 and re-evaluated the literature (Ichihara *et al.*, 1999, 2002, 2004a,b; Sekiguchi, 2002, Yamada *et al.*, 2003; WIL, 2001). Multiple benchmark analyses found a statistically significant decrease in the number of estrous cycles and increase in estrous cycle length associated with nPB exposure, consistent with other reproductive endpoints, namely reductions in sperm motility, decreased live litter size, and change in prostate weight (ICF, 2002a; ICF, 2006a; Stelljes and Wood, 2004; TERA, 2004). These more recent evaluations, which could lead to an HEC of 170 ppm and an AEL of 17 ppm, do not change EPA's acceptability determination for solvent cleaning, since the evidence supports the ability of users in this end use to consistently meet such a level.

Comment: Some commenters stated that data from the F1 generation is inappropriate for calculating occupational exposure, citing statements from some toxicologists that use of effects on adult F1 generation animals is inappropriate. They also stated that EPA has not required this for other chemicals and that the resulting value is more conservative than what is normal and appropriate for industrial toxicology (Morford, 2003d and e; Ruckriegel, 2003). One commenter claims that because EPA's review of nPB differed from EPA's review of other SNAP alternatives, the process violates equal protection (Morford, 2003d and e). Others stated that sperm motility effects on the F1 generation are appropriate to consider (Risotto, 2003; Farr, 2003), particularly because of the potential for *in utero* effects and because of the consistent presence of these reproductive effects in both generations and at multiple levels.

Response: EPA is not finalizing a specific AEL for the purposes of this final rule. EPA acknowledges that using data from the F1 offspring generation may be conservative because the pups in the F1generation were exposed to nPB between weaning and sexual maturity (WIL, 2001). During occupational exposure, this period of exposure would not occur because children under age 16 are not allowed to work in industrial settings. However, EPA believes that because of the potential for *in utero* effects that would only be seen in the offspring generation, looking only at the F0 parental generation could underestimate the adverse health impacts of a chemical. Therefore, it was appropriate for us to consider effects seen in both the F0 parental generation and the F1 offspring generation. Further, effects on sperm motility in the parental and offspring generations are seen at levels generally consistent with multiple reproductive effects seen in both generations and both sexes exposed to nPB, such as estrous cycle length, lack of estrous cycling, the number of estrous cycles in a given period of time, fertility indices, and the number of live pup births (TERA, 2004; ICF, 2006a; SLR International, 2001).

We also note that different substances have different toxicological effects and those effects must be considered based on the best scientific information and methodologies available. It is incorrect to claim that such reviews, which focus on the effects of different substances, resulted in disparate treatment of nPB [7].

2. Adjustments to Acceptable Exposure Level Based on Risk Management Principles

In the 2003 NPRM, EPA derived 18 ppm as the starting point for an acceptable exposure level based on reduced sperm motility in the offspring generation of animals exposed to nPB (WIL, 2001). Following a SNAP program principle that alternatives should be restricted only where it is ''clearly more harmful to human health and the

[7] We interpret the commenter's use of the term ''equal protection'' to mean that the commenter beleives that EPA has performend a harsher review of nPB than it has for other substitutes and not a claim that EPA has violated the 14th Amendment of the Constitution, which applies only to the states and not the Federal Government.

environment than other alternatives,'' we noted that ''a slight adjustment of the AEL may be warranted after applying judgment based on the available data and after considering alternative derivations''(69 FR 33294, 33295). The Agency proposed an upward adjustment of the AEL to 25 ppm based on principles of risk management, and based, among other things, on a determination that 25 ppm was between the level based on the most sensitive endpoint (sperm motility in the F1 offspring generation) and the second most sensitive endpoint (sperm motility in the F0 parental generation). We stated further that ''18 ppm is a reasonable but possibly conservative starting point, and that exposure to 25 ppm would not pose substantially greater risks, while still falling below an upper bound on the occupation[al] exposure limit.''

Comment: Commenters responded that: (1) The SNAP program does not create a presumption in favor of substances that are already available on the market, especially where other alternatives exist (Linnell, 2003; Werner, 2003); (2) EPA's AEL derivation of 18 ppm is not conservative enough (Werner, 2003; Risotto, 2003) and further adjustment upward further reduces protection; (3) the data do not support adjusting the AEL upward (EPA–HQ–OAR–2002–0064–0003); (4) EPA should first use the same methodology in establishing an AEL as for other chemicals to ensure that the program's guiding principle in comparing risks is not compromised (Werner, 2003); and (5) EPA should reconsider whether industrial exposures consistently occur or can be controlled at 25 ppm (Werner, 2003). No commenters specifically supported adjusting the AEL upward.

Response: EPA is not finalizing a specific AEL for the purposes of this final rule. In a separate proposed rulemaking for the aerosol, adhesive and coatings end uses, we will be providing the public an opportunity to comment on a range of exposure level values that are comparable to the levels discussed in the June 2003 proposal (69 FR 33295) that the Agency would consider to be acceptable. Because we have concluded that end users in the solvent sector are routinely able to meet even the lowest exposure level we considered recommending (U.S. EPA, 2003), we do not need to make a final determination as to the appropriate level for purposes of this rulemaking.

3. Uncertainty Factors

According to EPA risk assessment guidance for RfC (EPA 1994a), uncertainty factors of up to 10 may be applied to the ''human equivalent concentrations (which accounts for worker exposure patterns of 8 hours per day for 5 days a week), for each of the following conditions:

(1) Data from animal studies are used to estimate effects on humans;

(2) Data on healthy people or animals are adjusted to account for variations in sensitivity among members of the human population (inter-individual variability);

(3) Data from subchronic studies are used to provide estimates for chronic exposure;

(4) Studies that only provide a LOAEL rather than a NOAEL or BMD; or

(5) An incomplete database of toxicity information exists for the chemical.

Comment: Some commenters on the June 2003 NPRM stated that EPA should use an uncertainty factor of 1 or 2 to extrapolate from animals to humans (Weiss Cohen, 2003), while others suggested uncertainty factors of 2 or 3 for pharmacokinetics, or an overall uncertainty factor of 10 for rat to human extrapolation because of a lack of information on the metabolism and mode of action of nPB and because the rat is an insensitive model for effects on male reproduction in humans (Werner, 2003; Rusch and Bernhardt, 2003).

Response: EPA believes that two uncertainty factors are appropriate for this database to account for (1) physiological differences between humans and rats; and (2) variability within the working population. EPA RfC guidelines state that an uncertainty factor of 10 may be used for potential differences between study animals and humans. This factor of 10 consists in turn of two uncertainty factors of 3—the first to account for differences in pharmacodynamics[8] and the second to account for differences in pharmacokinetics[9] between the study animal and humans. (The value of three is the square root of 10 rounded to one digit, with 10 representing an order of magnitude [EPA,1994a, pp. 1–6, 4–73]. In practice, EPA uses the square root of 10 when there are two or four uncertainty factors of 3, yielding a total uncertainty factor of 10 or 100, and we use a value of 3 when multiplying by other uncertainty factors.) In general, EPA's RfC guidelines state that for the uncertainty factor extrapolating from animal to human data, ''Use of a 3 is recommended with default dosimetric adjustments.'' (U.S. EPA, 1994b, p. 4–73). By EPA RfC guidelines (US EPA, 1994b), no adjustment for differences in pharmacokinetics is necessary in this instance because the blood/air partition coefficient[10] for nPB in the human (7.1) is less than in the rat (11.7), indicating that the delivered dose of nPB into the bloodstream in rats is slightly higher than in humans. EPA has seen no data to indicate that (1) the toxicity is not directly related to the inhaled parent compound in the arterial blood, or that (2) the critical metabolic pathways do not scale across species, with respect to body weight, in the same way as the ventilation rate. Consistent with Appendix J of EPA's RfC guidelines for an inhaled compound that exerts its effects through the bloodstream, EPA applies an uncertainty factor of 1 for pharmacokinetics and an uncertainty factor of 3 for differences between animals and humans.

Recent studies provide additional data regarding metabolism of nPB in rats and mice (RTI, 2005), but data on human metabolism are still lacking. One analysis of these metabolic data suggested that mice are less sensitive to the effects of nPB than rats and hypothesized that humans would also be less sensitive than rats (Stelljes, 2005). This analysis makes numerous assumptions about toxic nPB metabolites and metabolic activation pathways that have not been confirmed by experimental data. A review of this analysis is available in the public docket (ICF, 2006c). Despite the difference in metabolic pathways for nPB in mice and rats (RTI, 2005), EPA finds no significant species-specific differences in toxicity exist between rats and mice at inhaled concentrations <500 ppm for 13 weeks (NTP, 2003; ICF, 2006c). However, these metabolic and subchronic inhalation studies conducted under the National Toxicology Program did not specifically examine for reproductive toxicity or nPB metabolism in target organs that control reproductive function. In summary, there is little available data about the metabolic activation or reactive metabolites responsible for reproductive toxicity in rodents. Similarly, for nPB, there is little information available about differences and similarities between rodents and humans. Given this circumstance, EPA assumes, in the absence of evidence to the contrary, that nPB toxicity is directly related to the inhaled parent

[8] Pharmacodynamics refers to the biochemical and physiological effects of chemicals in the body and the mechanism of their actions.

[9] Pharmacokinetics refers to the activity or fate of chemicals in the body, including the processes of absorption, distribution, localization in tissues, biotransformation, and excretion.

[10] The blood/air partition coefficient is the ratio of a chemical's concentration between blood and air when at equilibrium.

compound in the arterial blood and that the critical metabolic pathways scale across species in a manner similar to the ventilation rate (U.S. EPA, 1994b). Therefore, the Agency applied an uncertainty factor of 1 to account for interspecies differences in pharmacokinetics.

Given the available data on the blood/air partition coefficient and EPA RfC guidance in the absence of other information, EPA is applying the same rationale used for other compounds reviewed under EPA's SNAP program with a comparable amount of data where an uncertainty factor of 1 for pharmacokinetics was applied. To account for uncertainty in pharmacodynamics of nPB, EPA is applying the default uncertainty factor of 3. This follows the procedures in EPA's RfC guidelines for situations where there are no data to compare pharmacodynamics in rats versus humans (U.S. EPA, 1994b). Recently published data on humans and rodents do not decrease the uncertainty regarding the pharmacodynamics of nPB; therefore, modification of the uncertainty factor of 3 for differences between species was not justified.

Comment: One commenter stated that EPA did not cite any data that describes the size, condition, or existence of a subpopulation of men especially sensitive to the effects of nPB. In addition, this commenter asserted that sensitive populations are not traditionally considered when deriving an OEL, and that EPA has never mentioned a concern with sensitive subpopulations in previous SNAP reviews. Another commenter said that there is no evidence to support the assertion that nPB exposure below a 100 ppm average will further reduce sperm count or that the removal of nPB exposure will improve sperm count.

Response: EPA disagrees with the comments. There are preexisting reproductive conditions as well as significant variability in fertility among otherwise healthy adults in the workplace. Both male and female reproduction have been shown to be adversely affected by aging, with effects on the ovarian cycle and on sperm motility as major factors changing with increasing age for women and men, respectively (Dunson *et al.*, 2002). Adding damage from other factors, such as smoking or occupational exposure to chemicals such as nPB, therefore, can potentially harm an individual's ability to reproduce further (Dunson, *et al.* 2002). EPA did not issue a proposal based on sperm count, so that comment is not relevant to this rule. In addition, we note that EPA has used uncertainty factors in the past to protect sensitive subpopulations on other chemicals reviewed under the SNAP program (*e.g.*, trifluoroiodomethane at 60 FR 31092, 61 FR 25585 and IoGas™ Sterilant Blends at 69 FR 58903). For deriving AELs from health endpoints such as liver effects and neurotoxicity, the SNAP program typically has assigned an uncertainty factor of 1 for sensitive subpopulations because we assume that individuals who are especially susceptible to these effects will have greater difficulty working than most people. However, there is no connection between the ability to reproduce and the ability to work in the industrial sectors discussed in this rule. Thus, we find it appropriate to require an uncertainty factor greater than 1 for reproductive effects for variability within the working population.

Comment: Some commenters said that an uncertainty factor of 1 is appropriate for variability within the working population because sensitive subpopulations will not be present in the working population (Stelljes, 2003, Morford, 2003e). Other commenters stated that there will be very little difference in variability between the worker population and the general population and that it is unclear why EPA selected an uncertainty factor of 3 instead of 10 (Werner, 2003). Commenters suggested uncertainty factors for variability in the working population of 1, 2, and 5 (Stelljes, 2003, Weiss Cohen, 2003, Werner, 2003).

Response: EPA disagrees with the commenters. EPA's RfC guidelines recommend an uncertainty factor of 10 to account for intraspecies variability within the general population. However, in developing an AEL, EPA's focus is on worker exposure, which excludes some particularly vulnerable populations, such as children, most adolescents, and the elderly. Thus, we believe that a full uncertainty factor of 10, as for the general population, may be higher than necessary to protect workers. Certain individuals in the general population but not in the working population that might be particularly vulnerable would include children and adolescents under age 16 and individuals with immune deficiency disorders. However, because of variability in reproductive function due to factors present among workers, such as aging, smoking, and sexually transmitted disease (Dunson *et al.*, 2002), and because there is no screening of workers that would make workers more likely to have healthy reproductive systems than non-workers of the same age, we believe than an uncertainty factor of 1 is not sufficiently protective. Under EPA guidelines, 3 is a default value for an uncertainty factor where there is indication that a value less than an order of magnitude (10) but greater than one is appropriate, and where the available data are not sufficiently quantified to select a specific value.

4. Other Analyses of nPB's Toxicity

Comment: One commenter stated that documents by Drs. Doull, Rozman, Stelljes, Murray, Rodricks, and the KS Crump Group were not acknowledged (Morford, 2003d,e, and f). Another commenter requested that EPA take into account the scientific presentations presented by Drs. Doull, Rozman and Stelljes and mentions a review by Dr. Rodricks (Weiss Cohen, 2003).

Response: EPA specifically mentioned and responded to the occupational exposure limit recommendations from Drs. Rozman, Doull, and Stelljes in the preamble to the June 2003 NPRM at 68 FR 33298–33299. In addition, EPA included more detailed written responses to these derivations and the evaluation by Dr. Rodricks in the online docket prior to proposal (EPA–HQ–OAR–2002–0064–0017, –0018, and –0019). Here are abbreviated responses to the various documents cited by the commenter:

- Drs. Doull and Rozman's letter dated August 24, 2001, stating that a two-generational reproductive study is not appropriate (Docket A–2001–07, item II–D–26)—Drs. Doull and Rozman do not provide a rationale for their statement. Their statement is in conflict with their AEL derivation, in which they consider use of the F1 generation of the WIL Laboratories two-generation study. As discussed above in section V.B.1, EPA believes that data from a two-generation reproductive study are appropriate in developing a guideline for the workplace in order to assure that workers and their children are protected from any adverse health effects of workplace exposure, including exposure *in utero.* We acknowledge that this value may be more conservative than considering data only from the parental generation.
- Drs. Doull and Rozman's critique of ICF's AEL derivation (II-D–41b)—Drs. Doull and Rozman's primary stated reason for rejecting ICF Consulting's evaluation is that it does not reflect their own AEL derivation. They reiterate that they find neurotoxicity to be the appropriate basis for an AEL without addressing the reasons that ICF's derivation provides for finding reproductive toxicity to be of greater concern than neurotoxicity. We disagree with Doull and Rozman's conclusion that neurotoxicity is the more

appropriate endpoint for several reasons: (1) The human data are insufficient to draw conclusions because of a small number of subjects, limited exposure information, and lack of statistical significance; (2) the animal data on neurotoxicity are inconsistent and equivocal concerning the level at which nervous system effects occur, and they indicate that neurotoxic effects may be reversible; and (3) neurotoxicity is a less sensitive endpoint than reproductive effects. However, if we had used neurotoxicity as the endpoint for an AEL, we would have reached the same acceptability determination for solvent cleaning.

The basis of EPA's June 2003 NPRM is different from either one of these documents because it uses a different endpoint from Doull and Rozman's derivation (2001) and an uncertainty factor of 3 instead of 2 to 3 for variability within the working population (Doull and Rozman, 2001; ICF, 2002a). According to EPA guidance on establishing uncertainty factors, if a uncertainty factor is between 1 and 10 and the data are not sufficient to quantify the uncertainty between those values, the default uncertainty factor to be used is 3 (U.S. EPA, 1994b).

• Drs. Rozman and Doull's derivation of an AEL (II–D–63)—EPA discussed our evaluation of this document at length in the preamble of the June 2003 NPRM at 68 FR 33298. In particular, we disagree with Rozman and Doull's selection of the most sensitive endpoint. Rozman and Doull concluded that reproductive toxicity should not be considered the most sensitive endpoint, stating that a National Institute for Occupational Safety and Health (NIOSH) evaluation found that no human beings at a facility using nPB-based adhesives experienced reproductive health effects from the nPB. However, the NIOSH study in fact concluded that the survey questions would not be sufficient to determine if there were reproductive health effects, which is significantly different from saying that there was no health effect. The expert panel for the CERHR looked at the NIOSH report and a wide range of human and animal studies on nPB; in contrast to Rozman and Doull, the expert panel concluded that there was insufficient information on reproductive effects of nPB on humans and that the results of tests on animals were considered appropriate for evaluating potential reproductive health effects on humans.

Further, EPA disagrees with the specific AEL value of 60 to 90 ppm that Rozman and Doull derived. They used data on headaches from a draft NIOSH survey, selecting an endpoint of 190 ppm. However, the data in the final survey were not sufficient to detect any dose-response with any statistical significance (Custom Products HHE, II–A–49). Further, more recent studies on human exposure to nPB have found neurotoxic effects occurring at levels at least as low as 86 ppm, and possibly lower than 60 ppm (Ichihara 2004a, Beck and Caravati 2003). These data would indicate that an AEL of 60 to 90 ppm is not sufficiently protective against neurotoxic effects. Drs. Rozman and Doull themselves now suggest that an AEL of 25 ppm may be more appropriate for protecting against neurotoxic effects (Rozman and Doull, 2005).

• Dr. Rodricks' AEL derivation and comments on ICF's derivation (II–D–65)—EPA reviewed Rodricks (2002) in developing its June 2003 NPRM, although the study was not explicitly mentioned in that preamble. Rodricks (2002) suggests an AEL of 60 to 88 ppm for nPB, based on male reproductive effects. Dr. Rodricks says that the most sensitive endpoint that is relevant for occupational exposure is data from the parent generation of the two-generation reproductive study. Dr. Rodricks suggests that an uncertainty factor of only 1 to 2 is necessary for animal to human extrapolation because one should consider animals and workers of average sensitivity; although such an argument presumably could be made for any chemical used in the workplace, EPA has not seen other AEL derivations that use this approach. Dr. Rodricks appears to agree with ICF that an uncertainty factor for variability in reproductive function in the human population is reasonable, although he suggests a factor of 2 instead of the range of 2 to 3 in ICF's derivation. Dr. Rodricks and colleagues previously recommended an AEL for nPB of less than 10 ppm, and at that time suggested an uncertainty factor of 10 for variability in reproductive function in the human population (A–91–42, X–B–53). We discussed above the use of data from both the F0 and F1 generations and the use of an uncertainty factor of 3 for variability within the working population.

• Dr. Stelljes's critique of ICF's AEL derivation (II–D–41a)—Dr. Stelljes states that ICF should have used data from the parent generation rather than from the offspring generation because ''data from F1 animals is not directly applicable to a workplace exposure setting because both parents would not be exposed to nPB on a daily basis over the reproductive cycle, and also have their offspring exposed daily from weaning.'' EPA disagrees in part with Dr. Stelljes's reasoning. Data from F0 animals may not be sufficiently protective because effects on the F0 animals will not reflect effects of *in utero* exposure. However, we agree that exposure during weaning is not reflective of workplace exposure, and thus, data from F1 animals may be conservative. EPA proposed 25 ppm instead of 18 ppm in part to take this conservatism into account.

• Dr. Stelljes's (SLR International's) AEL derivation (II–D–13)—EPA discussed this AEL derivation at length in the preamble to the proposed rule at 68 FR 33298. We agreed with Dr. Stelljes's BMD modeling and his selection of reduced sperm motility in the F1 offspring generation of the WIL Laboratories study as the most sensitive endpoint. However, we disagree with Dr. Stelljes's selection of uncertainty factors. There is no information showing that human sex cells are less sensitive to nPB than rat sex cells, and there is considerable evidence that human males have less reproductive capacity than male rats (U.S. EPA, 1996). Therefore, it is appropriate to add an uncertainty factor of at least 3 to account for differences between rats and humans. Further, Stelljes dismisses the use of an uncertainty factor for differences within the human population. Although we agree that children and the elderly would not be present in the workplace as sensitive subpopulations, there certainly is variability in the reproductive abilities of different working-age people that would have no impact on the individual's ability to be hired or to work; therefore, EPA expects there is some variability in the susceptibility of working individuals to the effects of reproductive toxicants. EPA believes that male reproductive capacity is very susceptible to chemical insult (U.S. EPA, 1996).

• Dr. Murray's opinion on parent and offspring generations (II–D–58)—Dr. Murray says that because the offspring generation will not yet have developed sperm while *in utero,* it is more appropriate to use data from the parent generation of the two-generation study. However, Dr. Murray does not address the possibility that nPB exposure during pregnancy could influence the production of hormones that eventually would result in sperm production. Further, Dr. Murray's response does not address potential effects on ova, which would be present while a fetus is still in its mother's womb.

• Report on uncertainty factors used by ACGIH from K.S. Crump Group (IV–D–26/OAR–2002–0064–0047 and –48)—This report concluded that EPA's

approach to selecting uncertainty factors for use in risk assessment was more transparent, with justification for each value selected, and was more consistent than the values apparently used by the ACGIH in deriving TLVs. EPA agrees with these conclusions.

Comment: A commenter states that ''an uncertainty factor of 10 is NOT 'generally' used to derive occupational exposure limits and that in fact, uncertainty factors of 3 or less or more commonly used,'' citing the K. S. Crump Group's report.

Response: In the case of the TLV that ACGIH established for nPB, ACGIH appears to set an AEL that is a factor of 10 lower than the endpoint cited as lowest (100 ppm for effects on pup weight) (ACGIH, 2005). Thus, ACGIH has used an approach for nPB consistent with the total uncertainty factor of 10 assigned by EPA.

5. Overall Stringency of the Acceptable Exposure Limit

Comment: Some commenters supported the proposed AEL of 25 ppm, stating that it was derived using appropriate conservative and cautious scientific processes. Other commenters said that the proposed AEL of 25 ppm was too high, citing uncertainties in the data, the inappropriateness of adjusting the AEL upward from 18 ppm, reports of health effects on humans, and a need for higher uncertainty factors. Other commenters said that the proposed AEL of 25 ppm was too low, citing higher AELs derived by Drs. Stelljes, Doull, Rozman, and Rodricks, NIOSH studies, and a need for lower uncertainty factors. Commenters suggested alternate AEL values ranging from 1 ppm to 156 ppm.

Response: In this final rule, EPA is not recommending an acceptable exposure limit. We have based our determination of acceptability by comparing measured exposure levels from workers using nPB in solvent cleaning to exposure levels discussed by EPA in the proposal (see section IV.E). At the levels discussed in the NRPM or higher, we find nPB acceptable for solvent cleaning. After considering the available scientific studies on toxicity, exposure data, and alternative derivations of the acceptable exposure limit, we find that the exposure levels discussed in 2003 provide sufficient protection for human health and are consistent with EPA's derivations of AELs for other chemicals reviewed under the SNAP program and EPA guidance for risk assessment.

6. Skin Absorption

In the June 2003 NPRM, EPA discussed listing nPB with a skin notation, and proposed that this was not necessary (68 FR 33295).

Comment: Several commenters on the June 2003 proposal stated that a skin notation for nPB is appropriate, while another commenter agreed with EPA's proposal that no skin notation was necessary (Smith, 2003; HESIS, 2003; Werner, 2003, Weiss Cohen, 2003). One commenter said that EPA should require manufacturers, distributors, and marketers of nPB-containing products to communicate such information on the Material Safety Data Sheets (MSDS) and the product label.

Response: We agree with the commenter that said a skin notation is not necessary. However, today's decision includes a recommendation for users to wear protective clothing and flexible laminate gloves when using nPB to address the concerns about dermal exposure.

Rat studies indicate that dermal exposure to nPB results in neither appreciable absorption through the skin (RTI, 2005) nor systemic toxicity (Elf Atochem, 1995). Unlike methyl chloride and dichlorvos, which are absorbed through the skin and could contribute to systemic toxicity (ACGIH, 1991), EPA is not including a skin notation for nPB in the information provided to users associated with this rulemaking because of the relatively low level of absorption. The ACGIH provides no skin notation in its TLV documentation for several solvents, including nPB (ACGIH, 2005), methylene chloride, and perchloroethylene, and there is no evidence that absorption through the skin is greater for nPB than for the other halogenated compounds. The TLV documentation for nPB states, ''There is no basis for a skin notation because the dermal LD50 of 1-BP was >2 g/kg.'' Further, including a statement giving advice about how to reduce skin exposure in the ''Further Information'' column of listings is likely to be more informative to workers than a skin notation.

Given the possibility that some nPB can be absorbed through the skin in humans, and that the solvent can irritate the skin, EPA encourages users to wear protective clothing and flexible laminate gloves when using nPB and encourages manufacturers, distributors, and marketers of nPB-containing products to include such precautions in their MSDSs. EPA believes that our regulatory authority for the SNAP program is over the substitution (use) of ozone-depleting substances, and thus, we do not believe we have sufficient authority to regulate the manufacturers, distributors and marketers of nPB.

7. Iso-Propyl Bromide Limit

In the June 2003 proposed rule, we proposed as a use condition that nPB formulations contain no more than 0.05% isopropyl bromide (iPB) [11] by weight because of potential health effects associated with this isomer (68 FR 33301–33302).

Comment: Two commenters said that 0.05% iPB is an appropriate and achievable limit. (Smith, 2003; Weiss Cohen, 2003). One of these commenters stated that industry test studies showed that lower limits were neither toxicologically justified nor economical. Another commenter opposed the implementation of the proposed use restriction, stating that it places an undue legal burden on end users, rather than the manufacturers of raw materials, and would not benefit worker safety. This commenter also stated that this is the only instance that SNAP has regulated residual contaminants. This commenter also suggested that EPA defer to an AEL of 1 ppm for iPB established by the government of Korea and the Japan Society for Occupational Health. Moreover, this commenter said that the difference between the acceptable iPB exposure determined by EPA and that determined by ASTM–D6368–00 is very small and, thus, EPA's proposed regulation does not add any value to existing standards. Finally, this commenter noted that epidemiological data found no adverse effect on human workers exposed to 110 ppm of iPB (Ichihara, specific study not identified by the commenter). (Morford, 2003g and h).

Response: We agree that industry has achieved this contamination limit for several years without regulation. We also agree that the concentration of iPB likely to be breathed in by workers would be below 1 ppm even if workers were exposed to concentrations of nPB at 100 ppm or more, provided that the iPB content meets the ASTM–D6368–00 standard for nPB used in vapor degreasing. Further, even if iPB were present in nPB formulations in concentrations as high as 1%, if industry meets the AEL for nPB proposed in 2003 of 25 ppm, or lower, exposures still would be at most 0.25 ppm. This is below the level of 1 ppm established by the Korean government and by the Japan Society for Occupational Health (Morford, 2003h). Therefore, we are not adopting a use condition for iPB for the solvent cleaning end uses.

[11] iPB is also referred to as 2-bromopropane, 2-propyl bromide, or 2-BP. Its CAS registry number is 75–26–3.

8. Short-Term Exposure Limit (STEL)

In the June 2003 NPRM, EPA recommended a short-term exposure limit of 75 ppm (three times the AEL).

Comment: One commenter noted that there was no indication in the various applications as to how the exposures from those operations compared to the EPA recommendation for a STEL at 75 ppm. This commenter asserted that the potential for exceeding the STEL in solvent cleaning applications appears high and should, therefore, be investigated by EPA. This commenter also stated that, depending on the results of this investigation, EPA may choose to find nPB unacceptable in metals cleaning or restrict its use to where ventilation is employed and/or personal protective equipment is worn.

Response: EPA disagrees that it is necessary to use a short-term exposure limit in determining the acceptability of nPB in solvent cleaning. Acute, short-term exposures of nPB are not of significant health concern, so long as long-term exposures are below the 8-hour TWA limit (ERG, 2004). EPA provided the STEL recommendation in the June 2003 proposal to give guidance to the user community, consistent with the following recommendation of the American Conference of Governmental Industrial Hygienists (ACGIH): ''Excursions in worker exposure levels may exceed 3 times the [threshold limit value] TLV–TWA for no more than a total of 30 minutes during a workday'' (ACGIH 1999). We note that when the ACGIH developed a TLV for nPB, they said there were no data to support a short-term exposure limit (ACGIH, 2005).

C. Ozone Depletion Potential

We proposed that, since the ODP of nPB in the continental U.S. is only 0.013 to 0.018 relative to an ODP of 0.8 for CFC-113, 0.1 for methyl chloroform, and 0.1 for HCFC-141b, nPB should not be found unacceptable because of its ODP (68 FR 33303). The Agency recognized that nPB's ODP could be much higher in tropical regions, as high as 0.071 to 0.100, but since EPA is regulating nPB used in the U.S., we made our decision based on the ODP in the continental U.S.

Comment: One commenter on the June 2003 NPRM provided information (Wuebbles, 2002) and stated that ''even if the entire amount of nPB produced in 2002 was emitted across North American, European and Asian latitudes, the resulting effects on ozone depletion would be too small to measure.'' The same commenter said that the effects on ozone would only be larger if all emissions were to occur in the equatorial region. (Morford, 2003f).

Response: EPA agrees that, based on the current usage of nPB and its ODP in the U.S., there is not a significant impact on the ozone layer.

Comment: Comments on the June 2003 NPRM expressed concern that other countries, particularly those in equatorial regions, might assume that nPB does not pose a danger to the stratospheric ozone layer if the U.S. EPA's SNAP program finds nPB acceptable (Linnell, 2003; Steminiski, 2003).

Response: Because the ODP for nPB is higher when used in the tropics (see footnote 3 above in section IV.2), we recognize the concerns raised by these commenters. However, EPA is regulating use in the U.S. and cannot dictate actions taken by other countries. For example, other countries could choose to continue to use nPB even if EPA were to find it unacceptable in the U.S. We believe the more appropriate forum to address this concern is through the Parties to the Montreal Protocol.

At the most recent Meeting of the Parties to the Montreal Protocol, the Parties made the following decision with regard to n-propyl bromide, in order to ''allow Parties to consider further steps regarding n-propyl bromide, in the light of available alternatives'' (Decision XVIII/11):

1. To request the Scientific Assessment Panel to update existing information on the ozone depletion potential of n-propyl bromide, including ozone depleting potential depending on the location of the emissions and the season in the hemisphere at that location;

2. To request the Technology and Economic Assessment Panel to continue its assessment of global emissions of n-propyl bromide, * * * paying particular attention to:

(a) Obtaining more complete data on production and uses of n-propyl bromide as well as emissions of n-propyl bromide from those sources;

(b) Providing further information on the technological and economical availability of alternatives for the different use categories of n-propyl bromide and information on the toxicity of and regulations on the substitutes for n-propyl bromide;

(c) Presenting information on the ozone depletion potential of the substances for which n-propyl bromide is used as a replacement;

3. To request that the Technology and Economic Assessment Panel prepare a report on the assessment referred to in paragraph 1 in time for the twenty-seventh meeting of the Open-ended Working Group for the consideration of the Nineteenth Meeting of the Parties. (MOP 18, 2006)

D. Other Environmental Impacts

With respect to environmental effects other than ozone depletion potential, we stated in the June 2003 NPRM that users should observe existing Federal, state, and local regulations such as those under the Resource Conservation and Recovery Act or those for compliance with the National Ambient Air Quality Standards (68 FR 33304).

Comment: Commenters stated that, until the safety of nPB has been demonstrated conclusively, more stringent controls are necessary to protect the public and the environment. In particular, these commenters said that the potential for cross-media impacts was not given adequate consideration in the proposed rule. They also stated that EPA did not address the potential for nPB to bioaccumulate in the environment or its impact on sensitive species. One commenter said that he thought it was appropriate to ensure that nPB be kept out of wastewater, and an independent contractor also mentioned concerns about water pollution. Another commenter said that nPB hydrolyzes more quickly than the chlorinated solvents, and so would have less impact on water quality. Currently, the representative's company recommends that spent solvents be incinerated, and offers free pickup and disposal of spent solvent to its customers.

Response: EPA agrees that it should not be standard practice to dispose of spent nPB in water, and that nPB should be kept out of wastewater to the extent possible. This may be achieved by recycling or through incineration. These also are good practices with other spent halogenated solvents, whether or not they are specifically listed as hazardous wastes.

EPA's PBT (persistence/bioaccumulation/toxicity) profiler tool suggested that, based on its structure, nPB would not be considered persistent in water or soil and that nPB would have a low tendency to bioaccumulate (8.3, where 1000 is considered bioaccumulative and greater than 5000 is considered very bioaccumulative). Further, the calculated bioconcentration factor for nPB is only in the range of 18 to 23 (HSDB, 2004; ICF, 2004a). Under EPA's criteria for listing chemicals on the Toxics Release Inventory, this would not be a level of concern (ICF 2004a, EPA 1992). Therefore, we conclude further testing for bioaccumulation of this chemical is not needed before rendering a decision for

use of nPB in the solvent cleaning sector.

Currently, the estimated amount of nPB used in the U.S. in SNAP sectors is on the order of 10 to 12 million pounds per year, which corresponds to roughly 1% of the organic solvent cleaning market, a relatively small amount. It is unlikely that very large amounts of nPB will enter and remain in the nation's water supply, because:

- nPB tends to evaporate quickly, with a calculated half-life of 3.4 hours in a river or 4.4 days in a lake due to volatilization.
- nPB hydrolyzes readily, with a measured hydrolysis half-life of 26 days at 25° C and pH 7.
- If released to the atmosphere, nPB will exist solely in the vapor phase based on its vapor pressure of 110.8 mm Hg. Thus, it is unlikely to be redeposited in rainwater in significant amounts. (PBT Profiler, 2007; ICF, 2004a)

Further, because nPB is short-lived compared to ODS and many ODS substitutes, it is unlikely that nPB will create a substantially greater impact than other acceptable cleaning solvents and than the ODS it replaces. EPA is required by the Clean Air Act to consider whether a replacement for an ODS is more harmful, overall, to human health and the environment than other available or potentially available substitutes. The available information shows that nPB will not be more hazardous than other available, acceptable solvents if it pollutes water or soil.

E. Flammability

In the June 2003 NPRM, we proposed that nPB should not be restricted or found unacceptable because of flammability (68 FR 33303). EPA specifically requested data concerning the flashpoint of pure nPB, including the test method used to provide the data.

Comment: Several manufacturers of nPB and nPB-based solvents and an independent contractor stated that nPB has no flash point under a number of accepted consensus standards for flash point. In support of these statements, the manufacturers of nPB and nPB-based solvents provided flash point test data from a number of different test methods (ASTM D 92 open cup, ASTM D56 Tag closed cup, and ASTM D93 Pensky-Martens closed cup).

Response: EPA agrees. The test results provided by the commenters indicates that nPB has no flash point using a number of standard test methods, including ASTM D 92 open cup, ASTM D56 Tag closed cup, and ASTM D93 Pensky-Martens closed cup. Based on these data, we find that nPB is not flammable under standard test conditions. EPA concludes that nPB should not be considered unacceptable on the basis of flammability risks.

F. Legal Authority to Set Exposure Limits

Comment: Two commenters stated that EPA has no jurisdiction to develop any AEL designed to be applicable to a workplace environment, and that this right belongs to OSHA.

Response: As an initial matter, EPA notes that it has not established an AEL applicable to the workplace in this rule. Rather, EPA reviewed the available information to determine what a safe workplace exposure might be in order to determine whether use of nPB in the solvent cleaning sector poses substantially more risk than use of other available substitutes. The analysis performed by EPA imposes no binding obligation on anyone, particularly in this case where EPA determined that nPB is acceptable for use in the solvent cleaning sector.

Although the Occupational Safety and Health Act (OSH Act) gives the Occupational Safety and Health Administration (OSHA) authority to issue a rule setting or revising an occupational safety or health standard (29 U.S.C. 655(b)), it does not prohibit other Federal agencies from reviewing the safe level of exposure under other statutes that require consideration of the human health and environmental effects of a substance. Conversely, although section 4(b)(1) of the OSH Act prohibits OSHA from regulating a working condition addressed by another federal agency's regulations affecting occupational safety or health, this provision is overridden with respect to EPA's exercise of authority under the Clean Air Act by 42 U.S.C. 7610. That provision states: ''(a) Except as provided in subsection (b) of this section, this chapter shall not be construed as superseding or limiting the authorities and responsibilities, under any other provision of law, of the Administrator or any other Federal officer, department, or agency.''

Section 612 of the Clean Air Act expressly recognizes that some substitutes for ODS may pose more risk to human health and the environment than others and expressly requires EPA to prohibit use of substitutes that pose more risk than other substitutes that are currently or potentially available. Thus, in evaluating whether a substitute should be found acceptable, we must compare the risks to human health and the environment of that substitute to the risks associated with other substitutes that are currently or potentially available.

Our long-standing interpretation is that worker safety is a factor we consider in determining whether a substitute poses significantly greater risk than other available substitutes. In the original SNAP rule, we promulgated the criteria we would review for purposes of determining whether a substitute posed more risk than other available substitutes. Specifically, 40 CFR 82.178(a) specifies the information we require as part of a SNAP application and 40 CFR 82.180(a)(7) identifies the criteria for review. Notably, we require submitters to provide information regarding the exposure data (40 CFR 82.178(a)(10)) and we identify ''occupational risks'' as one of the criteria for review (40 CFR 82.180(a)(7)(iv)). In the preamble of the original SNAP rule, we said that we would use any available OSHA PELs, EPA inhalation reference concentrations, or EPA cancer slope factor data for a substitute together with exposure data to explore possible concerns with toxicity (March 18, 1994; 59 FR 13066). We have reviewed substitutes based on existing OSHA PELs, where available, and, where not available, based on our own assessment of what level is safe for workers. (See e.g., March 18, 1994, 59 FR 13044; Sept. 5, 1996, 61 FR 47012; June 8, 1999, 64 FR 30410; June 19, 2000, 65 FR 37900; December 18, 2000, 65 FR 78977; March 22, 2002, 67 FR 13272; August 21, 2003, 68 FR 50533). In making our own assessment, we review any existing recommended exposure guidelines and available scientific studies and use EPA's risk assessment guidelines (e.g., U.S. EPA, 1994b).

In the case of EPA's evaluation of nPB, there is no final OSHA PEL for EPA to use in evaluating workplace exposure risks. There is a wide variability in the workplace exposure guidelines recommended by manufacturers of nPB-based products, ranging from 5 ppm to 100 ppm, thus providing no definitive value for evaluating the human health risks of workplace exposure. The ACGIH has recently established a TLV for nPB of 10 ppm; however, as discussed above in section IV.E, EPA has concerns about the scientific basis for this TLV. As provided in the original SNAP rule, in the absence of a definitive workplace exposure limit set by OSHA, we evaluated the available information to establish our own health-based criteria for evaluating nPB's human health risks to workers.

Comment: A commenter said that EPA's authority for the SNAP program is under section 615 of the Clean Air Act and that the SNAP program only has authority to take action based on effects on the stratosphere. Specifically, the commenter claims section 615 of the CAA limits EPA's authority under title VI to regulating for purposes of protecting the stratospheric ozone layer. Citing section 618, the commenter also contends that section 618 identified SNAP requirements as ''requirements for the control and abatement of air pollution'' and cites the CAA and EPA policy documents as identifying ambient air as air external to buildings. The commenter also notes that title VI was intended to implement the Montreal Protocol and that it replaced former Part B. The commenter cites legislative history from the enactment of Part B that indicated EPA's authority under Part B was not intended to pre-empt authority of other agencies to take action with respect to hazards in their areas of jurisdiction and that EPA's authority under Part B was only to fill regulatory gaps and not to supersede existing authority of other agencies. With respect to the legislative history of the 1990 Amendments, the commenter argues that there is no suggestion that ''EPA has authority to set workplace worker-exposure standards.'' The commenter also cites legislative history from the Toxic Substances Control Act in which Congress indicated EPA's authority under that statute does not extend to setting workplace standards.

Response: While many provisions in title VI address the regulation of substances that deplete the stratospheric ozone layer, section 612 which governs the SNAP program is broader. The purpose of Section 612 is to review substitutes for ODS and Section 612 of the Clean Air Act clearly requires EPA to consider both the environmental effects as well as *human health,* which includes both the health of the general population and workers. EPA believes there is no doubt that the statutory language requires EPA to consider effects beyond those on the stratospheric ozone layer. In addition, the legislative history makes clear that this language is to be interpreted broadly. Specifically, the report of House Debate on the Clean Air Act Amendments provides ''the Administrator shall base risk estimates on the total environmental risk (toxicity, flammability, atmospheric, etc.) that is perceived to exist, not just the risk as it relates to ozone depletion.'' House Debate on the Clean Air Act Amendments of 1990 Conference Report, S–Prt 103–38 at 1337. The legislative history cited by the commenter is not pertinent. The legislative history for Part B of Title I of the Act is not relevant because that section was repealed in 1990. Public Law 101–549, section 601. Nor is the legislative history for other statutes, such as TSCA, relevant for determining what authority Congress granted to EPA under the CAA.

The commenter incorrectly states that sections 615 and 618 of the CAA place limits on EPA's authority under section 612 of the Act. These provisions expand, rather than restrict, the Administrator's authority. Section 615 is a separate provision of the statute and provides general authority for the Administrator to regulate for purposes of addressing adverse effects to the stratosphere. This provision does not explicitly or implicitly purport to limit the Administrator's authority under other provisions of the Act. Rather, it is a general provision authorizing the Administrator to regulate for protecting against adverse effects to the stratospheric ozone layer.

With respect to section 618, we first note that the commenter appears to equate the stratospheric ozone layer with ''ambient air.'' In fact, they are two different things. Ambient air is defined as ''that portion of the atmosphere, external to buildings, to which the general public has access.'' 40 CFR 50.1(e). The stratospheric level generally extends from 10 to 50 kilometers above the earth and is not considered air to which the public has access. [See *http://www.epa.gov/ozone/defns.html*]. The definition of ''air pollutant'' under the CAA is defined in terms of substances emitted to the ''ambient air.'' The purpose of section 618 is to make clear that for purposes of sections 116 (retention of state authority) and 118 (control of pollution from federal facilities), the provisions in Title VI governing protection of the stratospheric ozone layer shall be treated the same as if they were for the purpose of controlling and abating ''air pollution'' (i.e., pollution to the ambient air). Again, this is not for the purpose of restricting the Administrator's authority under any provision of the Act. Rather, it is for the purpose of extending the protections of Title VI to programs that otherwise only address air pollution (i.e., ambient air, which does not include the stratospheric ozone layer).

Comment: A commenter stated that EPA's claim to authority conflicts with the Department of Labor's administrative ''whistleblower'' case law. These cases hold that a whistleblower action may proceed under the CAA only when the complaint concerned substances emitted to the ambient air. Claims regarding air quality within the workplace are brought under the whistleblower provisions of the OSH Act.

Response: The commenter overstates the import of the decisions issued by the Administrative Review Board. In each of the cited decisions, the Board examined the specific circumstances before it to determine which statutory whistleblower provision provided the basis for the claimed action. While making general pronouncements that the CAA regulates ambient air and OSHA regulates air within the workplace, none of these opinions specifically addressed the scope of EPA's authority under section 612, the SNAP provisions of the Act.

Comment: A commenter stated that even if ventilation or other measures could reduce exposures to below 25 ppm, there is nothing to ensure that companies will take such measures. This commenter also stated that he is aware of nPB formulators that have already announced they will not adhere to this voluntary standard. Three commenters, all representing local environmental regulators, stated that a recommendation that worker exposure be limited to 25 ppm will not carry the enforcement powers of an OSHA standard, and that this lack of control will encourage the use of nPB in applications beyond those envisioned by EPA. Another commenter asserted that the proposed exposure limits (both the AEL and the STEL) should be established as use conditions, citing Section 612 as the basis for EPA's authority to do so. This commenter stated that a precedent has already been set for EPA to accept an alternative chemical subject to use conditions—including that observance of workplace concentration limits—in the adhesives, aerosols, and solvent cleaning sectors (e.g., HCFC–225 ca/cb, HFC–4310mee, monochlorotoluenes, benzotrifluorides; 40 CFR part 82, subpart G, appendices A, B, and D).

Response: EPA agrees that a recommended AEL from EPA does not provide the same level of protection as an enforceable standard from OSHA. We also agree that EPA has the authority under section 612 to require use conditions in those circumstances where use of a potentially promising substitute would otherwise be unacceptable unless those use conditions are met and there are significant concerns about the ability of industry to meet a safe level for use. In the preamble to the original SNAP rule,

we recognized that there may be cases where OSHA has not regulated worker exposure to a substitute. We went on to say that ''EPA anticipates applying use conditions only in the rare instances where clear regulatory gaps exist, and where an unreasonable risk would exist in the absence of any conditions.'' For the solvent cleaning end use, we do not believe that there is an unreasonable risk in the absence of a use condition. Available exposure data show that roughly 88% of samples from nPB users in solvent cleaning met an exposure level of 25 ppm, 81% met an exposure level of 18 ppm, and 70% met an exposure level of 10 ppm (U.S. EPA, 2003). One nPB supplier provided evidence that on the few occasions when nPB concentrations from vapor degreasers were higher than the company's recommended AEL of 25 ppm, users were able to reduce exposure easily and inexpensively by changing work practices, such as reducing drafts near the cleaning equipment (Kassem, 2003). Therefore, we expect that users of nPB in the solvent cleaning sector following typical industry practices and using typical equipment for vapor degreasing will continue to use nPB at levels considered safe for workers. As noted above, this is the approach we indicated we would follow at the time of the original SNAP rule and we have taken this same approach for many other solvents where users are readily able to meet a workplace exposure limit that will protect human health and there is no enforceable OSHA PEL (e.g., HFC–365mfc and heptafluorocyclopentane at 65 FR 78977, ketones, alcohols, esters, and hydrocarbons at 59 FR 13044).

Comment: One commenter claims that section 6 of the Occupational Safety and Health Act requires OSHA to make certain legal findings before promulgating a standard and that therefore EPA has no authority to develop any AEL applicable to a workplace environment. Furthermore, since OSHA is the only agency that can make standards applicable in the workplace, any level developed by EPA is misleading. The same commenter said that EPA offers no reasoning as to why a different methodology for setting an AEL (from that of OSHA) is necessary or advisable. Therefore, this commenter believes that the Agency's process violates equal protection unless EPA is publishing a new standard for chemical review under SNAP.

Response: In this rulemaking, EPA has not developed an AEL that is applicable in any workplace. Rather, EPA looked at a range of possible AELs for purposes of determining whether nPB will pose significantly greater risk than other substitutes that are available in the same end use. The range of levels EPA used for its analysis is not binding. Moreover, as explained above in section V.B.2, EPA has concluded that for purposes of finding nPB acceptable in the solvent cleaning end use, it is not necessary to provide a non-binding recommended workplace exposure limit because these users in the solvent cleaning sector are regularly able to comply with even the lowest level EPA considered in performing its evaluation.

For standards covering hazardous chemicals in the workplace, the OSH Act requires OSHA to set standards that, to the extent feasible, ensure that workers do not suffer material impairments of health. Standards established by OSHA under their statute have not typically prohibited the use of the chemical in any particular application, but instead establish performance goals for the use and handling of hazardous chemicals that reduce such risks to the extent feasible. The available information on health effects of nPB on workers is not sufficiently well-characterized to develop a standard based on avoiding material impairments of health in workers. Most manufacturers and organizations that set workplace exposure limits such as ACGIH and the American Industrial Hygiene Association use an approach similar to EPA's and do not base exposure limits on avoiding material impairments of health in workers. Because of the need for large amounts of well-characterized data from the workplace on exposures and associated health effects to prepare an AEL to prevent material impairment, if EPA were to develop AELs for nPB and other chemicals based on the approach required by section 6 of the OSH Act, EPA would effectively be unable to assess the human health effects of ODS alternatives in time to assist industry in transitioning away from ODS. In order to provide for a more timely assessment of human health effects, as well as one that is consistent with federal guidelines of the National Academies of Science (NAS, 1983), we have considered exposure levels following EPA guidance (U.S. EPA, 1994b). Different substances have different toxicological effects and those effects must be considered based on the best scientific information and methodologies available. It is incorrect to claim that such reviews, which focus on the effects of different substances, resulted in disparate treatment of nPB.

VI. How can I use nPB as safely as possible?

Below are actions that will help nPB users minimize exposure levels:

All End Uses

- All users of nPB should wear appropriate personal protective equipment, including chemical goggles, flexible laminate protective gloves (e.g., Viton, Silvershield) and chemical-resistant clothing. Special care should be taken to avoid contact with the skin since nPB, like many halogenated solvents, can be absorbed through the skin. Refer to OSHA's standard for the selection and use of Personal Protective Equipment, 29 CFR 1910.132.
- Limit worker exposure to solvents to minimize any potential adverse health effects. Workers should avoid staying for long periods of time in areas near where they have been using the solvent. Where possible, shorten the period during each day when a worker is exposed. Where respiratory protection is necessary to limit worker exposures, respirators must be selected and used in accordance with OSHA's Respiratory Protection standard, 29 CFR 1910.134.
- Use less solvent, or use a different solvent, either alone or in a mixture with nPB.
- Follow all recommended safety precautions specified in the manufacturer's MSDS.
- Workers should receive safety training and education that includes potential health effects of exposure to nPB, covering information included on the appropriate MSDSs, as required by OSHA's Hazard Communication Standard (29 CFR 1910.1200).
- Request a confidential consultation from your State government on all aspects of occupational safety and health. You can contact the appropriate state agency that participates in OSHA's consultation program. These contacts are on OSHA's Web site at *http://www.osha.gov/oshdir/consult.html.* For further information on OSHA's confidential consultancy program, visit OSHA's web page at *http://www.osha.gov/html/consultation.html.*
- Use the employee exposure monitoring programs and product stewardship programs where offered by manufacturers and formulators of nPB-based products.
- If the manufacturer or formulator of your nPB-based product does not have an exposure monitoring program, we recommend that you start your own exposure monitoring program, and/or request a confidential consultation from your State government. A medical monitoring program should be

established for the early detection and prevention of acute and chronic effects of exposure to nPB. The workers' physician(s) should be given information about the adverse health effects of exposure to nPB and the workers' potential for exposure.

• For non-aerosol solvent cleaning, follow guidelines in the National Emissions Standards for Hazardous Air Pollutant (NESHAP) for halogenated solvents cleaning if you are using nPB. The equipment and procedural changes described in the halogenated solvents NESHAP can reduce emissions, reduce solvent losses and lower the cost of cleaning with organic solvents. For more information on the halogenated solvents NESHAP, visit *http://www.epa.gov/ttn/atw/eparules.html* and *http://www.epa.gov/ttn/atw/degrea/halopg.html.* We note that these steps are useful for reducing exposure to any industrial solvent, and not just nPB.

VII. Statutory and Executive Order Reviews

A. Executive Order 12866: Regulatory Planning and Review

Under Executive Order (EO) 12866 (58 FR 51735, October 4, 1993), this action is a ''significant regulatory action.'' It raises novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in the Executive Order. Accordingly, EPA submitted this action to the Office of Management and Budget (OMB) for review under EO 12866 and any changes made in response to OMB recommendations have been documented in the docket for this action.

In addition, EPA prepared an analysis of the potential costs and benefits associated with this action. This analysis is contained in the document ''Analysis of Economic Impacts of nPB Rulemaking.'' A copy of the analysis is available in the docket for this action (Ref. EPA–HQ–OAR–2002–0064) and the analysis is briefly summarized here.

In our analysis, we assumed that capital costs are annualized over 15 years or less using a discount rate for determining net present value of 7.0%. The acceptability determination for solvents cleaning imposes no requirements and thus creates no additional cost to users.

EPA also considered potential costs end users could incur to meet acceptable exposure levels if they are not already achieving it. EPA found that those users using nPB-based solvents in a vapor degreaser would save money by reducing solvent losses, and that the savings would recover the costs of emissions controls (e.g., secondary cooling coils, automated lifts or hoists) within a year of installation. Based on evidence from solvent suppliers, EPA believes that some of those users would have chosen to use nPB in order to avoid meeting requirements of the national emission standard for halogenated solvents cleaning and that they would only become aware of the potential savings due to reduced solvent usage as a result of this proposal (Ultronix, 2001; Kassem, 2003; Tattersall, 2004). Based on available exposure data for each sector, we assumed that 81% of nPB users in the non-aerosol solvent cleaning sector already achieve exposure levels at the lowest level that we considered, i.e., 18 ppm (U.S. EPA, 2003). Of those nPB solvent users with exposure levels above that, we examined the cost associated with reducing emissions on average by 60%.

If all nPB users in solvent cleaning reduced exposures to 18 ppm, EPA estimates that users would save up to $2 million dollars per year, overall (U.S. EPA, 2007). The value will depend on the number of users that attempt to meet an acceptable exposure level which is already being achieved with existing equipment, the initial exposure level of cleaning solvent users, the price of nPB, and the amount of emission control equipment installed.

B. Paperwork Reduction Act

There are no new requirements for reporting or recordkeeping or information collection associated with this final rule. The final rule merely allows the use of substitutes for ozone-depleting substances, without requiring the collection, keeping, or reporting of information. OMB has previously approved the information collection requirements contained in the existing regulations in subpart G of 40 CFR part 82 under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 *et seq.* and has assigned OMB control number 2060–0226 (EPA ICR No. 1596.06). This ICR included five types of respondent reporting and record-keeping activities pursuant to SNAP regulations: submission of a SNAP petition, filing a SNAP//Toxic Substance Control Act (TSCA) Addendum, notification for test marketing activity, record-keeping for substitutes acceptable subject to use restrictions, and record-keeping for small volume uses. A copy of the OMB approved Information Collection Request (ICR) may be obtained from Susan Auby, Collection Strategies Division; U.S. Environmental Protection Agency (2822T); 1200 Pennsylvania Ave., NW., Washington, DC 20460 or by calling (202) 566–1672.

Burden means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed to review instructions; develop, acquire, install, and utilize technology and systems for the purposes of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of information; and transmit or otherwise disclose the information.

An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. The OMB control numbers for EPA's regulations in 40 CFR are listed in 40 CFR part 9.

C. Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) generally requires an agency to prepare a regulatory flexibility analysis of any rule subject to notice and comment rulemaking requirements under the Administrative Procedure Act or any other statute unless the agency certifies that the rule will not have a significant economic impact on a substantial number of small entities. Small entities include small businesses, small organizations, and small governmental jurisdictions. The RFA provides default definitions for each type of small entity. Small entities are defined as: (1) A small business as defined by the Small Business Administration's (SBA) regulations at 13 CFR 121.201; (2) a small governmental jurisdiction that is a government of a city, county, town, school district or special district with a population of less than 50,000; and (3) a small organization that is any not-for-profit enterprise which is independently owned and operated and is not dominant in its field. However, the RFA also authorizes an agency to use alternate definitions for each category of small entity, ''which are appropriate to the activities of the agency'' after proposing the alternate definition(s) in the **Federal Register** and taking comment. 5 U.S.C. 601(3)—(5). In addition, to establish an alternate small business definition, agencies must consult with SBA's Office of Advocacy.

For purposes of assessing the impacts of EPA's June 2003 proposed rule on

small entities, EPA proposed to define ''small business'' as a small business with less than 500 employees, rather than use the individual SBA size standards for the numerous NAICS subsectors and codes to simplify the economic analysis. We solicited comments on the use of this alternate definition for this analysis in the June 2003 NPRM and received no public comments. EPA also consulted with the SBA's Office of Advocacy on the use of an alternate small business definition of 500 employees. The Office of Advocacy concurred with EPA's use of this alternate definition to analysis the economic impacts on small businesses from the use of n-propyl bromide as an acceptable substitute for use in metals, precision, and electronics cleaning, and in aerosols and adhesives end-uses. Therefore, EPA used this alternate definition for this final rule. We believe that no small governments or small organizations are affected by this rule. This approach slightly reduced the number of small businesses included in our analysis and slightly increased the percentage of small businesses for whom the analysis indicated the use of nPB in metals, precision, and electronics cleaning may have an economically significant impact. The number and types of small businesses that are subject to this rule have not changed significantly since the June 2003 proposal. EPA intends to use this alternate definition of ''small business'' for regulatory flexibility analyses under the RFA for any other rule related to the use of nPB as a chemical alternative to ozone-depleting substances (ODS) for the same end uses in the June 2003 NPRM (e.g., adhesives and aerosol solvents).

After considering the economic impacts of this rule on small entities, I certify that this action will not have a significant economic impact on a substantial number of small entities. EPA estimates that approximately 1470 users of nPB industrial cleaning solvents (e.g., cleaning with vapor degreasers) would be subject to this rule. This rule lists nPB as an acceptable substitute for ODS. This rule itself does not impose any binding requirements on users of nPB, and therefore will not have a significant economic impact on a substantial number of small entities. EPA did however analyze the potential economic impacts on small businesses that use nPB for cleaning solvents for metals cleaning, electronics cleaning, or precision cleaning. The details of EPA's analysis are described in the supporting materials for this rulemaking (U.S. EPA, 2007). Based on its analysis, EPA believes businesses using nPB-based cleaning solvents for metals cleaning, electronics cleaning, or precision cleaning would experience significant cost benefits by reducing spending on solvent.

D. Unfunded Mandates Reform Act

Title II of the Unfunded Mandates Reform Act of 1995 (UMRA), Public Law 104–4, establishes requirements for Federal agencies to assess the effects of their regulatory actions on State, local, and tribal governments and the private sector. Under section 202 of the UMRA, EPA generally must prepare a written statement, including a cost-benefit analysis, for proposed and final rules with ''Federal mandates'' that may result in expenditures to State, local, and tribal governments, in the aggregate, or to the private sector, of $100 million or more in any one year. Before promulgating an EPA rule for which a written statement is needed, section 205 of the UMRA generally requires EPA to identify and consider a reasonable number of regulatory alternatives and adopt the least costly, most cost-effective or least burdensome alternative that achieves the objectives of the rule. The provisions of section 205 do not apply when they are inconsistent with applicable law. Moreover, section 205 allows EPA to adopt an alternative other than the least costly, most cost-effective or least burdensome alternative if the Administrator publishes with the final rule an explanation why that alternative was not adopted. Before EPA establishes any regulatory requirements that may significantly or uniquely affect small governments, including tribal governments, it must have developed under section 203 of the UMRA a small government agency plan. The plan must provide for notifying potentially affected small governments, enabling officials of affected small governments to have meaningful and timely input in the development of EPA regulatory proposals with significant Federal intergovernmental mandates, and informing, educating, and advising small governments on compliance with the regulatory requirements. EPA has determined that this rule does not contain a Federal mandate that may result in expenditures of $100 million or more for State, local, and tribal governments, in the aggregate, or the private sector in any one year. This final rule does not affect State, local, or tribal governments. This rule contains no enforceable requirements. The impact of users meeting the AEL range discussed in the preamble is from a savings of $2 million per year to a cost of $0 million per year. Therefore, the impact of this rule on the private sector is less than $100 million per year. Thus, this rule is not subject to the requirements of sections 202 and 205 of the UMRA. EPA has determined that this rule contains no regulatory requirements that might significantly or uniquely affect small governments. This regulation applies directly to facilities that use these substances and not to governmental entities.

E. Executive Order 13132: Federalism

Executive Order 13132, entitled ''Federalism'' (64 FR 43255, August 10, 1999), requires EPA to develop an accountable process to ensure ''meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications.'' ''Policies that have federalism implications'' is defined in the Executive Order to include regulations that have ''substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.''

This final rule does not have federalism implications. It will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132. This regulation applies directly to facilities that use these substances and not to governmental entities. Thus, Executive Order 13132 does not apply to this rule.

F. Executive Order 13175: Consultation and Coordination With Indian Tribal Governments

Executive Order 13175, entitled ''Consultation and Coordination with Indian Tribal Governments'' (65 FR 67249, November 6, 2000), requires EPA to develop an accountable process to ensure ''meaningful and timely input by tribal officials in the development of regulatory policies that have tribal implications.'' ''Policies that have tribal implications'' is defined in the Executive Order to include regulations that have ''substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and the Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.''

This final rule does not have tribal implications. It will not have substantial direct effects on tribal governments, on the relationship between the Federal government and Indian tribes, or on the

distribution of power and responsibilities between the Federal government and Indian tribes, as specified in Executive Order 13175.

This final rule would not significantly or uniquely affect the communities of Indian tribal governments, because this regulation applies directly to facilities that use these substances and not to governmental entities. Thus, Executive Order 13175 does not apply to this final rule.

G. Executive Order 13045: Protection of Children From Environmental Health and Safety Risks

Executive Order 13045: ''Protection of Children from Environmental Health Risks and Safety Risks'' (62 FR 19885, April 23, 1997) applies to any rule that: (1) Is determined to be ''economically significant'' as defined under Executive Order 12866, and (2) concerns an environmental health or safety risk that EPA has reason to believe may have a disproportionate effect on children. If the regulatory action meets both criteria, the Agency must evaluate the environmental health or safety effects of the planned rule on children, and explain why the planned regulation is preferable to other potentially effective and reasonably feasible alternatives considered by the Agency.

This final rule is not subject to the Executive Order because it is not economically significant as defined in Executive Order 12866, and because the Agency does not have reason to believe the environmental health or safety risks addressed by this action present a disproportionate risk to children. The exposure limits and acceptability listings in this final rule apply to the workplace. These are areas where we expect adults are more likely to be present than children, and thus, the agents do not put children at risk disproportionately.

H. Executive Order 13211: Actions That Significantly Affect Energy Supply, Distribution, or Use

This rule is not a ''significant energy action'' as defined in Executive Order 13211, ''Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use'' (66 FR 28355 (May 22, 2001)) because it is not likely to have a significant adverse effect on the supply, distribution, or use of energy. This action would impact manufacturing of various metal, electronic, medical, and optical products cleaned with solvents containing nPB and products made with adhesives containing nPB. Further, we have concluded that this rule is not likely to have any adverse energy effects.

I. National Technology Transfer and Advancement Act

Section 12(d) of the National Technology Transfer and Advancement Act of 1995 (''NTTAA''), Public Law 104–113, section 12(d) (15 U.S.C. 272 note) directs EPA to use voluntary consensus standards in its regulatory activities unless to do so would be inconsistent with applicable law or otherwise impractical. Voluntary consensus standards are technical standards (e.g., materials specifications, test methods, sampling procedures, and business practices) that are developed or adopted by voluntary consensus standards bodies. The NTTAA directs EPA to provide Congress, through OMB, explanations when the Agency decides not to use available and applicable voluntary consensus standards.

This action does not involve technical standards. Therefore, EPA did not consider the use of any voluntary consensus standards.

J. Congressional Review Act

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, as added by the Small Business Regulatory Enforcement Fairness Act of 1996, generally provides that before a rule may take effect, the agency promulgating the rule must submit a rule report, which includes a copy of the rule, to each House of the Congress and to the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. A major rule cannot take effect until 60 days after it is published in the **Federal Register**. This action is not a ''major rule'' as defined by 5 U.S.C. 804(2). This rule will be effective July 30, 2007.

VIII. References

The documents below are referenced in the preamble. All documents are located in the Air Docket at the address listed in section I.B.1 at the beginning of this document. Unless specified otherwise, all documents are available electronically through the Federal Docket Management System, Docket # EPA–HQ–OAR–2002–0064. Some specific items are available only in hard copy in dockets A–2001–07 or A–92–42 (legacy docket numbers for SNAP nPB rule and for SNAP program and submissions). Numbers listed after the reference indicate the docket and item numbers.

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Dated: May 15, 2007.

Stephen L. Johnson,

Administrator.

Appendix A: Summary of Decision

SOLVENT CLEANING ACCEPTABLE SUBSTITUTE

End uses	Substitute	Decision	Further information
Metals cleaning, electronics cleaning, and precision cleaning.	n-propyl bromide (nPB) as a substitute for CFC–113 and methyl chloroform.	Acceptable	EPA recommends the use of personal protective equipment, including chemical goggles, flexible laminate protective gloves and chemical-resistant clothing. EPA expects that all users of nPB would comply with any final Permissible Exposure Limit that the Occupational Safety and Health Administration issues in the future under 42 U.S.C. 7610(a). nPB, also known as 1-bromopropane, is Number 106–94–5 in the Chemical Abstracts Service (CAS) Registry.

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Toxicological assessment of industrial solvents using human cell bioassays: assessment of short-term cytotoxicity and long-term genotoxicity potential

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There is an increasing demand for simple toxicological screening methods to assess the human health risk associated with exposure to environmental toxicants. Such screening tools should allow for risk evaluation in terms of both short-term/acute toxicity and longer-term genetic damage, which may lead to mutagenicity and carcinogenicity. We employed a battery of human cell bioassays using the human hepatoma cell-line, HepG2, to assess the cytotoxic and genotoxic potential of environmental pollutants. Here, we demonstrate direct application of these human cell bioassays to the toxicological assessment of a number of industrial solvents that are in common use worldwide. HepG2 cells were exposed to various solvents at concentrations ranging from 25 to 500 ppm. The cells were then analysed using specific protocols for four different adverse effects: cell death/acute cytotoxicity using a neutral red uptake assay, altered enzyme function (often an indicator of cell stress) using the ethoxyresorufin *O*-deethylase (EROD) bioassay, DNA single strand breaks (SSB), and DNA repair induction, which evaluates mutagenic activity. Using the positive controls, linear dose–response curves were achieved for all four bioassays. The high sensitivity of the tests allowed for environmentally meaningful assessments, and precision studies showed excellent reproducibility for all four bioassays. Comparing the results of the four bioassays on each of 16 industrial solvents allowed for ranking of the anticipated relative human toxicity of these solvents, which were comparable with data from standard toxicity tests and human occupational data. Overall, the study clearly supports the application of the HepG2 cell bioassay system for rapid toxicological screening of many candidate toxicants for both short- and long-term toxicity potential. *Toxicology and Industrial Health* 2006; **22:** 301–315.

Key words: *bioassay; solvents; cytotoxicity; genotoxicity*

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Introduction

There is an urgent need to develop and establish new toxicological approaches to assess the potential cytotoxic and genotoxic effects of toxicants found in the environment (Hasspieler *et al.*, 1996; Bakand *et al.*, 2005; Bhogal *et al.*, 2005). In response to such growing demand, the development of rapid, simple, and sensitive toxicological screening methods for the biomonitoring of environmental pollutants that affect human health, is a universal goal. In previous years, numerous *in vitro* and *in vivo* assays have been utilized to assess the effects of environmental pollutants on their cellular targets. Increasing public interest in these issues has created a demand for alternatives to using animals in such testing. Bacterial assays are used for fundamental studies of mutagenesis and for screening of environmental samples as potential genotoxins. Mammalian cell culture systems have also been used in risk evaluation in order to investigate the mechanisms of chemical carcinogenesis and as bioassay systems for monitoring environmental genotoxins. Isolated cells have been extensively used in toxicological studies *in vitro* (Andreoli *et al.*, 2003; Bakand *et al.*, 2005; Hayashi, 2005; Dambach *et al.*, 2005).

The types of organ and cell systems – including the liver, kidney, neural tissue, the hematopoietic system, the immune system, the reproductive organs and the endocrine system – currently available to perform *in vitro* tests for toxicity testing have been extensively reviewed (Tahti *et al.*, 2003; O'Brien *et al.*, 2004; Farkas and Tannenbaum, 2005). Perfused organs, such as the liver and kidney, brain, lung etc., are examples of one model used for *in vitro* testing (Speilman *et al.*, 1998). The prime advantage of using entire organs is that the general morphology and cell–cell interactions are preserved. Primary cell cultures from organs of interest (liver, kidney, etc.) may also be prepared. Their use permits longer-term studies encompassing a few days and/or a few passages. Some differentiated functions may be retained, and co-culture is possible with other cellular types (Speilman *et al.*, 1998; Pfaller and Gstraunthaler, 1998; Costa, 1998). On the contrary, primary cell cultures have unstable phenotypes, and may quickly lose many differentiated functions. The use of immortalized and continuous cell lines offers ease of propagation, and the ability to generate unlimited numbers of cells for testing (Speilman *et al.*, 1998; Pfaller and Gstraunthaler, 1998; Costa, 1998). Many different cell types have been used in toxicity studies, including continuous renal epithelial cell lines to assess nephrotoxicity (Pfaller and Gstraunthaler, 1998; Prieto, 2002), neuroblastoma or glioma cell lines to assess neurotoxicity (Costa, 1998; Lindahl *et al.*, 1999; Tahti *et al.*, 2003; Madia *et al.*, 2004), embryonic stem cells and ovarian and testicular cell types to assess reproductive and developmental toxicity (Spielmann, 1998; Riecke and Stahlmann, 2000; Bishop, 2003; Bremer *et al.*, 2005). Such lines are useful for specific mechanistic studies and may be co-cultured. They may also be genetically manipulated to express proteins of interest, and can be cryopreserved. As with all primary cell cultures, their disadvantage is they may have lost a variety of specific cell functions and have an unstable genotype.

One organ of particular importance to toxicological research is the liver. The use of *in vitro* hepatic systems for toxicity studies has received increasing attention in recent years (Hasspieler *et al.*, 1996; Andreoli *et al.*, 2003; Tahti *et al.*, 2003; O'Brien *et al.*, 2004; Bakand *et al.*, 2005; Bhogal *et al.*, 2005; Dambach *et al.*, 2005; Farkas and Tannenbaum, 2005; Hayashi, 2005). These have been used advantageously in hepatocyte-based cytotoxicity and genotoxicity assays *in vitro*. One human hepatic cell line, HepG2, provides a convenient and sensitive tool for the rapid screening of environmental samples for potential genotoxic and cytotoxic effects (Hasspieler *et al.*, 1996). The human hepatocyte, HepG2, retains many functions of the normal hepatocyte (liver cell), including the synthesis and secretion of hepatic-specific proteins (Adeli and Sinkevitch, 1990), and expression of xenobiotic-metabolizing enzymes (Dufresne *et al.*, 1993), and has been used extensively for many biological studies. Our laboratory previously used the HepG2 cell culture system to develop a number of toxicity bioassays, in order to assess both acute cytotoxicity as well as genotoxic potential, as assessed by measurement of DNA strand breaks (Ali *et al.*, 1994), and DNA repair activity (Hasspieler *et al.*, 1995).

Genetic approaches to measuring toxicological effects are becoming increasingly popular, as our expertise in this area of technology quickly advances. Over the past decades, many *in vitro* assays have been used to assess the genotoxic effects of xenobiotics, such as heavy metals, on target organisms. For example, bacterial assays, such as the *Salmonella* mutagenicity assay (Ames *et al.*, 1975), have been used, not only for fundamental studies of mutagenesis, but also for the screening of environmental samples for potential genotoxicity. The methods used in this test system have been extensively reviewed elsewhere (Claxton *et al.*, 2004; Chung *et al.*, 2006). Several mammalian cell lines have also been used to investigate the mechanisms of chemical carcinogenesis, and as bioassay systems for monitoring environmental genotoxins (Maurici *et al.*, 2005; Ohno *et al.*, 2005; Fernandes *et al.*, 2005; Lambert *et al.*, 2005).

Of the various endpoints that have been used as indices of genotoxic insult, the formation of DNA single-strand breaks (SSB) has experienced increasing use. This trend may be attributed to the relatively high sensitivity of the SSB response to xenobiotic exposure, as well as to the toxicological sequelae that are associated with the SSB response, including clastogenesis, heritable mutations, and cancer. The methods of quantifying SSBs are generally based on exposing the DNA strand to alkaline conditions (pH >11.5), so that unwinding of the helix occurs at the SSB sites. If an appropriate, fixed period of unwinding is used, the formation of single-strand (SS) DNA will be proportional to the number of 'alkali-labile' break sites present. At least four procedures have been developed to assess SSBs including: (1) alkaline unwinding and DNA quantification using a fluorescent DNA-binding stain (Hoechst 33258) (Shugart, 1998); (2) alkaline elution of SS DNA using a porous membrane (Kohn *et al.*, 1980), where the DNA is quantified radiometrically using cells that are prelabeled in culture with [^{3}H]thymidine; (3) the single-cell gel electrophoresis assay (Singh *et al.*, 1988); and (4) hydroxylapatite DNA chromatography (Daniel *et al.*, 1985). We have previously improved upon this latter method for use with human cells in culture (Hasspieler *et al.*, 1995).

Another approach to assessing genotoxicity is monitoring DNA repair activity in cells after genotoxic insult. The most widely used approach involves quantifying unscheduled DNA synthesis (UDS), which indicates the repair of DNA lesions. UDS assays are based on the incorporation of radiolabeled nucleotides (commonly [^{3}H]thymidine) into the DNA of cells that are not undergoing replicative (scheduled) DNA synthesis. The two general methods for quantifying [^{3}H]thymidine incorporation are (1) autoradiography (Dusenbery and Lee-Chen, 1988), and (2) liquid scintillation counting (LSC) (Martin *et al.*, 1978). In the interest of developing methods to assess genotoxicity in ways that are sensitive and rapid, our laboratory has optimized the LSC-based UDS assay for use in human cultured cell lines, following the procedures described by Martin *et al.* (1978). This technique differs from the autoradiography assay in that the cellular DNA is assessed in a batchwise manner rather than by the visual examination of individual cells (Martin *et al.*, 1978).

This study focuses on the application of a panel of *in vitro* human cell bioassays to provide a toxicological assessment of a number of industrial solvents that are currently in common use worldwide. A combination of assays that measure acute cytotoxicity and enzyme induction, together with genotoxic assays that assess DNA damage and repair induction, should allow for a comprehensive assessment of both short- and long-term toxicity potential. Data presented from the screening of 16 industrial solvents supports the potential use of such a test battery for mass screening of suspected environmental toxicants, providing useful information for human health risk assessment.

Materials and methods

Materials

HepG2 cells were obtained from the American Type Culture Collection (Rockville, MD, USA). Cell culture media were obtained from Life Technologies (Burlington, Canada). [^{3}H]Thymidine was obtained from ICN Biomedicals (Mississauga, Canada). Tissue culture equipment was obtained from Corning Inc. (New York, NY, USA). NTB-2 emulsion was purchased from Eastman Kodak

(Rochester, NY, USA). Hydroxylapatite gel (DNA grade) was obtained from Bio Rad Laboratories (Richmond, CA, USA). All other reagents were purchased from Sigma Chemical Co. (St Louis, MO, USA).

Table 1 lists the chemicals tested, their CAS numbers, and structural formulas.

Cell culture

HepG2 monolayer cell cultures were maintained in α-Minimal Essential Medium (MEM) (supplemented with 5% fetal bovine serum (FBS), 0.1 U/L penicillin (base), 100 mg/L streptomycin (base), and 0.25 mg/L amphotericin B) in a humidified atmosphere of 5% CO_2 at 37°C. The cell lines were subcultured weekly by digesting the cells with 0.25% Trypsin/1 mM sodium EDTA (Gibco) at 37°C for 7 min. The cells were then separated by four passages through a 20-gauge needle and dilution in complete medium. Culture plates were inoculated with the appropriate number of cells to reach confluence within a given time period. The culture medium was replaced with fresh medium every two to three days.

Neutral red uptake assay for cytotoxicity

The cytotoxicity of a test compound was quantified using the neutral red dye uptake (NRU) assay, as described previously (Hasspieler *et al.*, 1996). Approximately 3×10^4 cells in 0.2 mL complete medium were added to each well of a 96-well tissue-culture microtiter plate. The cell cultures were incubated at 37°C for 24 h and then treated with fresh medium containing various concentrations of a test compound delivered in solvent (eg, acetone, DMSO). Solvent alone (to a final concentration of 1% (v/v)) was used as a negative control. The cells were then incubated for a given time period (eg, 0–24 h), and then the treatment medium (pre-incubated overnight at 37°C) containing 50 mg/L NR was introduced. After incubation for another 3 h to allow uptake of the dye into viable cells, the cells were immediately washed with a fixative, and the NR dye was extracted. After a brief agitation on a microtiter plate shaker, the absorbance of the extracted dye was measured using a Dynatech MRX spectrophotometric plate reader (Dynatech Laboratories Inc., Chantilly, VA, USA) with a 540-nm filter.

Table 1. Chemicals quantitatively evaluated

Chemical name	Trade name	CAS No(s)	Structural formula
Isopropylbromide	Several	75-26-3	C3H7Br
n-Propylbromide	Several	106-94-5	C3H7Br
n-Propylbromide (stabilized)	EnSolv	106-94-5	C3H7Br
Perchloroethylene	Several	127-18-4	C2Cl4
trans-1,2-Dichloroethylene	Several	540-59-0	C2H2Cl2
Trichloroethylene	Several	79-01-6	C2HCl3
1,1,1,2,3,4,4,5,5,5-Decafluoropentane/ trans-1,2-dichloroethylene	VERTREL MCA	NA/540-59-0	C5F10H2/C2H2Cl2
1,1,1,2,3,4,4,5,5,5-Decafluoropentane/ trans-1,2-dichloroethylene/methanol	VERTREL SMT	NA/540-59-0/67-56-1	C5F10H2/C2H2Cl2/CH2OH
1,1,1-Trichloroethane	Several	71-55-6	C2HCl3
3,3-Dichloro-1,1,1,2,2-pentafluoropropane/ 1,3-dichloro-1,1,1,2,2-pentafluoropropane	DPF	422-56-0/NA	C3Cl2HF5 (two isomers)
3,3-Dichloro-1,1,1,2,2-pentafluoropropane/ 1,3-dichloro-1,1,1,2,3-pentafluoropropane	AK225ca/cb	422-56-0/507-55-1	C3Cl2HF5 (two isomers)
Methoxy-nonafluorobutane	HFE-7100	163702-08-7/163702-07-6	Two isomers: (CF3)2CFCF2OCH3/ CF3CF2CF2CF2OCH3
Ethoxynonafluorobutane	HFE-7200	163702-06-5/163702-05-4	Two isomers: (CF3)2CFCF2OC2H5/ CF3CF2CF2CF2OC2H5
Methylnonafluorobutylether/ethylnonofluorobutylether/ trans-1,2-dichloroethylene	HFE-72DE	NA/NA/540-59-0	C4F9OCH3/C4F9OCH3/C2H2Cl2
Methylnonafluorobutylether/trans-1,2-dichloroethylene	HFE-71DE	NA/540-59-0	C4F9OCH3/C2H2Cl2
Methylnonafluorobutylether/ trans-1,2-dichloroethylene/ethanol	HFE-71DA	NA/540-59-0/64-17-5	C4F9OCH3/C2H2Cl2/CH2OH

NA, not available.

Ethoxyresorufin *O*-deethylase (EROD) bioassay

The EROD bioassay presented here is a modification of the method described by Pohl and Fouts (1980). HepG2 cells were grown to confluence in 96-well tissue culture microtiter plates and then treated with test compounds for 24 h under standard culture conditions. After a 24-h exposure period, the cells were washed and preincubated for 5 min in medium containing 40 μM digitonin (to permeabilize cells), glucose 6-phosphate dehydrogenase, and ethoxyresorufin (8 μM). The reaction was started by the addition of glucose 6-phosphate (5 mM) and NADPH (0.5 mM). EROD, measured as an increase in fluorescence, was monitored at 37°C in a Labsystems Fluoroskan II plate reader, at the respective excitation and emission wavelength optima of 538 and 591 nm. The rates of resorufin production were determined using resorufin standards, and the protein content for the same microtiter plates was measured using a modification of the method described by Lowry *et al.* (1951), using bovine serum albumin in incubation medium as standard. To each microtiter well containing cells and medium, sodium dodecyl sulfate was added to solubilize protein, and the plates were shaken on an orbital shaker. The solubilized protein from each microtiter well was transferred to corresponding wells in a new plate containing 200 μL of premixed copper/tartrate reagent. The plates were shaken, diluted Folin reagent was added to each well, and the plates were shaken at room temperature. The absorbance at 650 nm was read in a spectrophotometric plate reader (MRX, Dynatech Laboratories Inc.). The standard protein assay was simultaneously used to calculate protein content. The specific enzyme activity was expressed as pmol resorufin produced/mg protein/min.

DNA SSB assay

The procedure used for analysing DNA SSB is a modification of the procedure described by Hasspieler *et al.* (1995). HepG2 cells were grown to confluence in 24-well (16 mm diameter) tissue culture plates containing complete medium supplemented with 50 nCi/mL [^{3}H]thymidine. The cells were later treated for a given period of time with test compounds, as described above. After the treatment period, the treatment medium was replaced, and immediately followed by alkalinization with sodium hydroxide. After this alkaline unwinding period, the samples were neutralized with hydrochloric acid, followed by the immediate addition of 2% sodium lauryl sarcosinate/20 mM EDTA. The plates were then sonicated and the cell lysates stored at 4°C until hydroxylapatite chromatography. Hydroxylapatite chromatography was performed using a circulating, heated water bath that was fitted with 24 disposable columns, with the thermostat set at 60°C. The hydroxylapatite gel was prepared as a slurry containing 2.5 g gel suspended in 25 mL potassium phosphate buffer (PB). The slurry was mixed, heated to boiling, allowed to cool, and then the gel slurry (1 mL) was combined with each cell lysate. The mixtures were incubated at 60°C, poured into individual columns, and the columns were washed. The SS DNA fraction and the DS DNA fraction were eluted, and each DNA fraction was combined with concentrated hydrochloric acid and the samples were digested. Each digested sample was combined with scintillation cocktail and the radioactivity was measured in a β-liquid scintillation counter. Data are expressed as *F*-values, corresponding to the radioactivity (disintegrations/min) in the DS fraction divided by the sum of the radioactivity in the SS and DS fractions.

UDS-DNA repair assay

To minimize scheduled (replicative) DNA synthesis, HepG2 cells were grown to confluence in 35-mm Petri dishes, maintained at this stage for four days in 0.5% FBS, and then incubated for 1 h with hydroxyurea, to inhibit residual scheduled DNA synthesis. Test compounds were added to the cells in solvent (to a final concentration of 1%) together with [^{3}H]thymidine. After incubating for a given time period, the cells were collected onto 0.6 μm Sartorius filters, and washed successively with PBS, 5% trichloroacetic acid, and 95% ethanol. The filters were air-dried, combined with scintillation cocktail, and the radioactivity was measured in a β-liquid scintillation counter. In this assay, an increase in the incorporation of [^{3}H]thymidine over background levels indicated the induction of UDS.

Results

In the present study, we screened a number of industrial solvents for potential short-term cytotoxicity and long-term genotoxic potential using a battery of four human cell bioassays. Two bioassays were developed to assess the carcinogenic and mutagenic potential of suspected toxicants at the cellular and DNA levels. These assays were combined with two other bioassays that measure cytoxicity as well as enzyme induction, and this four-test battery was used to screen a number of industrial solvents for acute and chronic toxicity potential.

The cell death/cytotoxicity bioassay is based on the ability of normal, healthy cells to take up nutrients. A toxic response lowers this rate of uptake, indicating loss of cell viability. The positive control used for this test is menadione, which is known to be cytotoxic and affects, among other things, calcium transport across the cell membrane. The test introduces a non-toxic dye into the culture medium, which is then taken into living cells, but not into damaged or dead cells. Toxicity is quantified by extracting the dye from the cells, measuring the absorbance with a spectrophotometer, and comparing the results to the positive control. Figure 1(A) shows a typical standard curve generated using different concentrations of menadione to induce cytotoxicity assessed by decreasing uptake rate of NRU. This is a highly reproducible assay with intra-assay (within-run) and inter-assay (between-day) imprecision of 8.6 and 8.5%, respectively, at 18.8 μM menadione. The lowest concentration of menadione that showed a toxic effect on cells was 15.6 μM.

The altered enzyme function bioassay is based on the increased enzyme activity, primarily mixed function oxidases (MFOs), that often results from exposure to toxic chemicals. The positive control for this test is 2,3,7,8-TCDD (dioxin), which is known to induce MFO activity at very low levels. The specific MFO activity measured in the test focuses on the CYP1A1/2 P450 enzymes. The test measures enzyme activity with a fluorometer after 24-h exposure to the chemical of interest. Toxicity is quantified by comparison with the positive control. Figure 1(B) shows a typical standard curve generated using different concentrations of TCDD to induce EROD. The assay is very reproducible with intra-assay (within-run) and inter-assay (between-day) imprecision of 5.6 and 13.6%, respectively, at 60 and 115.0 pM TCDD ($N=24$ for both studies). The lowest concentration of TCDD to consistently show a statistically significant increase in EROD activity over the negative control was 15.6 pM.

The DNA damage bioassay evaluates the ability of a chemical to cause damage to DNA by monitoring strand breakage. The positive control for this test is 4-nitroquinoline *N*-oxide, a known mutagen that induces SSBs. For this test, the cells are labeled with radioactive DNA, exposed to the chemical, and then analysed. Analysis involves separating SS DNA (ie, broken strands) from double-stranded (DS) DNA (ie, intact DNA), and then counting the radioactivity of both types of DNA in a liquid scintillator. Toxicity is quantified by comparing the ratio of SS to DS DNA to the positive control. Figure 2(A) shows a typical standard curve generated using different concentrations of 4-NQO. This assay was optimized to ensure precision and typically has intra-assay (within-run) and inter-assay (between-day) imprecision of 4.8 and 7.1%, respectively ($N=25$ for each study). The lowest concentration of 4-NQO that showed a statistically significant genotoxic effect on cells was 125 nM. This sample concentration yielded an average F value of 89.9%, compared to 96.8% for the control.

The DNA repair bioassay evaluates the ability of a chemical to both damage and repair DNA. This activity is often an indicator of mutagenicity. Repair of damaged DNA is measured by the test. The positive control for this test is the same as for the DNA damage bioassay. In this test, the incorporation of healthy nucleotides at a previously damaged DNA site is measured. When combined with the DNA strand break assay above, this test provides an indicator of the genotoxic potential of a chemical. Figure 2(A) shows a typical standard curve generated using different concentrations of 4-NQO. This assay was optimized to ensure precision and typically has intra-assay (within-run) and inter-assay (between-day) imprecision of 5.5 and 8.3%, respectively.

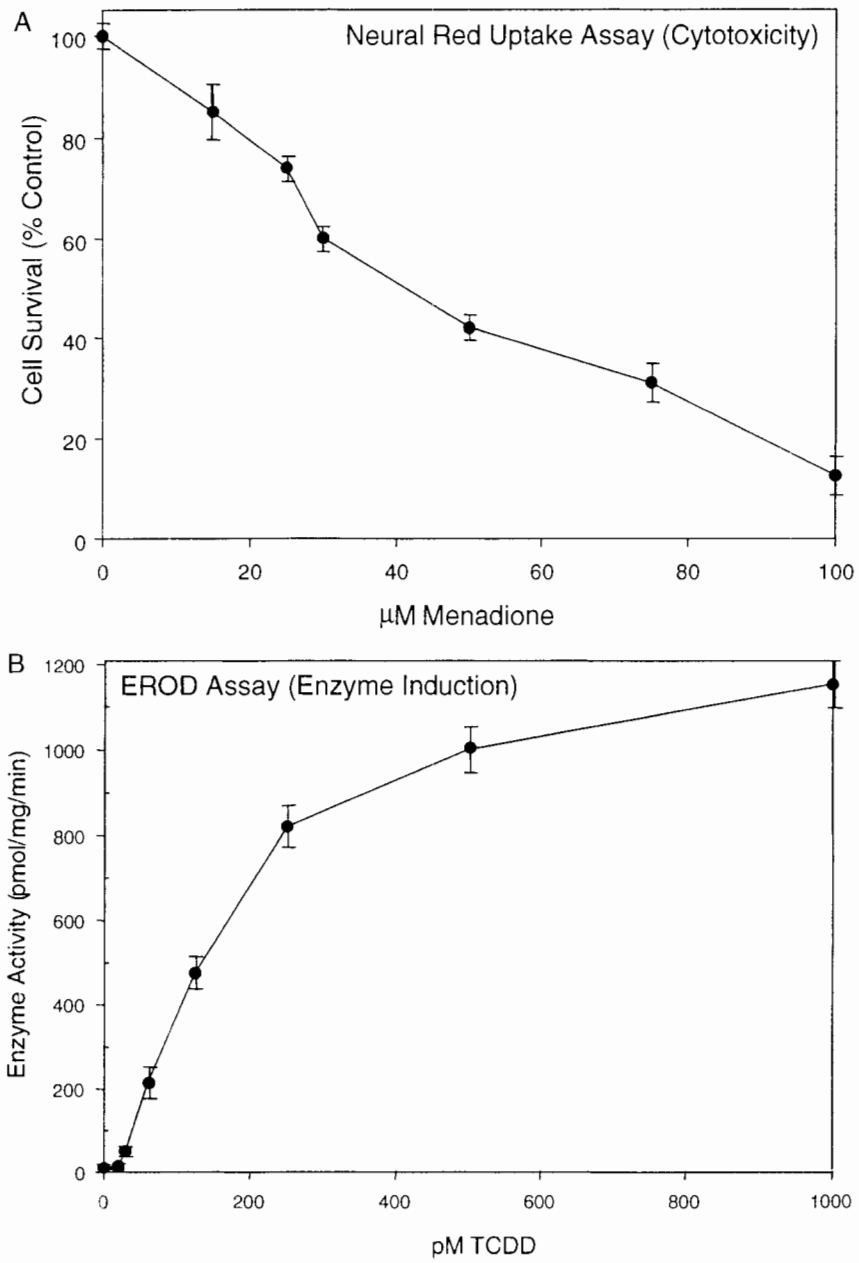

Figure 1. Dose response curves for the neural red dye uptake and EROD assays in HepG2 cells. (A) Effect of menadione on HepG2 cells in the neutral red uptake assay for cytotoxicity. Vertical axis represents absorbance at 540 nm expressed as percent of solvent-treated controls. (B) Effect of TCDD on EROD activity in HepG2 cells. A typical profile of percent maximum EROD activity versus TCDD concentration is shown. The dose–response relationship is readily evident from these plots. Vertical bars represent standard error of the mean of four replicates.

Once all four human cell bioassays were fully optimized, this battery of assays was used to screen a number of industrial solvents. A series of comparative human cell bioassay tests was carried out on 16 solvents, and the results of these tests were interpreted in terms of relative toxicity. The comparative human cell bioassay tests were carried out for two groups of compounds. The first group included *n*-propyl bromide (nPB), stabilized nPB, 1,1,1-trichloroethane (TCA), trichloroethylene (TCE), perchloroethylene (PCE), and isopropyl bromide (iPB). The second group of solvents included a mixture of 3,3-dichloro-1,1,1,2,2-pentafluoropropane and 1,3-dichloro-1,1,

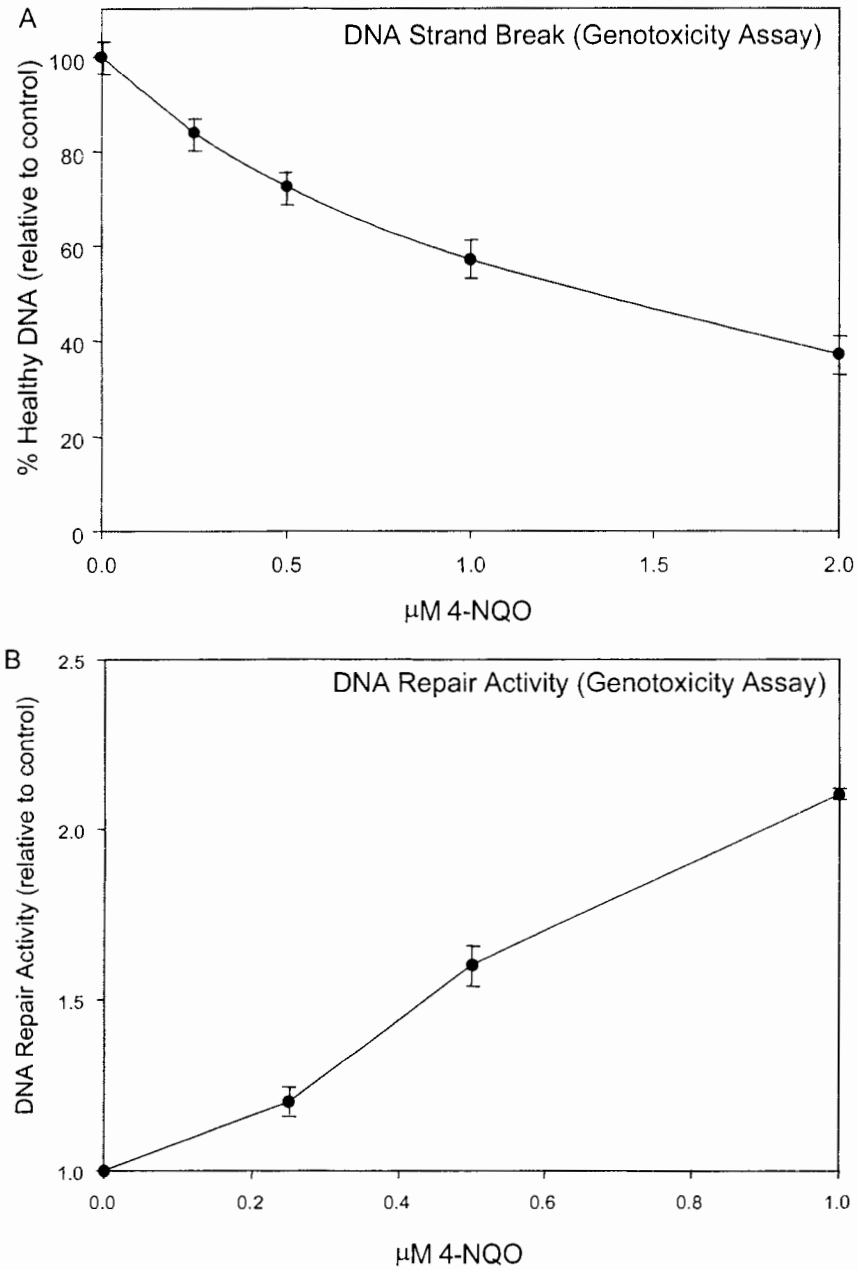

Figure 2. Dose response curves for the DNA break and DNA repair assays. (A) Effect of 4-NQO on HepG2 cells in the DNA single stranded break assay for gentotoxicity. Vertical axis represents percent of healthy DNA calculated based on the *F* value (ratio of single stranded to double stranded DNA) at each concentration of 4-NQO. (B) Effect of 4-NQO on DNA repair activity in HepG2 cells. Liquid scintillation assay for unscheduled DNA synthesis was performed in the presence of different concentrations of 4-NQO. Vertical axis represents [^{3}H]thymidine uptake relative to solvent-treated controls. Vertical bars represent standard error of the mean of four replicates.

1,2,2-pentafluoropropane (AK225ca/cb), 3,3-dichloro-1,1,1,2,2-pentafluoropropane/1,3-dichloro-1,1,1,2,2-pentafluoropropane (DPF), a mixture of methyl nonafluorobutyl ether, ethyl nonafluorobutyl ether and trans-1,2-dichloroethylene (HFE-72DE); methoxy-nonafluorobutane (HFE-7100), ethoxy-nonafluorobutane (HFE-7200), a hydrofluoroether, methylnonafluorobutyl ether in an azeotrope formulation with trans-1,2-dichloroethylene (HFE-71DE), a hydrofluoroether, methylnonafluorobutyl ether in an azeotrope formulation with trans-1,2-dichloroethylene and ethanol (HFE-71DA), 1,1,1,2,3,4,4,5,5,5-decafluoropentane, trans-1,2-dichloroethylene and stabilizer

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(VERTEL SMT), 1,1,1,2,3,4,4,5,5,5-decafluoropentane, trans-1,2-dichloroethylene (VERTEL MCA), and trans 1,2-dichloroethylene (TDE).[1]

Both nPB and a stabilized nPB product (EnSolv®[2] stabilized nPB) were tested to evaluate the comparative toxicity of the compound and a stabilized formulation. Other stabilizing formulations for nPB exist, but were not tested. Since the components of these other stabilizing formulations vary widely from those used in the EnSolv formulation, extrapolation from the results of the EnSolv stabilized nPB to any product with a different stabilizing formulation is not warranted or advised.

Four tests for all compounds tested were run using a range of concentrations from 25 to 500 ppm (Table 2). Figures 3–5 show the results of human cell bioassays for three of the 16 compounds (nPB, iPB, and TCE). Each chemical was tested using all four bioassays. The results for the 16 chemicals are summarized in Table 2. Graphs are not shown for the remaining chemicals to limit the number of figures shown to 5. The tissue concentrations tested reflect higher actual workplace air concentrations because only a portion of chemicals in inhaled air are actually absorbed, and then only a fraction of the chemical mass actually absorbed reaches target tissues and cells. Therefore, these tissue concentrations provide a good biomarker of the potential toxicity of the chemical product in humans exposed to them in the workplace. The sensitivity of these tests was sufficient to identify impacts due to nPB at low concentrations that are environmentally meaningful. The sensitivity of these tests ranged from 0.02 ng/m^3 (0.00004 parts per million (ppm)) for the EROD enzyme induction test, to 0.02 mg/m^3 (0.004 ppm) for the cytotoxicity assay.

Discussion

There are a number of important general considerations to take into account when choosing a system and method to measure *in vitro* toxic effects (Tiffany-Castiglioni *et al.*, 1999). If permanent cell lines are used (which have both technical and economic advantages), the observations and conclusions made may differ greatly from what actually occurs *in vivo* after toxicant exposure. Many continuous cell lines are hardy, and may not show realistic exposure effects unless they are subjected to unusually high toxicant concentrations. Continuous lines do not exhibit the usual cellular stages of development. When primary cell cultures are used, batch-to-batch cellular variability may influence observed toxicant responses. If tissue slices are used, it is important to consider the method by which they are prepared. Cell–cell interactions may also be crucial to toxic effects, and should be taken into consideration when a test system is selected. Cell–cell interactions between different cell types may be implicated in toxic effects. Concentrations of toxicants that are effective *in vivo* may be very different than those relevant *in vitro*. If the results obtained from *in vitro* studies are to be meaningful, they must mimic as closely as possible those conditions present *in vivo*. It is important to generate both time and dose response curves to cover a variety of scenarios and gain meaningful information. It is also important to note that *in vitro* systems only allow monitoring of short-term effects and that a clear understanding of the advantages and limitations of such *in vitro* systems will need to be considered when interpreting data generated from *in vitro* toxicological assessments.

We believe this study is the first time these solvents have been subjected to an identical set of *in vitro* cell bioassay tests on human cells. This is one of the important functions of this testing, as it affords a basis for comparing the anticipated relative human toxicity of these solvents. What follows is a critical analysis of relative toxicity, based strictly on the outcome of the human bioassay tests.

Six chemicals were positive in three of the four tests (isopropyl bromide, AK225ca/cb, DPF, HFE-72DE, Vertrel SMT, and Vertrel MCA). Four chemicals were positive in only one of the four tests (TCA, *n*-propylbromide, EnSolv, and HFE-7100). The other six were positive in two of the four tests. For the purposes of discussion, it was

[1]AK225ca/cb is a registered trademark/tradename of Asahi Glass Company. HFE-71DA, HFE-71DE, HFE-72DE, HFE-7100 and HFE-7200 are tradenames and/or trademarks of 3M Corp. Vertrel, VERTEL MCA and VERTEL SMT are trademarks and tradenames of DuPont, Inc.

Table 2. Toxicological assessment of organic solvents using human cell bioassays

	Cytotoxicity	EROD	DNA strand break	DNA repair activity
TCE	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Negative (at 25–500 ppm)
PCE	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Negative (at 25–500 ppm)
TCA	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)
n-Propyl bromide (nPB)	Positive (at 500 ppm)	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)
EnSolv® (stabilized nPB)	Positive (at 500 ppm)	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)
Isopropyl bromide	Positive (at >150 ppm)	Negative (at 25–500 ppm)	Positive (at >150 ppm)	Positive (at >150 ppm)
AK225ca/cb	Positive (at >100 ppm)	Positive (at >200 ppm)	Negative (at 25–500 ppm)	Positive (at 500 ppm)
DPF	Positive (at >200 ppm)	Positive (at 500 ppm)	Negative (at 25–500 ppm)	Positive (at 500 ppm)
HFE-72DE	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Positive (at >200 ppm)
HFE-7100	Positive (>25 ppm)	Negative (at 25-500 ppm)	Negative (at 25–500 ppm)	Negative (at 25–500 ppm)
HFE-7200	Positive (>100 ppm)	Negative (at 25–500 ppm)	Positive (>200 ppm)	Negative (at 25–500 ppm)
HFE-71DE	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>100 ppm)	Negative (at 25–500 ppm)
HFE-71DA	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Negative (at 25–500 ppm)
VERTREL SMT	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Positive (>200 ppm)
VERTREL MCA	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Positive (>100 ppm)
TDE	Positive (>25 ppm)	Negative (at 25–500 ppm)	Positive (>25 ppm)	Negative (at 25–500 ppm)

Each solvent was tested at various doses of 25–500 ppm using each of four cell bioassays in HepG2 cells to assess cytotoxicity, EROD activity, DNA strand breakage, and DNA repair activity. A test was scored as positive when percent change in activity was statistically different from the negative control ($P<0.05$)

on the combined basis of the number of positive tests and the concentrations at which significant results were obtained. On this basis, the six chemicals that were positive in three of the four tests would be considered most toxic. Based on the relative concentrations in the three positive tests across these chemicals, the comparative relative toxicity across these six tested compounds is as

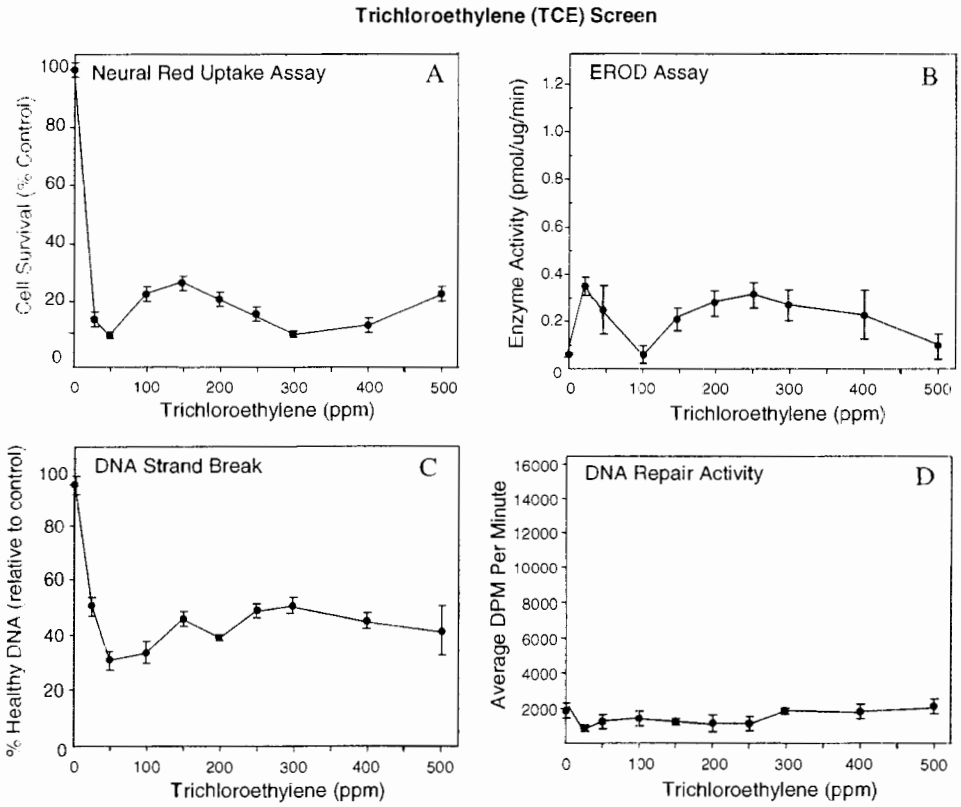

Figure 3. Dose–response curves for trichloroethylene (TCE) in the neural red dye uptake, EROD, and DNA break and repair activity assays. The effect of TCE at concentrations of 25–500 ppm was tested on HepG2 cells using the four cell bioassays. (A) Neutral red dye uptake assay, (B) EROD assay, (C) DNA stand break assay, and (D) DNA repair activity assay. Positive controls (4-NQO and TCDD) were run in parallel with each chemical to validate each of the four assays. Vertical bars represent standard error of the mean of four replicates.

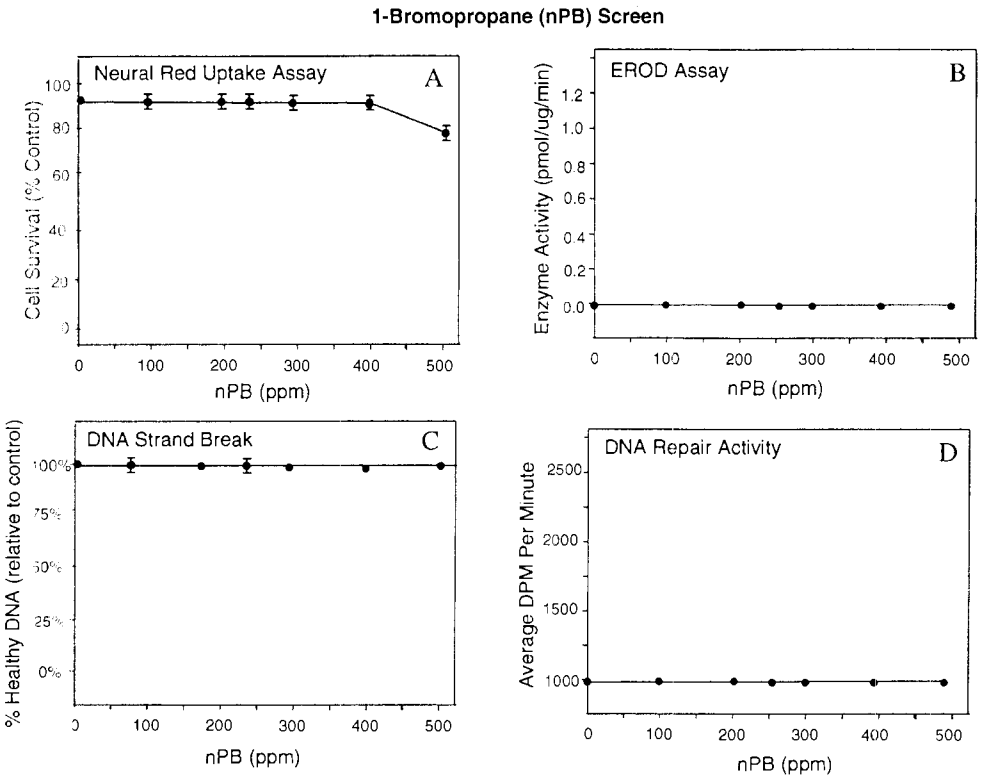

Figure 4. Dose–response curves for 1-bromopropane (nPB) in the neural red dye uptake, EROD, and DNA break and repair activity assays. The effect of nPB at concentrations of 25–500 ppm was tested on HepG2 cells using the four cell bioassays. (A) Neutral red dye uptake assay, (B) EROD assay, (C) DNA strand break assay, and (D) DNA repair activity assay. Positive controls (4-NQO and TCDD) were run in parallel with each chemical to validate each of the four assays. Vertical bars represent standard error of the mean of four replicates.

follows: Vertrel MCA (most toxic) > Vertrel SMT and HFE-72DE > iPB > AK225ca/cb > DPF.

For the group of chemicals that tested positive in two of the four assays, the comparative relative toxicity, using the same concentration scale, is as follows: TCE = PCE = TDE = HFE-71DA > HFE-71DE > HFE-7200. Finally, for the group of chemicals that tested positive in only one of the four assays, the comparative relative toxicity is estimated as follows: HFE7100 > TCA > nPB and stabilized nPB (least toxic). nPB, stabilized nPB, and HFE-7100 were positive only for cytotoxicity, and TCA was positive only in the DNA repair assay. While nPB and stabilized nPB were positive at only the highest tested dose (500 ppm), HFE-7100 and TCA were positive at all dose levels except 25 ppm. TCA was ranked lower in toxicity than HFE-7100 because cytotoxicity was considered a more direct toxic effect than DNA repair activity, considering the effects occurred at the same dose levels. nPB and stabilized nPB were considered least toxic because the only positive result was at the highest tested dose level. This was not the case for the other 14 solvents. The tests showed that a particular set of compounds, comprising the stabilizing formulation (about 7% of the total mixture for EnSolv®) added to nPB, had no effect on overall toxicity. Other formulations of nPB were not tested. nPB was also negative in standard genotoxicity tests conducted elsewhere (Elf Atochem, 1994). In addition, the human bioassay testing clearly indicates that nPB, although a structural analog of iPB, has neither the mutagenic nor inherent toxicity indicated by the test for iPB. The chlorinated solvents were tested only in their neat form due to the wide variety of stabilizing compounds used with these materials.

Of those solvents comprised of a single active chemical constituent, iPB appears to have the most potential for genotoxicity, inducing DNA strand breaks and repair activity at concentrations > 150 ppm. TDE was positive for strand breakage at a lower concentration, but was negative for repair activity. The genotoxic potential of TDE appears to be enhanced when combined with

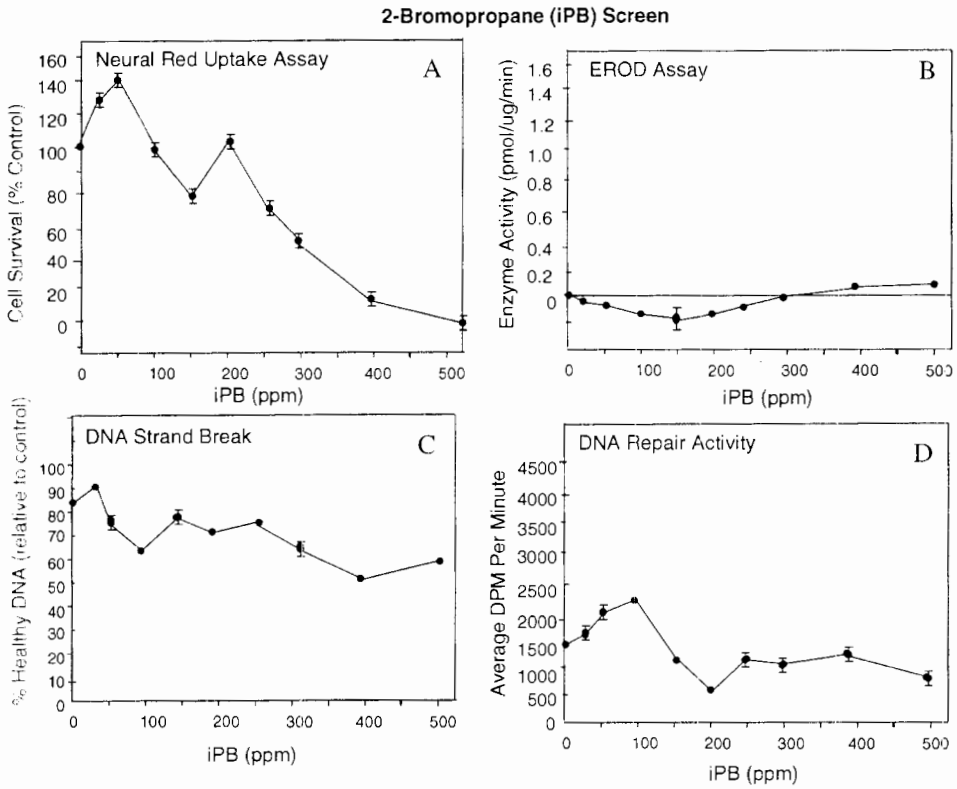

Figure 5. Dose–response curves for 2-bromopropane (iPB) in the neural red dye uptake, EROD, and DNA break and repair activity assays. The effect of iPB at concentrations of 25–500 ppm was tested on HepG2 cells using the four cell bioassays. (A) Neutral red dye uptake assay, (B) EROD assay, (C) DNA strand break assay, and (D) DNA repair activity assay. Positive controls (4-NQO and TCDD) were run in parallel with each chemical to validate each of the four assays. Vertical bars represent standard error of the mean of four replicates.

nonafluorobutyl ether and ethyl nonafluorobutyl ether (ie. HFE-72DE), resulting in both DNA strand breaks as well as DNA repair induction. TDE tested negative in other standard genotoxic tests, but the *cis*-isomer of 1,2-dichloroethylene tested positive (Agency for Toxic Substances and Disease Registry, 1996). HFE-7100 and HFE-7200 exhibited significant potential for cytotoxicity, but only ethoxy-nonafluorobutane showed activity in the DNA break assay. Of the products containing mixtures of active chemicals, AK225ca/cb induced cytotoxicity, DNA strand breaks, and DNA repair induction, and DPF induced cytotoxicity, EROD activity, and DNA repair induction, but generally at higher concentrations than other mixtures (500 ppm).

Use of human *in vitro* bioassays provides an indication of potential chemical toxicity. Such tests evaluate cellular biomarkers for potential toxicity. Chemical activity *in vitro* cannot be assumed to completely reflect *in vivo* effects, but provides critical information when attempting to relate the results of whole body animal toxicity tests to humans. The US Environmental Protection Agency (USEPA) has incorporated *in vitro* data into their revised approach to evaluate potential carcinogens (United States Environmental Protection Agency, 2005). They state that '[t]he application of techniques for measuring cellular and molecular alterations due to exposure to specific environmental agents may allow conclusions to be drawn about the mechanisms of carcinogenesis.'

Although specific in this case to carcinogenic analysis, this indicates that the USEPA has realized that human cellular studies can provide important information when evaluating the potential human toxicity of a chemical. USEPA further states that '...cells and tissues [can] serve as biomarkers of exposure in both animals and humans.' Such tests can '...aid in interspecies extrapolations when data are available from both experimental animal and human cells'. Clearly, use of *in vitro* bioassays alone does not provide conclusive evidence regarding potential whole body toxicity in humans. As the

USEPA also says '...although important information can be gained from *in vitro* test systems, a higher level of confidence is generally given to data that are derived from *in vivo* systems. However, such *in vitro* tests can provide useful information when included as part of an overall weight-of-evidence analysis for a chemical'.

Such a weight-of-evidence analysis is provided below for all tested solvents. The solvents containing only a single active ingredient included two chemicals with no toxicity-based standards (nPB and iPB), and four other solvents with toxicity-based standards (TCA, TDE, TCE, PCE). The latter two chemicals are suspected human carcinogens and all four have known non-cancer toxicity, especially on the liver. Based on the USEPA human health-based criteria (eg, reference doses), the non-cancer potency of these four chemicals can be ranked from high to low as follows: TCE > PCE > TDE > TCA.

Results obtained for all six solvents tested at seven dose levels ranging from 25 to 500 ppm are summarized in Table 2. Based on these results, it may be concluded there is no significant toxicity posed by nPB or stabilized nPB at concentrations in the range 100–400 ppm. These results indicate that TCE, TDE, and PCE are similarly toxic of the four tested chlorinated chemicals, and TCA is less toxic, which is consistent with the USEPA's ranking of these chemicals. Although TCA is not a suspected human carcinogen, it was positive in the DNA repair bioassay. This result suggests that TCA has an inherent induction effect on DNA repair activity. As this activity does not involve DNA strand breaks (negative response on DNA break test), the positive result in DNA repair assay may not be an indicator of significant DNA damage. These data indicate that the *in vitro* results obtained from human liver cells are consistent with the relative toxicity of chemicals based on whole animal toxicity testing. Compared with these *in vitro* results, nPB has less inherent toxicity to humans than TCA, TDE, TCE, and PCE. In addition, it clearly lacks the genotoxic potential of TCE and PCE. Results for iPB, a structural analog of nPB, but with *in vivo* evidence of greater inherent toxicity than nPB, indicated that only the EROD test was negative at all dose levels. The cytotoxicity test was positive at concentrations of 150 ppm and higher, while the two DNA-based tests were positive at concentrations of 100 ppm and higher. These results support the contention, based on standard toxicity tests and human occupational data, that iPB is mutagenic and more inherently toxic than nPB. Such results further support the likelihood that the metabolism of nPB is different to iPB. Specifically, it seems likely that the formation of radicals (ie, charged, highly reactive oxygen atoms) that can interact with DNA or impact cellular transport, either does not occur with nPB, or occurs at such a low rate that no cellular toxicity results from target tissue concentrations <500 ppm. Again, we believe this study marks the first time these solvents have been subjected to an identical series of human cell bioassay tests.

Acknowledgements

The bioassays and toxicological interpretation were supported by funding from EnviroTech International, who also provided the nPB and EnSolv® materials for testing.

Conflict of interest statement

The bioassays discussed in this article were performed by EnviroMed Laboratories of Windsor, Canada, at the request of Enviro Tech International, Inc., which also funded the studies. Enviro Tech International, Inc., is the manufacturer of the EnSolv stabilized nPB-based solvent discussed in the article. Enviro Med Labs and Enviro-Tech International, Inc., are unrelated entities with no affiliation of any kind. Three of the authors (Bruce Hasspieler, Douglas Haffner and Khosrow Adeli) were employed by EnviroMed at the time the bioassays were conducted. In addition, SLR International Corp., an environmental consulting firm, received fees from Enviro-Tech International, Inc., to provide critical review of the bioassay results and to prepare text evaluating the relative toxicity of the first group of tested chemicals. There is no corporate relationship between Enviro-Tech and SLR. One author, Mark Stelljes, is employed by SLR International Corp.

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ICF CONSULTING

HQ-RIN-00812-02-A

MEMORANDUM

To: Erin Birgfeld

From: Lauren Shapiro, Stacey Zee, Puttanna Honaganahalli, Edward Carr, Kara Altshuler, Reva Rubenstein, Mark Wagner

Date: January 21, 2002

Re: General Population Exposure Assessment for n-Propyl Bromide (EPA Contract Number 68-D-00-266, WA 1-05 Task 02)

INTRODUCTION

N-propyl bromide (NPB) is used in various solvent, aerosol, and adhesive formulations as an alternative to ozone-depleting substances (ODS) such as methyl chloroform. However, NPB has been shown to exhibit toxicity to the liver and reproductive system following inhalation exposure. To date, the potential for significant exposure of the general populations living near facilities that use n-propyl bromide has not been adequately assessed. This document attempts to provide a brief assessment of these exposures.

In general, the adhesive application industry is the largest emitter of n-propyl bromide and it is expected that the largest general population exposures will occur during the day-to-day adhesive application operations. Thus this assessment focuses on the long-term general population exposure as a result of routine adhesive application.

APPROACH

A risk screening exposure assessment has been conducted with the objective of determining the most reasonable foreseeable worst-case scenario for general population exposure associated with the use of n-propyl bromide. The exposure assessment uses a hypothetical adhesive application facility based on data collected from actual facilities (EPA 2001). The collected data have been used in this analysis to characterize the typical high-use adhesive application facility and an average-use adhesive application in an urban locale, assuming a row-house-type warehouse setting.

Two emission release scenarios were considered in the analysis:

1. Emissions released from the average-size adhesive application facility for the bonding of furniture and mattresses (S5); and

2. Emissions released from the urban row-house-type warehouse setting in which application of n-propyl bromide is used to bond furniture and mattresses (S6).

Please refer to the document entitled, "Occupational Exposure Assessment for NPB" for a description of the potential exposure setting in adhesives operations.

Average Size Adhesive Application Facility (S5)

The general characteristics used in the modeling of the average adhesive-application facility for the bonding of furniture and mattresses are:

- Average size facility: 65.7 meters x 65.7 meters;
- Average height of the facility: 7 meters;
- Typical lot size of 100 x 100 meters (~ 2.5 acres);

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- Urban setting;
- Average high use adhesive emission rate of 12.3 g/s;
- Facility operates 2000 hours per year (40 hr/week, 50 weeks/year);
- Average breathing height of 1.8 meters; and
- For the vented scenario the facility operates a ventilation system at the ASHRAE recommended flow rate of 0.50 cubic feet per minute/ft^2 of floor space. (i.e., 1.3 air exchanges per hour) (ASHRAE 1999). The stack was located on the roof, a short 0.3-m stack with an inside diameter of 0.8-m was assumed. Estimates of concentration included the effects of building downwash within cavity region, for both the near- and far-wake regions.

Within S5, three types of releases were considered:

1. Emissions released as a fugitive (non-vented) area source released upwards through the roof of the facility;

2. Emissions released as a single point source (vented) upwards on the roof of the facility; and

3. Emissions released as a fugitive (non-vented) source horizontally through cracks, leaks, window ventilation and shaft ventilation (natural ventilation).

Urban Row-house-type Warehouse Adhesive Application Operation (S6)

The general characteristics used in the modeling of the urban row-house-type warehouse adhesive application operation are:

- Three-story (30 feet) house, with a footprint of 25 feet x 40 feet;
- Urban setting;
- Average high use adhesive emission rate of 1.23 g/s;
- Facility operates 50 weeks per year, 8 hours per day, 5 days per week;
- Average breathing height of 1.8 meters;
- Nearest resident is adjacent to the house at a distance of 3-m; and
- For the vented scenario the facility operates a ventilation system at the ASHRAE recommended flow rate of 0.50 cubic feet per minute/ft^2 of floor space (i.e., 1.3 air exchange per hour) (ASHRAE 1999). The stack was located on the roof with a short 0.3-m stack with an inside diameter of 0.8-m. Estimates of concentration included the affects of building downwash within cavity region, for both the near- and far-wake regions.

Within S6, four types of releases were considered:

1. Emissions released as a fugitive (non-vented) area source upwards through the roof of the house;

2. Emissions released as a single point source (vented) upwards on the roof of the house;

3. Emissions released as a fugitive (non-vented) source horizontally through cracks, leaks, window ventilation and shaft ventilation (natural ventilation); and

4. Emissions released as a fugitive source horizontally using commercially available fans capable of accomplishing at least 1.3 air exchanges per hour.

Modeling System

EPA's SCREEN3 (EPA 1995) air dispersion model was used to assess dispersion of emissions using the full range of meteorological conditions (all stability classes and wind speeds) to estimate the highest 1-hour concentration. The SCREEN3 model is a "screening" model used to assess the likely maximum-potential concentration from a single source. The technique used here is typically used to evaluate air quality impacts of sources pursuant to the requirements of the Clean Air Act, such as prevention of significant deterioration (PSD), new source review, and existing sources of air pollutants, including air

toxics. The approach applied here is the initial-phase approach used to determine if either (1) the source clearly poses no air quality problem or (2) the potential for an air quality problem exists. If a potential problem exists then a more refined analysis is necessary following approaches discussed in the Guideline on Air Quality Models (Revised) (40 CFR Parts 51 and 52).

EPA's screening procedures (EPA 1992) for annual average concentration require that estimates be developed by multiplying the maximum 1-hour concentration determined by SCREEN3 by a factor of 0.10. This conservative number represents a worst-case maximum annual average concentration based on the likelihood that for these adhesive application facilities aerodynamic downwash and/or low emission height may be a problem. The multiplying factors are based upon general experience with relationships between maximum short-term concentrations and annual average concentrations based on observations. The factors account for the fact that the meteorological conditions that produce the highest 1-hour concentrations do not occur throughout the year (i.e., variations in wind speed, direction, atmospheric stability). The factors are intended as a way to estimate the maximum annual concentrations from short-term averages; a degree of conservatism is incorporated in the factors to provide reasonable assurance that maximum annual values will not be underestimated. For a site-specific analysis using site-specific meteorological data the use of the long-term dispersion model, Industrial Source Complex Long Term (ISCLT) is preferred, but unfortunately this approach cannot be used in this analysis because the site-specific meteorological data are not available.

Additionally, the SCREEN3 model can provide estimated concentrations for distances less than 100 meters (down to one meter as in other regulatory models). However EPA/OAQPS recommends caution when using results at distances of less than 100 meters, as concentrations may be suspect. A recent model validation study (EPA 1998) for similar conditions (flat terrain, non-buoyant, near-surface release, measurements at arcs positioned 50 m to 800 m downwind) using the short-term Prairie Grass tracer study have shown that the ISC3 model[1] predicts well within a factor of 2 for all downwind distances. The robust highest concentration statistic shows how the model predicts for the tail end of the distribution. For the Prairie Grass study Industrial Source Complex (ISC3) shows an overall tendency to over predict by an average of 50% for all downwind distances. This gives further support that the screening results are conservatively based and fair estimates of the near source concentration.

The certainty to which the ISC3 and SCREEN3 type model estimates are considered accurate have been evaluated in past studies (EPA 1982; EPRI 1983) by comparison with observed concentrations. The studies found that: (1) these types of models are more reliable for estimating longer time-averaged concentrations than for short-term concentrations; and (2) the models are reasonably reliable in estimating the magnitude of the highest concentrations occurring sometime, somewhere within an area. Errors in the highest estimated concentrations of 10 to 40 percent are found to be typical which is well within the factor of 2 accuracy that has long been recognized for these models as noted in the Guideline on Air Quality Models (Revised) (40 CFR Parts 51 and 52).

RESULTS

Results from the two scenarios are presented in Table 1 and 2 with a comparison to the reference concentration (RfC) for NPB. For the average sized high adhesive use facility (S5) the vented emission concentrations are lower than the non-vented emissions and are well below the RfC. These values include building downwash. The additional momentum from the ventilation system appears to be of sufficient magnitude to lower the concentrations over the non-vented scenario. All ventilation scenarios for S5 show no concentration exceeding the RfC.

For urban row-house-type warehouse (S6), again none of the scenarios show an exceedance of the RfC, although it is worth noting that the non-vented horizontal release with fans case shows relatively high values compared to other S6 cases. The two vertical release scenarios show maximum concentrations occurring at a distance of 30 meters from the house due to the height and upward momentum associated with the release.

[1] The basic dispersion algorithms contained within the SCREEN3 are identical to ISC3 – the ISC3 model allows the user more flexibility in inputting meteorological data, multiple sources, and source locations.

Table 1. Scenario 5: Maximum annual average air concentrations in the vicinity of an average sized high adhesive application facility using n-propyl bromide (S5)

Distance	Non-Vented Vertical Release Scenario	Vented Vertical Release Scenario	Non-Vented Horizontal Release Scenario	Reference Concentration Level
(m)	(ppm)	(ppm)	(ppm)	(ppm)
100	0.06	0.01	0.08	1
200	0.04	0.01	0.04	1
300	0.03	0.01	0.03	1
400	0.01	0.01	0.01	1
500	0.01	0.01	0.01	1
600	0.01	0.01	0.00	1
700	0.00	0.00	0.00	1
800	0.00	0.00	0.00	1
900	0.00	0.00	0.00	1

Table 2. Scenario 6: Maximum annual average air concentrations in the vicinity of a average adhesive using operation located in an urban row-house-type warehouse using n-propyl bromide (S6)

Distance	Vented Vertical Release Scenario*	Non-Vented Vertical Release Scenario	Non-Vented Horizontal Release (natural vent) Scenario	Non-Vented Horizontal Release (w/fans) Scenario	Reference Concentration Level
(m)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)
3	0.00	0.00	0.06	0.24	1
5	0.00	0.00	0.06	0.19	1
10	0.00	0.00	0.04	0.13	1
20	0.00	0.01	0.03	0.08	1
30	0.03	0.01	0.01	0.05	1
40	0.03	0.01	0.01	0.04	1
50	0.03	0.01	0.01	0.04	1
60	0.01	0.01	0.01	0.03	1
70	0.01	0.01	0.01	0.03	1
80	0.01	0.01	0.00	0.01	1
90	0.01	0.01	0.00	0.01	1
100	0.01	0.01	0.00	0.01	1

* Maximum cavity region annual average concentration of 0.02 ppm assuming half of all hours when facility is operating are conducive to downwash conditions

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Memorandum

To: Rich Morford, EnviroTech International

From Mark Stelljes, SLR

Re: Ambient Air Sampling at Sacramento Dry Cleaner

This memorandum summarizes methods and results of the ambient air sample collected during the August 22 and October 21, 2008 sampling events at Plant G located in Sacramento, California. The target analyte for this work was 1-bromopropane (n-propylbromide; nPB), the active ingredient in DrySolv® used to dry clean clothing at the store.

The dry cleaning machine using DrySolv® is a 1970s third-generation machine that had been using tetrachloroethylene (PCE) until it was recently reconfigured to use the new solvent. Since the machine is old, it should provide a reasonable worst-case estimate of air emissions from proper use of DrySolv®. Newer machines should have fewer leaks during use leading to lower emissions and exposure levels.

Methods

The methodology for this investigation was developed consistent with the California Environmental Protection Agency (CalEPA) Department of Toxic Substances Control (DTSC) for indoor air sampling. Since the purpose of the investigation was to identify potential exposure to nPB and to estimate potential daily exposure, the sampling plan was designed to identify "reasonable worst case" conditions within the building during typical operations. Part of the sampling program included collection of ambient air samples. One was located on a raised planter box just outside the front entrance of the facility. The planter box is approximately 2 feet off the ground. The other was located on the ground just outside the rear door of the facility; the door was kept open all day.

Sample containers were provided by the contracted laboratory, Air Toxics, Ltd. Individually certified Summa® canisters were used with flow controllers calibrated by the laboratory for TWA sampling. Seven (7) micrometer (µm) filters provided by the laboratory were used to prevent particulates from entering the containers. The vacuum of each sample container was

measured before, during, and after sampling to verify that the container was not leaking and that the flow controller was working properly. One trip blank canister was prepared by the laboratory and accompanied the other canisters during the investigation. The trip blank was filled with "zero air" at the laboratory following the sampling event.

The first round of sampling was conducted on August 22, 2008. The 8-hour time-weighted average (TWA) samples were collected beginning at approximately 5:55 am and continuing until approximately 1 pm. The dry cleaning machine was started at 5:50 am, so was operational during the period when the samples were being collected. All cleaning cycles were complete by 1 pm. The canister pressures were checked at the start, middle, and end of the sampling period. An SLR technician was present at the site during the entire sampling period. At 7 am, a photoionization detector (PID) was used that identified the presence of low levels of nPB throughout the back area of the facility. No odor was present except for immediately behind the machine. The presence of an odor indicates that some nPB may have escaped from the equipment during use. The odor threshold for nPB is approximately 10 ppm, implying that the concentration immediately behind the machine at this time exceeded 10 ppm.

Ambient conditions were recorded during the sampling period. Interior temperatures averaged approximately 75 degrees Fahrenheit during the morning and approximately 80 degrees Fahrenheit during the afternoon. Outside temperatures were in the upper 60s at the beginning of the sampling, and near 90 degrees at the end of the period. No rain events occurred at the facility in the ten days preceding the sampling event and the observable soil conditions were dry. Winds were calm during the majority of the morning.

One ambient sample was collected on August 22. Sample AS-6 was located on a raised planter box outside the front door of the facility. This sampling event was compromised by because one canister did not remain at this location over 8 hours. The sample container originally placed at this location was functioning normally. However, one of the canisters located indoors, closest to the dry cleaning machine, exhibited substantial pressure drop over the first few minutes indicating that the flow controller was not operating properly and was allowing air to enter the canisters too quickly. The flow into this container was stopped 13 minutes after the sampling period was initiated. Then this faulty controller sample container was moved to location AS-6, since during this initial sampling event we were more focused on obtaining accurate data from inside the facility to evaluate worker safety.

A second round of sampling was conducted on October 21, 2008 and two ambient samples (AMB-1 and AMB-3) were collected at the locations previously described. Both controllers worked effectively and no issues were reported during this second sampling event. The data resulting from this second sampling event represent the more accurate estimates of ambient concentrations; the sample from the first event contained air from a location close to the dry cleaning machine before it was moved outside. Temperatures were between 45 and 55 degrees during the sampling period, which ran from 6:15 am to 2:15 pm and again covered all cleaning cycles for the day.

SLR contracted Air Toxics Ltd. to provide certified containers, filters, flow controllers and a trip blank. Air Toxics Ltd. completed the analyses for the target analytes using TO-15 SIM. This method has a detection limit of 2.0 parts per billion (ppb) for nPB.

The ending pressures of all canisters were recorded on the chain-of-custody and checked upon receipt by the laboratory.

Results

Sample container AS-6 had a measured nPB 8-hour time weighted average concentration of 3 ppm (Table 1). However, the outdoor sample (AS-6) was moved from its initial location closest to the dry cleaning machine. The trip blank was non-detect for nPB.

Results from the second round of sampling were much lower. Location AMB-1, duplicating the AS-6 location from the August event, had a concentration of 0.016 ppm (16 ppb). Location AMB-3, just outside the open back door on the ground surface, recorded a TWA concentration of 0.19 ppm (190 ppb).

Table 1. Indoor Air Sampling Results
Swanson's Cleaners
1620 W. El Camino Blvd
Sacramento, California

Sample ID	Location	1-Bromopropane Concentration [a]	
		ppmv	mg/m^3
AS-6[b]	Outside Front Door	3.0	15
AMB-1	Outside Front Door	0.016	0.08
AMB-3	Pressing Area	0.19	0.95

Abbreviations:

ppmv = parts per million by volume;

mg/m^3 = micrograms per cubic meter.

Footnotes:
[a] 8-hour time weighted average as reported by Air Toxics, Ltd.
[b] Sample was compromised and data are considered suspect.

Discussion and Interpretation

As discussed under Methods, sample AS-6 was contaminated with air from the source of the dry cleaning solvent. Sample AMB-1 from the same location, collected following proper procedures, yielded a concentration of 16 ppb, which should be considered representative of ambient air immediately outside the building. This is well below any level of potential concern to human health.

Sample AMB-3 represents a worst-case outdoor air concentration. The HVAC system inside the facility was operating, creating a positive pressure at the back door. This forces air out of the building. The dry cleaning machine is located between the vent for fresh air and the back door. Therefore, air from around the machine is physically pushed out the door by the fan and the positive pressure. Since nPB is heavier than air, it sinks as it moves. The canister at AMB-3 was placed on the ground, where vapors will be higher than in the breathing zone. Therefore the worst-case ambient air estimate is 0.19 ppm. This is about 12 times greater than the concentration outside the front door, which is kept closed unless people are entering or exiting the store, and is located on the opposite side of the facility from the dry cleaning machine.

The back door is typically kept closed and locked, so the concentration at AMB-3 should be much lower under normal operating conditions.

Memorandum

To: Rich Morford, EnviroTech International

From Mark Stelljes, SLR

Date: January 19, 2010

Re: Ambient Air Sampling at Sacramento Dry Cleaner

This memorandum summarizes methods and results of the ambient air sample collected during the August 22, 2008 sampling event at Swanson's Cleaners, located at 1620 West El Camino Avenue in Sacramento, California. The target analyte for this work was 1-bromopropane (n-propylbromide; nPB), the active ingredient in DrySolv® used to dry clean clothing at the store.

The dry cleaning machine using DrySolv® is a 1970s vintage machine that had been using tetrachloroethylene (PCE) until it was recently reconfigured to use the new solvent. Since the machine is old, it should provide a reasonable worst-case estimate of air emissions from proper use of DrySolv®. Newer machines should have fewer leaks during use.

Methods

The methodology for this investigation was developed consistent with the California Environmental Protection Agency (CalEPA) Department of Toxic Substances Control (DTSC) for indoor air sampling. Since the purpose of the investigation was to identify potential exposure to nPB and to estimate potential daily exposure, the sampling plan was designed to identify "reasonable worst case" conditions within the building during typical operations. Part of the sampling program included collection of an ambient air sample, which was located on a raised planter box just outside the front entrance of the facility. The planter box is approximately 2 feet off the ground.

Sample containers were provided by the contracted laboratory, Air Toxics, Ltd. Individually certified Summa® canisters were used with flow controllers calibrated by the laboratory for TWA sampling. Seven (7) micrometer (µm) filters provided by the laboratory were used to prevent particulates from entering the containers. The vacuum of each sample container was

measured before, during, and after sampling to verify that the container was not leaking and that the flow controller was working properly. One trip blank canister was prepared by the laboratory and accompanied the other canisters during the investigation. The trip blank was filled with "zero air" at the laboratory following the sampling event.

The 8-hour time-weighted average (TWA) samples were collected on August 22, 2008 beginning at approximately 5:55 am and continuing until approximately 1 pm. The dry cleaning machine was started at 5:50 am, so was operational during the period when the samples were being collected. All cleaning cycles were complete by 1 pm. The canister pressures were checked at the start, middle, and end of the sampling period. An SLR technician was present at the site during the entire sampling period. At 7 am, a photoionization detector (PID) was used that identified the presence of low levels of nPB throughout the back area of the facility. No odor was present except for immediately behind the machine. The presence of an odor indicates that some nPB may have escaped from the equipment during use. The odor threshold for nPB is approximately 10 ppm, implying that the concentration immediately behind the machine at this time exceeded 10 ppm.

Ambient conditions were recorded during the sampling periods. Interior temperatures averaged approximately 75 degrees Fahrenheit during the morning and approximately 80 degrees Fahrenheit during the afternoon. Outside temperatures were in the upper 60s at the beginning of the sampling, and near 90 degrees at the end of the period. No rain events occurred at the facility in the ten days preceding the sampling event and the observable soil conditions were dry. Winds were calm during the majority of the morning.

SLR contracted Air Toxics Ltd. to provide certified containers, filters, flow controllers and a trip blank. Air Toxics Ltd. completed the analyses for the target analytes using TO-15 SIM. This method has a detection limit of 1.0 part per million (ppm) for nPB.

Two of the six canisters exhibited substantial pressure drop over the first few minutes, indicating that the flow controllers were not operating properly and were allowing air to enter the canisters too quickly. These canisters were originally located closest to the dry cleaning machine. The flow into these containers was stopped 13 minutes after the sampling period was initiated, and these containers were moved to peripheral areas and air was allowed to intermittently flow into the canisters for 10-15 minutes each hour. This allowed for the collection of a sample over the 8-hour sampling period, at discrete intervals. The ending pressures of all canisters were recorded on the chain-of-custody and checked upon receipt by the laboratory.

One of these two canisters (AS-6) was moved to the outdoor location and became the "ambient air" sample. This canister was originally at the location of AS-1, directly in front of the dry cleaning machine door. The beginning pressure at the start of the sampling period was 30 millimeters of mercury (mmHg), and had dropped to 7 mmHg by 6:08 am, or 13 minutes after sampling was initiated. Therefore, 75% of the vacuum was lost over this short interval. Over the next 7.5 hours with intermittent sampling (average of 12 minutes per hour), the vacuum pressure dropped to a final reading of 4 mmHg. At the midpoint of the sampling event, the

pressure reading on this canister was 5.5 mmHg. Based on how the intermittent sampling was conducted, ambient air was collected for approximately 85 minutes over the course of the sampling duration (10-15 minutes hourly for 7 hours). Adding the 13 minutes from the initial indoor location, AS-6 was operational for a total of approximately 100 minutes. Therefore, a total of 26 mmHg of vacuum was used during the 100 minutes (30 mmHg minus a final reading of 4 mmHg), and 23 mmHg of this total was lost during the first 13 minutes. Overall, this implies that 88% of the air entering this canister was from its initial location near the dry cleaning machine.

Results

Sample container AS-6 had a measured nPB 8-hour time weighted average concentration of 3 ppm (Table 1). Sample AS-1, located closest to the dry cleaning machine for all but the first 15 minutes of the sampling event, had a measured nPB concentration of 9.2 ppm.

Other samples had 8-hour time weighted average concentrations between 1.2 and 4.0 ppm, with lower concentrations reported from locations away from the dry cleaning machine (see Table 1). The 1.2 ppm sample was located among the sorting racks about 30 feet away from the dry cleaning machine. Based on these results, concentrations in the samples at the front counter (AS-5), located furthest from the dry cleaning machine (about 60 feet, with a partition between the counter and the working area of the facility), and the outdoor sample should both be lower than 1.2 ppm. However, the outdoor sample (AS-6) was moved from its initial location closest to the dry cleaning machine, and the front counter sample was also moved from its initial location near the dry cleaning machine (at location AS-2) due to similar vacuum issues discussed for AS-6. The trip blank was non-detect for nPB.

Discussion and Interpretation

The dry cleaning machine cycle lasts approximately 90 minutes; concentrations tend to be highest at the start of the cycle and at the end of the cycle when the door is opened to remove the clean clothes. The machine was used for 3 cycles that day, so the majority of vapor mass is assumed to be dominated by the short durations when the machine door is opened. This is supported by the low 1.2 ppm concentration from a sample located only 30 feet from the machine (AS-4).

PID readings from directly in front of the machine when first opened can be around 50 ppm, but were not that high at this location. Since nPB is heavier than air, it tends to sink to the ground, reducing the air concentration in the breathing zone quite rapidly after the machine is opened, which may stay open for 10 minutes as the laundry loads are changed.

Assuming the 9.2 ppm reading from AS-1 located closest to the machine is representative of the first 13 minutes of sampling, then the ambient air concentration over the 85 minutes when AS-6 was operational outdoors should be 1.6 ppm (9.2 ppm for 13 minutes and 1.6 ppm for 85 minutes results in an overall TWA of 3 ppm). However, the sorting rack sample (AS-4) had a time weighted average concentration of 1.2 ppm. This concentration should be higher than the

outdoor concentration, particularly since the indoor air is vented to the roof and not through the front door of the facility.

If we then assume that the nPB concentration at location AS-1 during the first 13 minutes was 15 ppm (which is consistent with the slight odor detected early in the day, indicating the concentration was in excess of 10 ppm), then the outdoor TWA concentration would be 0.75 ppm (13 minutes at 15 ppm and 85 minutes at 0.76 ppm results in an overall TWA of 3 ppm). This reflects a lower expected concentration outdoors than at AS-4, as discussed above.

Applying this same approach to the highest recorded sample (9.2 ppm at AS-1), we can assume air concentrations of 15 ppm over a 10-minute period three times during the day. Over the rest of the day, concentrations are likely consistent with those reflected from samples collected in the pressing area (2.8 ppm) and sorting racks (1.2 ppm; AS-3). The average concentration across these two latter locations was 2.0 ppm. The TWA assuming 15 ppm for 30 minutes and 2.0 ppm for 7.5 hours is 9.4 ppm, or essentially the same as the TWA measured in AS-1.

Therefore, the assumptions used to calculate an ambient air TWA of 0.75 ppm are validated by results from indoor air data. This TWA is below the analytical detection limit of 1.0 ppm.

Table 1. Indoor Air Sampling Results
Swanson's Cleaners
1620 W. El Camino Blvd
Sacramento, California

Sample ID	Location	1-Bromopropane Concentration [a]	
		ppmv	mg/m^3
1	Machine Source	9.2	46
2	Back Exit - inside	4.0	20
3	Pressing Area	2.8	14
4	Sorting Racks	1.2	6.1
5	Lobby	4.0	20
6	Outside - front	3.0	15

Abbreviations:

ppmv = parts per million by volume;

ug/m^3 = micrograms per cubic meter.

Footnotes:
[a] 8-hour time weighted average as reported by Air Toxics, Ltd.

Neurologic Abnormalities in Workers of a 1-Bromopropane Factory

Gaku Ichihara,[1] Weihua Li,[2] Eiji Shibata,[3] Xuncheng Ding,[2] Hailan Wang,[1] Yideng Liang,[4] Simeng Peng,[5] Seiichiro Itohara,[1] Michihiro Kamijima,[1] Qiyuan Fan,[2] Yunhui Zhang,[2] Enhong Zhong,[2] Xiaoyun Wu,[2] William M. Valentine,[6] and Yasuhiro Takeuchi[7]

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We reported recently that 1-bromopropane (1-BP; *n*-propylbromide, CAS Registry no. 106-94-5), an alternative to ozone-depleting solvents, is neurotoxic and exhibits reproductive toxicity in rats. The four most recent case reports suggested possible neurotoxicity of 1-BP in workers. The aim of the present study was to establish the neurologic effects of 1-BP in workers and examine the relationship with exposure levels. We surveyed 27 female workers in a 1-BP production factory and compared 23 of them with 23 age-matched workers in a beer factory as controls. The workers were interviewed and examined by neurologic, electrophysiologic, hematologic, biochemical, neurobehavioral, and postural sway tests. 1-BP exposure levels were estimated with passive samplers. Tests with a tuning fork showed diminished vibration sensation of the foot in 15 workers exposed to 1-BP but in none of the controls. 1-BP factory workers showed significantly longer distal latency in the tibial nerve than did the controls but no significant changes in motor nerve conduction velocity. Workers also displayed lower values in sensory nerve conduction velocity in the sural nerve, backward recalled digits, Benton visual memory test scores, pursuit aiming test scores, and five items of the Profile of Mood States (POMS) test (tension, depression, anxiety, fatigue, and confusion) compared with controls matched for age and education. Workers hired after May 1999, who were exposed to 1-BP only (workers hired before 1999 could have also been exposed to 2-BP), showed similar changes in vibration sense, distal latency, Benton test scores, and depression and fatigue in the POMS test. Time-weighted average exposure levels in the workers were 0.34–49.19 ppm. Exposure to 1-BP could adversely affect peripheral nerves or/and the central nervous system. ***Key words:*** **1-bromopropane, distal latency, nerve conduction velocity, neurobehavioral testing, neurotoxicity, ozone-depleting solvents, postural sway testing, reproductive toxicity, vibration sense.** ***Environ Health Perspect*** **112:1319–1325 (2004). doi:10.1289/ehp.6995 available via *http://dx.doi.org/* [Online 30 June 2004]**

Ozone-depleting solvents, such as specific chlorofluorocarbons and 1,1,1-trichloroethane, have been banned since 1996 in developed countries. Because they were used in large amounts in various industries, alternative compounds were introduced to the workplace. One such alternative compound is 1-bromopropane (1-BP; *n*-propylbromide, CAS Registry no. 106-94-5), which is used in the United States and Japan as a cleaning agent for metals, precision instruments, electronics, optical instruments, and ceramics (Ichihara, in press). It is also used in spray form as an adhesive in the United States (Ichihara et al. 2002). Environ Tech (2001) estimated the total amount of 1-BP commercially available for sale in the United States in the year 2000 was 1,967.9 metric tons (4,338,583 lb), which is comparable to 9.0, 31.0, and 10.6% of the amount of methylene chloride, perchloroethylene, and trichloroethylene used in adhesive/foam fabrication and metal cleaning in the same year in the United States. In Japan, the amount of 1-BP sold in 2003 was 1,125 metric tons, which is about double the 645 metric tons sold in 1998 (Association of Bromopropane Producers of Japan, unpublished data). In addition, in the workplace where cases of neurotoxicity had been reported, 1-BP was introduced as an alternative for methylene chloride (Ichihara et al. 2002). The benefits of using 1-BP instead of the chlorinated carbons are not clear. However, under pressure to regulate the use of chlorocarbons, 1-BP has been used as a surrogate, which is encouraged by the lack of measures to define the exposure limits. In this regard, previous animal studies revealed neurotoxicity and reproductive toxicity of 1-BP (Ichihara et al. 2000a, 2000b; Wang et al. 2002, 2003; Yamada et al. 2003; Yu et al. 1998, 2001). Exposure to 1-BP resulted in a dose-dependent limb muscle weakness and reduction of nerve conduction in rats (Ichihara et al. 2000a). It also resulted in myelin degeneration of peripheral nerves and swelling of preterminal axons in the medulla oblongata (Ichihara et al. 2000a). It was also revealed that 1-BP exhibits reproductive toxicity in both male and female rats (Ichihara et al. 2000b; Yamada et al. 2003). Thus, animal studies preceded human studies and warned about the potential neurotoxicity and reproductive toxicity of 1-BP in humans. The most recently reported cases also confirmed the neurotoxicity of 1-BP in humans (Ichihara et al. 2002; Sclar 1999). However, these case reports have limitations in terms of quantitative analysis. In 1999 we investigated a 1-BP factory, but this investigation was also limited because it was originally oriented to study the effects of 2-bromopropane (2-BP), which targets mainly reproductive and hematopoietic systems (Ichihara et al. 2004).

The aim of the present study was to assess the neurologic function and other health-related changes in workers exposed to 1-BP and compare the results with those of control workers in a beer factory.

Materials and Methods

Factories and workers. The subjects were female workers of a 1-BP production factory located in Yixing, Jiangsu Province, China. The survey was conducted 16–18 January 2001. The same factory mainly produced 2-BP in 1996 (Ichihara et al. 1999), but shifted the main production to 1-BP between 1996 and 1999 (Ichihara et al. 2004), and the product was only 1-BP at the time of the present survey. 1-BP was synthesized by incubating *n*-propranolol and hydrogen bromide under concentrated sulfuric acid. The product was purified by distillation and temporarily stored in ceramic containers. The crude product was then transferred to 20-L plastic vessels through hose pipe from the cock of the container and subsequently neutralized with hydrogen carbonate. The product was finally transferred to 1,000-L drums for storage and transport. The

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workers were at risk of exposure to 1-BP when *a*) placing the chemicals into the reaction pots; *b*) sitting close to the reaction pots to observe and record the temperature; *c*) taking out the crude product; *d*) adding the hydrogen carbonate and stirring; and *e*) pouring the product into the drums. In the final step, the workers added the product with hand scoops to adjust the product volume in the drum.

The surveyed factory has two similar-sized manufacturing plants, each measuring 9.7 × 24.4 × 7 m (width × depth × height). In each plant, a ventilating fan was ineffectively installed 6 m from the floor; no local ventilation fan was installed in the vicinity of the areas where workers might be exposed to 1-BP. The 27 surveyed workers who were engaged in the production of 1-BP in the factory were all female. As controls, we selected age-matched (± 2 years) females at random from 202 female workers in a beer factory in the same city. The control workers lived in the same area.

In the analysis of paired *t*-tests between 1-BP workers and controls, four 1-BP workers were excluded because no corresponding match of control workers from the beer factory could be recruited. However, the analysis by exposure level or period of exposure included those 1-BP female workers for whom no corresponding age-matched controls could be recruited. All workers who were hired after 1991 and for whom corresponding age-matched controls could be recruited were identified as 1991 workers. Among them, the workers who were hired after 1999 and were exposed only to 1-BP were defined as 1999 workers.

Medical examination. Signed informed consent was obtained from each worker for all examinations and interviews, according to the Declaration of Helsinki (World Medical Association 2002). All female workers in the 1-BP factory and the 23 age-matched beer-factory workers were clinically examined by a trained Chinese neurologist who was conducting medical research at the Department of Neurology, Nagoya University, Japan, and had a good command of both Chinese and Japanese languages.

The vibration sensation was evaluated using a vibrating tuning fork (128 Hz); the fork was placed on the dorsum of the metatarsophalangeal joint of the big toe or the dorsum of the metacarpophalangeal joint of the thumb, and the worker was asked to report when the vibration ceased. Immediately after reporting, the tuning fork was moved to the same site (big toe or thumb) of the examiner and the duration of the lasting vibration after the worker's report was recorded. It was difficult to assess the actual time when the delay time was < 2 sec, because it took some time (but < 2 sec) to move the tuning fork from the worker's body to the examiner's body. In addition, one worker reported total loss of vibration sense in the right toe. Therefore, the value could not be treated as a continuous value in the statistical analysis. The examiner was a trained female (38-year-old) neurologist who worked with every worker throughout the investigation.

Electrophysiologic studies. We conducted electrophysiologic studies in an air-conditioned room maintained at 24°C. The workers were acclimated to the room temperature for 30 min before the electrophysiologic studies. We examined distal latency (DL), motor nerve conduction velocity (MCV), F-wave conduction velocity (FWCV), and sensory nerve conduction velocity (SNCV). Electric stimulation and recordings were performed with a Neuropack evoked potential/electromyogram measurement system (model MEB5508; Nihon Kohden, Co., Tokyo, Japan). For measurement of DL and MCV, the stimulation site was just behind the medial malleolus (distal) and the center of poples (proximal), and the recording site was fixed 11 cm distal to the distal stimulation site on the abductor hallucis muscle.

Blood tests. The following blood tests were performed in each worker: red blood cell (RBC) count, hemoglobin, hematocrit, white blood cell (WBC) count, and platelet count, using a hematocell counter (Coulter JT, Coulter Electronics, Hialeah, FL, USA), as well as fructosamine (colorimetric method), blood urea nitrogen [urease ultraviolet (UV) method], creatinine (enzyme method), total protein (Biuret method), total cholesterol (enzyme method), creatine kinase (UV *N*-acetylcysteine method), aspartate aminotransferase (UV method), alanine aminotransferase (UV method), γ-glutamyl transferase (L-γ-glutamyl-3-carboxy-4-nitroanilide substrate method), lactate dehydrogenase (Wroblewski-LaDue method), alkaline phosphatase (*p*-nitrophenol substrate method), serum creatinine (alkaline picric acid method), vitamin B_1 (HPLC method), iron [2-nitroso-5-(*N*-propyl-*N*-sulfopropylamino)phenol method], ferritin, thyroid-stimulating hormone [radioimmunoassay (RIA)], luteinizing hormone (LH; RIA), follicle-stimulating hormone (FSH; RIA), and estradiol (RIA).

Neurobehavioral tests and postural sway test. Neurobehavioral testing [simple reaction time, digit span, Santa Ana, digit symbol, Benton, pursuit aiming test, Profile of Mood States (POMS)] was conducted based on the Chinese edition of the World Health Organization Neurobehavioral Core Test Battery (Chen 1988; Liang 1987) by trained Chinese researchers. Because neurobehavioral tests can be influenced by education level, we also conducted analyses with controls matched for age and education level. Postural balance was measured with a Gravicorder GS-30 stabilometer (Anima Co., Tokyo, Japan). The same instrument was used in all subjects throughout the investigation. Postural sway testing was performed as described previously (Yamamoto et al. 2001; Yokoyama et al. 1997). Briefly, the subject was asked to stand with big toes touching each other on the platform of the Gravicorder. The center of gravity was recorded every 50 msec with both eyes open for 1 min and closed for 1 min. The calculated values based on the center of gravity were *a*) the total length of excursion; *b*) envelope area; *c*) length of excursion per envelope area; *d*) rectangular area, representing the product of the range of the x-component (lateral) and that of the y-component (anteroposterior); *e*) root mean square area; *f*) the mean of *x*-axis or *y*-axis component of each recorded point; *g*) the center of range of the *x*-axis or *y*-axis component of points; *h*) power spectrum of the *x*-axis or *y*-axis at 0.02–0.2 Hz, 0.2–2.0 Hz, and 2.0–10.0 Hz, obtained by frequency analysis, with both eyes open and closed; and *i*) the Romberg quotient, representing the ratio of values measured with eyes closed to the value with eyes open for items *a* through *h*.

Assessment of exposure to 1-BP. Individual exposure levels during work shifts were evaluated with passive samplers (Sibata Scientific Technology Ltd., Tokyo, Japan) using the method described previously by Ichihara et al. (2004). A passive sampler was attached to each worker during one 8-hr shift and was collected immediately after the shift and kept in separate sealed bags at 4°C until analysis. The absorbed solvent in the sampler was analyzed 2 weeks after the investigation. In our previous study (Ichihara et al. 2004), we confirmed the stability of absorbed 1-BP in charcoal at 4°C for 2 weeks. For analysis, activated charcoal particles were taken from the samplers and then immersed in 2 mL carbon disulfide (Wako Pure Chemicals, Osaka, Japan) in a glass tube with a screw cap. The tube was shaken vigorously for 5 min and left to stand

Table 1. Characteristics of workers.

Characteristic	1-BP exposed (*n* = 23)	Control (*n* = 23)
Age (years)	36.2 ± 5.7[a]	36.2 ± 5.2
Height (cm)	160.3 ± 6.6[a]	158.8 ± 5.9
Education		
Elementary school	4	4
Junior high school	19	12
High school	0	6
University	0	1
Job duration (months)	27 ± 31	168 ± 67
Past job exposure to chemicals	0	4[b]
Previous medical condition	2[c]	8[d]

Data for age, height, and job duration are mean ± SD. Other values are numbers of workers.
[a]Not significantly different from the controls (paired *t*-test). [b]Includes formalin (2), ammonia (1), alkaline (1). [c]Includes cholecystitis (1), contraceptive use (1). [d]Includes anemia (2), gastritis (2), hysteromyoma (2), oophoritic cyst (1), cholecystitis (1), taking antihypertensive medications (1).

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for 1 hr; the supernatant was then injected into a gas chromatograph equipped with an electron ionization detector (GCD system G1800A, Hewlett Packard, Palo Alto, CA, USA). The concentration of 1-BP was quantified by the selected ion mode. The detection limit was 0.007 ppm by this method. The time-weighted average (TWA) was calculated based on the formula

$$\text{TWA} = \frac{\text{absorbed solvent (}\mu\text{g)}}{\text{sampling rate}\left[\frac{\mu\text{g}}{(\text{ppm} \times \text{min})}\right] \times \text{sampling time (min)}}$$

In our calculations, we used the value of 0.134 as the sampling rate of 1-BP. The value was determined by the diffusing cell method.

Statistical analysis. We used the paired *t*-test to compare continuous parameters of the exposure group and controls matched for age or age and education level. In this analysis, all indices of electrophysiologic studies, neurobehavioral tests, POMS test, stabilometer testing, and blood tests were compared with the age-matched controls, and the indices of neurobehavioral tests and POMS were also compared with controls matched for age and education level. We used the Wilcoxon test and Fisher's exact test to compare the delay time and abnormality of menstrual cycles, respectively, of the exposure group and the age-matched controls. In the analysis by exposure levels, the 27 exposed workers were classified into two groups: ≤ 2.64 ppm (n = 17) and ≥ 8.84 ppm (n = 7); data missing (n = 3). For analysis by length of exposure, the 27 exposed workers were again classified into two groups: ≤ 9.31 months (n = 10) and ≥ 16.33 months (n = 16); data missing (n = 1). We selected these cutoff values because they divided the two peak distributions when the histograms with column width of 2.5 ppm and 5 months, respectively, were drawn, whereas no values were found between 2.64 and 8.84 ppm and 9.31 and 16.33 months. In comparisons between groups stratified with fructosamine [≤ 246 µmol/L (n = 14) and 248–284 µmol/L (n = 13)] or vitamin levels [20–30 ng/mL (n = 13) and ≥ 31 ng/mL (n = 13); data missing (n = 1)], the groups were divided according to the median because there was no split in the distribution that formed two peak distributions. The *t*-test was applied when comparing continuous variables (electrophysiologic tests, neurobehavioral tests, POMS test, stabilometer tests, and blood tests) by exposure levels or length of exposure as well as the levels of fructosamine or vitamin B_1. For the analysis of delay time and frequency of menstrual cycles, we used Wilcoxon test and Fisher's exact test, respectively, for comparison according to exposure levels, length of exposure, and the level of fructosamine or vitamin B_1. We defined significance as the probability of $p < 0.05$.

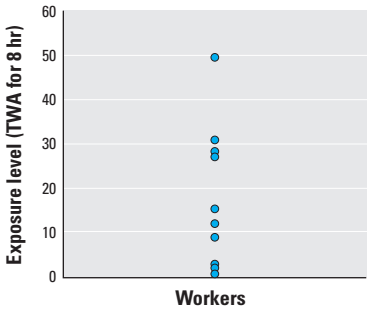

Figure 1. Exposure levels of each worker in a 1-BP factory (TWA for 8-hr shift). Values were obtained with passive samplers from workers who had age-matched controls (n = 23). Maximum = 49.19; minimum = 0.34; median = 1.61; geometric mean = 2.92 ppm.

Results

There were no differences in age and height between 1-BP workers and the age-matched controls (Table 1). The control group had a higher education level than the exposure group. Job duration of the exposure group was shorter than for the controls, probably because the area where the workers lived had been developed quite recently, so they had engaged in agriculture before employment in the factory. Four workers in the beer factory (controls) had been exposed to various chemicals (formalin, n = 2; ammonia, n = 1; alkaline reagent, n = 1) in occupational settings before their present jobs. None of the workers investigated was a smoker, and only one exposed worker and one control worker were alcohol drinkers. None of the workers investigated had a history of diabetes mellitus, which could cause polyneuropathy. Individual exposure levels ranged from 0.34 to 49.2 ppm (median, 1.61 ppm; geometric mean, 2.92; Figure 1).

Bromopropane workers, all of whom were hired after 1991 (1991 workers), had significantly longer DL and lower SNCV than did the age-matched controls (Table 2). Because the main product in the factory had shifted from 2-BP to 1-BP between 1996 and May 1999 (Ichihara et al. 2004), we also analyzed data for 1999 workers to examine the effects of exposure to 1-BP only. Examination of these workers showed the only significant change to be an increase in the DL compared with age-matched controls. However, the extent of the change in any electrophysiologic parameter in the 1999 workers tended, in general, to be similar to that of the 1991 workers. Reduced vibration sensation as tested on the right toe, left toe, right finger, and left finger was detected in 15, 13, 4, and 4 female workers, respectively (Tables 3 and 4). One worker showed complete loss of vibration sense on the right toe by tuning fork stimulation. The exposure level for this worker was 1.10 ppm, and she had a relatively high DL (8.8 msec) and low MCV (43.1 m/sec), FWCV (53.7 m/sec), and SNCV (38.8 m/sec). In contrast, none of the age-matched beer workers showed any abnormalities in vibration sensation in the toe and finger. The Wilcoxon test showed significant differences in the delay time bilaterally both in the feet and in the fingers between 1991 workers and controls. Analysis of 1999 workers also showed significant prolongation of the delay time on the toes bilaterally but not in the fingers. The percentage of 1999 workers who showed reduced vibration sensation (delay time ≥ 2 sec) on both sides of the foot and in the fingers was similar to that of 1991 workers.

Neurobehavioral tests showed lower values for the forward and backward digit span, Benton visual memory test, pursuit aiming test, POMS test (scores for tension, depression, anxiety, fatigue, and confusion) in the 1-BP workers than in the controls (Tables 5 and 6). Because the education level of 1-BP workers was different from that of the age-matched controls and because the education level could affect the results of neurobehavioral tests, these tests were analyzed after matching both education level and age (Tables 5 and 6). 1-BP workers had lower levels of backward digit span; correct scores in the Benton visual memory test; completed response in the pursuit aiming test; and tension, depression, anxiety, fatigue, and confusion in the POMS test than did controls matched for age and education level. Further analysis was conducted for these neurobehavioral tests on 1999 workers (Tables 5 and 6). Significant differences with the controls were found only in the Benton visual memory test and in POMS depression and fatigue.

The postural sway tests showed significantly lower power spectrum of the *x*-axis at 2.0–1.0 Hz with eyes open and *y*-axis at 0.02–0.2 Hz with eyes closed and significantly

Table 2. Electrophysiologic indices of workers exposed to 1-BP and of the controls.

	1991 workers	Age-matched controls for 1991	1999 workers	Age-matched controls for 1999
No. of pairs	23		12	
DL of nervus tibialis (msec)	8.05 ± 2.17*	5.96 ± 1.38	8.36 ± 2.38*	6.06 ± 1.43
MCV of nervus tibialis (m/sec)	49.8 ± 10.3	49.9 ± 8.2	51.3 ± 12.0	51.7 ± 10.7
FWCV of nervus tibialis (m/sec)	52.8 ± 3.5	55.1 ± 3.2	51.8 ± 2.8	55.0 ± 2.9
SNCV of nervus suralis (m/sec)	39.2 ± 3.5*	46.2 ± 6.6	39.2 ± 2.6	47.5 ± 8.5

Data are mean ± SD.
*$p < 0.05$ compared with age-matched controls (paired *t*-test).

higher power spectrum of the *y*-axis at 0.2–2.0 Hz with eyes closed (Table 7) in the 1999 workers than in the age-matched controls, but other parameters were not significantly different between the two groups (Table 7; Romberg quotients for all items, which also did not show any statistical difference, are not shown). The comparison of the 1999 workers and age-matched controls did not show any significant differences in postural sway tests (Table 7; Romberg quotients not shown).

Laboratory tests did not show any significant differences between the 1991 workers and age-matched controls (data not shown) except for significantly lower levels of vitamin B_1 (31.0 ± 5.6 vs. 34.3 ± 5.4 ng/mL) and low WBC count (5.7 ± 1.7 × 10^3/µL vs. 6.7 ± 1.8 × 10^3/µL) in the 1991 workers than in age-matched controls. For 1999 workers, only the WBC count was significantly lower than in the age-matched controls. In only one worker (42 years of age) in the control group, the fructosamine level (286 µmol/L) was above the upper limit of reference value (205–285 µmol/L). This worker had rather high DL (8.24 msec) and low levels of MCV (42.5 m/sec), FWCV (49.8 m/sec), and SNCV (39.5 m/sec) but did not show abnormal vibration sensation. This worker was not included in the education-matched testing because she had no education-matched individual in the exposure group. Comparison between the two groups stratified by fructosamine levels within all exposed workers (n = 27) showed significant differences only in higher levels of total protein (8.22 ± 0.53 g/dL), total cholesterol (197.7 ± 32.1 mg/dL), choline esterase (ChE; 366.1 ± 86.7 IU/L), LH (14.3 ± 14.3 IU/L), WBC (6.62 ± 5.15 × 10^3/µL), RBC (4.19 ± 0.38 × 10^6/µL), POMS confusion (5.31 ± 4.35), and lower estradiol level (35.4 ± 25.1 pg/mL) in the high-fructosamine group compared with the low-fructosamine group (total protein, 7.64 ± 0.24 g/dL; LH, 4.2 ± 3.4 IU/L; total cholesterol, 166.5 ± 28.7 mg/dL; ChE, 288.4 ± 37.8 IU/L; WBC, 5.16 ± 0.97 × 10^3/µL; RBC, 3.84 ± 0.38 × 10^6/µL; POMS confusion, 2.36 ± 1.91; estradiol, 63.2 ± 38.3 pg/mL).

Fisher's exact test did not show any difference between the 1991 and 1999 worker groups and their corresponding age-matched control groups with regard to the frequency of menstrual abnormalities after starting working in the 1-BP factory. Two workers in the exposure group had a short menstrual cycle. Similarly, one worker in the control group had a short menstrual cycle, and another reported a prolonged period of menstrual bleeding.

On the other hand, a comparison based on the exposure levels (≤ 2.64 or ≥ 8.84 ppm) showed that workers with high exposure levels showed significantly high values of MCV (56.4 ± 12.9 m/sec), FWCV (54.7 ± 2.8 m/sec), hematocrit (0.393 ± 0.032), and POMS tension (5.14 ± 1.77) and lower values of FSH (9.0 ± 6.3 mIU/mL) and POMS vigor (18.6 ± 2.5), compared with the low-exposure group (MCV, 47.3 ± 8.3 m/sec; FWCV, 52.0 ± 1.9 m/sec; hematocrit, 0.356 ± 0.034; POMS tension, 2.73 ± 1.49; FSH, 27.7 ± 35.3 mIU/mL; POMS vigor, 24.3 ± 4.0) but did not show any significant association with other examined indices. In the comparison by the length of exposure (≤ 9.31 or ≥ 16.33 months), the longer-exposure group had high levels of LH (13.5 ± 13.7 mIU/mL) and FSH (34.9 ± 34.9 mIU/mL) and lower levels of total protein (7.77 ± 0.30 g/dL) and vitamin B_1 (29.2 ± 5.1 ng/mL) than did the shorter-exposure group (LH, 3.3 ± 1.8 mIU/mL; FSH, 5.5 ± 2.1 mIU/mL; total protein, 8.18 ± 0.66 g/dL; vitamin B_1, 33.2 ± 5.0 ng/mL) but did not show any significant association with other examined indices.

Because the mean concentration of vitamin B_1 was significantly lower in the exposure group than in the controls, the values were compared between the two groups stratified by vitamin B_1 level within all exposed workers (n = 27). The comparison did not reveal any difference in the frequency of low vibration sensation or results of electrophysiologic tests, apart from lower levels of alkaline phosphatase (ALP; 129.3 ± 30.7 IU/L) and ChE (293.8 ± 52.8 IU/L) in the low vitamin group than high vitamin group (ALP, 169.5 ± 43.1 IU/L; ChE, 361.8 ± 84.1 IU/L).

Discussion

In the tested factory, isopropanol, hydrogen bromide, and sulfuric acid were also used as materials in the process of producing 1-BP. These chemicals are not considered to have neurotoxic effects, so it is unlikely that the low vibration sensation or change in DL is due to these chemicals. In the last survey of the same factory (Ichihara et al. 2004), we found that the main product of this factory was shifted from 2-BP to 1-BP. 1991 Workers include the workers who were hired before May 1999 and might have been exposed to not only 1-BP but also 2-BP before 1999 (Ichihara et al. 1999). In contrast, 1999 workers were exposed to 1-BP only. Therefore, the observed changes in the DL, vibration sense in both feet bilaterally, Benton visual memory test score, and depression and fatigue in the POMS test that were noted in 1999 workers are considered to be due to exposure to 1-BP. However, the effects of 2-BP cannot be excluded in 1991 workers. The SNCV showed significant changes in the analysis of 1991 workers but not in 1999 workers with age-matched controls. This is most likely due to the lack of power as a result of the reduction in the number of subjects, given the fact that the extent of change in sensory nerve conduction, as well as other electrophysiologic parameters, and the percentage of workers who showed reduced vibration sense among 1999 workers was similar to that of 1991 workers. This explanation might also be valid for other parameters that showed significant change in 1991 workers but not in 1999 workers.

Table 3. Number of workers with reduced vibration sensation in the foot.

Delay time[a] (sec)	1991 workers and age-matched controls (n = 23 pairs)				1999 workers and age-matched controls (n = 12 pairs)			
	Right foot*		Left foot*		Right foot*		Left foot*	
	1-BP workers	Controls	1-BP workers	Controls	1-BP workers	Controls	1-BP workers	Controls
< 2	8	23	10	23	5	12	5	12
2	0	0	1	0	0	0	1	0
3	3	0	1	0	1	0	1	0
4	2	0	4	0	1	0	1	0
5	2	0	1	0	1	0	0	0
6	4	0	4	0	3	0	2	0
8	3	0	1	0	1	0	1	0
10	0	0	1	0	0	0	1	0
∞[b]	1	0	0	0	0	0	0	0

[a]Delay time for vibration sensation by tuning fork stimulation (see "Materials and Methods" for details); time 0 is the time when the worker reported becoming unaware of the vibration. [b]One worker felt no vibration sense in the right foot. *$p < 0.05$, Wilcoxon test.

Table 4. Number of workers with reduced vibration sensation in the finger.

Delay time[a] (sec)	1991 workers and age-matched controls (n = 23 pairs)				1999 workers and age-matched controls (n = 12 pairs)			
	Right finger*		Left finger*		Right finger		Left finger	
	1-BP workers	Controls	1-BP workers	Controls	1-BP workers	Controls	1-BP workers	Controls
< 2	19	23	19	23	10	12	10	12
2	3	0	2	0	2	0	2	0
3	1	0	2	0	1	0	0	0

[a]Delay time for vibration sensation by tuning fork stimulation (see "Materials and Methods" for details); time 0 is the time when the worker reported becoming unaware of the vibration. *$p < 0.05$, Wilcoxon test.

Our animal studies (Ichihara et al. 2000a; Yu et al. 1998) preceded human case reports in revealing the neurotoxicity of 1-BP, which is far more potent than that of 2-BP (Yu et al. 1999, 2001). However, the results of animal studies had certain limitations in predicting symptoms or signs in human cases; for example, animal studies cannot detect any subjective symptoms that might reflect abnormalities of sensation or the central nervous system. It is sometimes difficult especially for morphologic studies to substantiate the adverse effects on the central nervous system because the structure of the central nervous system is far more robust than that of peripheral nerves or other organs. It is also difficult to evaluate imbalance during walking in rodents because four-footed animals are completely different from bipedal humans regarding the clinical signs of imbalance. Thus, information from human cases should help us understand the toxicologic targets of 1-BP. The first case was reported by Sclar (1999), and three other cases were recently reported by our group (Ichihara et al. 2002). All four cases showed diminished vibration sensation in the toe. Moreover, the present study showed that more than half of the workers exposed to 1-BP suffered from reduced vibration sensation. Considered together, these results suggest that vibration sensation in the toe might be susceptible to exposure with 1-BP. The previously reported cases also complained of urinary incontinence; numbness in the perineum, low back, and front of the thighs or buttocks; or headache (Ichihara et al. 2002); however, our factory workers did not report any such symptoms. This difference might depend on the levels or period of exposure to 1-BP because it is possible that our workers adapted to low levels but longer periods of exposure, leading to unawareness of symptoms.

In comparisons with age-matched controls, both the 1991 workers and 1999 workers showed prolonged DL but no change in MCV. This prolongation of DL without decrease in MCV parallels the results of animal studies, which showed earlier changes in DL than MCV in the tail nerve (Ichihara et al. 2000a). Such a pattern of changes might indicate predominant deterioration of the distal portion of the peripheral nerve or delay in chemical transmission between nerve terminals and muscle.

Comparison of data of 1991 workers with age-matched controls showed that the exposure group had lower levels of forward and backward digit span, Benton scores, pursuit aiming test scores, and POMS tension, depression, anxiety, fatigue, and confusion than did the controls. Because education level could influence the results of neurobehavioral tests, the results of the tests were reanalyzed after matching age and education levels. This reanalysis also revealed changes in the above items excluding forward digit span. When the analysis was limited to the 1999 workers, significant differences were found only in Benton visual memory test scores, POMS depression, and POMS fatigue, which could reflect the lack of power due to the small sample number. Digit span, pursuit aiming test, and the POMS test are considered the most sensitive indicators of exposure to organic solvents or neurotoxic agents such as lead (Zhou et al. 2002). Poorer performance in the POMS test was also observed in a Venezuelan study of workers exposed to organic solvents (Escalona et al. 1995). The present results of neurobehavioral tests could also suggest that 1-BP adversely affects the central nervous system in humans. Postural sway tests showed higher power of the *y*-axis (anterior–posterior sway) at 0.2–2.0 Hz and lower at 0.02–0.2 Hz with eyes closed, although such significant differences were not observed in 1999 workers. These results might be important because the cases found in the United States also showed unstable balance in walking. Clinically, patients with cerebellar disease and anterior lobe atrophy show anteroposterior sway, often with a spontaneous high-frequency body tremor of around 3 Hz (Diener et al. 1984). This anteroposterior sway might resemble the present result of the increase in the power of the *y*-axis at 0.2–2 Hz. However, the results of the postural sway tests noted in our study await further confirmation because the presence of cerebellar disorder in the formerly reported cases or present workers is not conclusive, and it is possible to attribute the unstable balance to a disorder of the peripheral nerves or spinal cord.

Diabetes mellitus could be a common confounding factor related to neurologic disorders by solvent intoxication. HbA1C and fructosamine are used as long-term (Bunn et al. 1976) and intermediate-term (1–3 weeks) (Baker et al. 1983) indicators of glucose levels in clinical settings. In the present study, we measured serum fructosamine levels. For the measurement of HbA1C, the blood samples had to be kept at 4°C but not frozen. However, the long transportation from the factory site to the laboratory could have potentially caused

Table 5. Results of neurobehavioral tests in the 1-BP group and controls matched for age or for age and education (mean ± SD).

Test	1991 workers (age-matched controls)	1991 workers (age/education-matched controls)	1999 workers (age/education-matched controls)
No. (pairs)	22	12	6
Simple reaction time (sec)	0.38 ± 0.12 (0.36 ± 0.12)	0.38 ± 0.12 (0.36 ± 0.12)	0.40 ± 0.14 (0.39 ± 0.12)
Digit span (digits recalled) forward	10.6 ± 2.3* (11.7 ± 1.4)	10.8 ± 2.5 (11.8 ± 1.3)	10.2 ± 3.1 (12.0 ± 1.1)
Digit span (digits recalled) backward	4.5 ± 2.2* (5.8 ± 1.8)	5.0 ± 2.6* (5.6 ± 1.4)	4.2 ± 2.3 (6.2 ± 1.6)
Santa Ana preferred hand	35.2 ± 3.6 (36.6 ± 4.8)	35.3 ± 4.0 (36.1 ± 4.3)	36.0 ± 2.4 (35.8 ± 5.2)
Santa Ana nonpreferred hand	33.5 ± 4.6 (32.8 ± 5.1)	33.8 ± 5.2 (33.7 ± 5.6)	32.8 ± 4.4 (35.5 ± 5.9)
Digit symbol (no. completed)	47.0 ± 17.5 (54.0 ± 10.2)	48.6 ± 19.8 (55.5 ± 5.6)	45.3 ± 21.9 (56.7 ± 6.7)
Benton (no. correct)	7.2 ± 1.7* (8.3 ± 1.4)	7.8 ± 1.5* (8.2 ± 1.3)	7.3 ± 1.8* (8.3 ± 1.0)
Pursuit aiming test (no. completed)	103.1 ± 16.9* (119.9 ± 19.1)	101.6 ± 17.9* (119.3 ± 20.4)	98.0 ± 11.4 (125.7 ± 17.0)

*$p < 0.05$, paired *t*-test.

Table 6. Results of POMS tests in the 1-BP group and controls matched for age or for age and education (mean ± SD).

Test	1991 workers (age-matched controls)	1991 workers (age/education-matched controls)	1999 workers (age/education-matched controls)
No. (pairs)	20	12	6
Profile of mood state			
Tension	4.4 ± 3.9* (7.7 ± 7.1)	4.1 ± 5.2* (10.2 ± 8.5)	6.8 ± 7.0 (9.6 ± 7.2)
Depression	4.8 ± 7.5* (10.5 ± 13.0)	5.6 ± 10.1* (13.3 ± 17.1)	10.0 ± 14.4* (12.8 ± 16.0)
Anxiety	4.1 ± 5.0* (10.2 ± 10.2)	4.7 ± 6.3* (12.6 ± 13.2)	7.0 ± 9.0 (13.4 ± 12.7)
Vigor	22.2 ± 4.3 (20.7 ± 6.7)	23.7 ± 3.9 (20.9 ± 6.9)	23.4 ± 4.5 (21.4 ± 9.2)
Fatigue	3.1 ± 2.6* (6.4 ± 4.0)	3.0 ± 3.4* (6.7 ± 5.2)	4.4 ± 4.8* (7.2 ± 3.8)
Confusion	3.7 ± 3.7* (7.1 ± 4.3)	3.3 ± 4.4* (7.7 ± 5.6)	5.0 ± 6.2 (5.6 ± 5.0)

*$p < 0.05$, paired *t*-test.

hemolysis of the collected blood and thus may have resulted in marked variability and errors in estimations. For this reason, HbA1C was not measured in the present study. The comparison between the exposed group and the controls did not show any difference in the level of fructosamine, and the comparison between the high-fructosamine group and low-fructosamine group within the exposed group also did not show any difference in indices related to the nervous system.

The levels of vitamin B_1 were lower in the entire exposure group than in the controls and in the longer-exposure group compared with the shorter-exposure group. Lack of vitamin B_1 is known to cause polyneuropathy, but the relatively low level of vitamin B_1 in the 1-BP factory workers could not fully explain the neurologic abnormalities. First, the level of vitamin B_1 in the exposed workers ranged from 20 to 43 ng/mL, which was within the normal range (20–50 ng/mL). Second, the low-level vitamin B_1 group showed no neurologic deficit such as vibration sensation or electrophysiologic indices, apart from a low score of POMS confusion, which would be weak evidence in substantiating the adverse effects on the nervous system.

Letz and Gerr (1994a, 1994b) investigated the confounding factors that could affect nerve conduction velocity and amplitude as well as vibrotactile and thermal thresholds, based on data from 4,464 subjects. Their studies revealed that the major covariates were height, examiner, skin temperature, and body mass index for sural sensory nerve and height, examiner, age, and body mass index for peroneal motor nerve conduction velocities. For vibrotactile threshold in toe, the major covariates were height, examiner, age, and body mass index. Our study design could control for the effect of examiner-, sex-, and age-matching pairs but not skin temperature-, body height-, or body mass index-matching pairs. Although body height was comparable on average between the exposure group and the controls and workers were acclimated to the room temperature before the electrophysiologic studies, the lack of pair matching for height, skin temperature, and body mass index should be carefully noted as a limitation of this study. Previous animal experiments demonstrated that exposure to 1-BP disrupted the estrous cycle and inhibited follicular development (Yamada et al. 2003). Two patients who worked in a cushion company in the United States also reported temporary irregularities of menstrual cycle (Ichihara et al. 2002). Although the exposure level for the two patients was not evaluated directly, such levels would be higher than 60–261 ppm, which were determined with the third case from the same factory after the former two cases were identified and ventilation was improved in the workplace. On the other hand, our study did not demonstrate significant differences in the prevalence of menstrual cycle abnormalities between the two groups. This might be due to the difference in exposure levels between U.S. cases (≥ 60–261 ppm) and our Chinese 1-BP factory workers (0.34–49.19 ppm).

Comparisons based on the exposure period showed higher levels of FSH and LH in the longer-exposure group than in shorter-exposure group. One explanation for this difference is that our group included four elderly women, who were excluded from the paired *t*-test analysis because of the lack of matched controls and who had high levels of FSH (42–100 mIU/mL) and LH (16–42 mIU/mL). Analysis based on exposure level did not show any relationship between exposure levels and these parameters, which were different between the exposure group and age-matched controls (paired *t*-test). The present analysis by exposure period and level has certain limitations. First, the number of subjects was too small and did not control for age. Second, the experimental design allowed only a single measurement of the exposure level, although the task of workers was not fixed and thus the exposure levels could vary. The exposure levels in 1999 in the same factory ranged from 0.9 to 170.5 ppm (geometric mean = 52.5 ppm) (Ichihara et al.

Table 7. Stabilometer test results of 1-BP exposure group and controls.

	1991 Workers	Age-matched controls	1999 Workers	Age-matched controls
No. (pairs)	23		12	
LNG (cm)				
Eyes open	71.7 ± 15.5	69.9 ± 20.8	71.5 ± 19.3	74.0 ± 19.4
Eyes closed	100.4 ± 25.1	91.1 ± 27.3	106.3 ± 29.7	95.0 ± 26.0
E AREA (cm^2)				
Eyes open	3.38 ± 1.26	3.69 ± 2.86	3.60 ± 1.52	3.88 ± 2.64
Eyes closed	4.94 ± 2.27	4.56 ± 3.62	5.65 ± 2.67	4.80 ± 4.15
LNG E AREA (per cm)				
Eyes open	22.9 ± 6.3	24.9 ± 10.9	21.8 ± 6.6	26.3 ± 13.7
Eyes closed	23.1 ± 7.9	26.3 ± 10.4	22.0 ± 8.8	28.8 ± 12.2
REC AREA (cm^2)				
Eyes open	7.53 ± 2.76	8.26 ± 6.39	7.87 ± 3.42	8.51 ± 6.08
Eyes closed	10.5 ± 5.6	10.3 ± 8.6	12.8 ± 6.1	10.5 ± 9.6
RMS (cm^2)				
Eyes open	1.62 ± 0.70	1.98 ± 1.67	1.82 ± 0.91	2.09 ± 1.46
Eyes closed	2.05 ± 1.01	2.05 ± 1.65	2.30 ± 1.25	2.22 ± 2.01
Mx (cm)				
Eyes open	0.019 ± 0.581	–0.123 ± 1.162	–0.166 ± 0.485	–0.008 ± 0.724
Eyes closed	0.010 ± 0.573	0.053 ± 1.228	–0.044 ± 0.557	0.217 ± 0.679
My (cm)				
Eyes open	–2.43 ± 1.15	–2.09 ± 1.37	–2.70 ± 1.05	–2.20 ± 1.41
Eyes closed	–2.29 ± 1.06	–2.06 ± 1.28	–2.50 ± 0.95	–2.41 ± 1.07
XO (cm)				
Eyes open	–0.004 ± 0.621	–0.142 ± 1.170	–0.186 ± 0.627	–0.009 ± 0.756
Eyes closed	0.119 ± 0.657	–0.003 ± 1.347	0.106 ± 0.771	0.231 ± 0.788
YO (cm)				
Eyes open	–2.50 ± 1.15	–2.07 ± 1.39	–2.79 ± 1.14	–2.22 ± 1.41
Eyes closed	–2.29 ± 1.01	–2.30 ± 1.42	–2.48 ± 0.86	–2.48 ± 1.09
Power spectrum of *x*-axis (lateral)				
Eyes open (%)				
0.02–0.2 Hz	61.1 ± 12.4	54.7 ± 17.0	62.5 ± 12.1	53.7 ± 14.5
0.2–2.0 Hz	38.5 ± 12.3	42.1 ± 13.6	37.1 ± 11.9	45.8 ± 14.4
2.0–10 Hz	0.36 ± 0.21*	0.46 ± 0.21	0.38 ± 0.24	0.46 ± 0.21
Eyes closed (%)				
0.02–0.2 Hz	45.7 ± 17.3	47.9 ± 12.2	48.5 ± 17.8	46.1 ± 12.7
0.2–2.0 Hz	52.5 ± 19.7	49.2 ± 16.3	48.4 ± 21.8	49.2 ± 19.7
2.0–10 Hz	0.53 ± 0.37	0.59 ± 0.33	0.60 ± 0.44	0.58 ± 0.34
Power spectrum of *y*-axis (anteroposterior)				
Eyes open (%)				
0.02–0.2 Hz	66.6 ± 14.0	70.7 ± 11.4	73.5 ± 11.1	70.9 ± 10.1
0.2–2.0 Hz	32.4 ± 12.8	28.9 ± 11.4	26.1 ± 11.1	28.6 ± 10.1
2.0–10 Hz	0.97 ± 2.62	0.42 ± 0.28	0.35 ± 0.16	0.45 ± 0.35
Eyes closed (%)				
0.02–0.2 Hz	51.6 ± 14.0*	61.2 ± 13.7	54.0 ± 11.6	55.0 ± 11.2
0.2–2.0 Hz	47.3 ± 13.0*	38.3 ± 13.7	45.4 ± 11.6	44.4 ± 11.2
2.0–10 Hz	1.03 ± 2.38	0.50 ± 0.28	0.56 ± 0.26	0.57 ± 0.25

Abbreviations: E, envelope; LNG, length of excursion; Mx, mean of *x*-axis (lateral) component of each recorded points; My, mean of *y*-axis (anteroposterior) component of each recorded points; REC AREA, rectangular area; RMS, root mean square area; XO, center of range of *x*-axis component of points; YO, center of range of *y*-axis component of points. Data are mean ± SD.

*$p < 0.05$, paired *t*-test. No significant difference was found between the exposed group and the controls in the Romberg quotient for all items (the ratio of values measured with eyes closed to the values with eyes open; data not shown).

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2004), which was far higher than in the present study. It is possible that the workers were exposed to 1-BP at higher levels than those measured in our study. Further assessment of long-term exposure levels is required to determine the relationship between 1-BP and exposure levels.

In summary, the present study suggested that exposure to 1-BP produces adverse effects on peripheral sensory and motor nerves and/or the central nervous system in humans. Estimation of long-term exposure levels is required to confirm the precise association between the health effects of 1-BP and exposure levels.

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Correction

In the manuscript published online, the numbers of workers listed in Table 1, especially in the footnotes, were incorrect; also, the statistical significance of values for the right and left fingers for 1999 workers and age-matched controls was incorrect. These errors have been corrected here.

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Derivation of an Occupational Exposure Limit (OEL) for n-Propyl Bromide Using an Improved Methodology

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n-Propyl bromide is an industrial solvent with increasing production volume due to its use as a replacement for fluorohydrocarbons. Therefore, the number of occupationally exposed workers is growing accordingly. This manuscript presents a thorough evaluation of available animal and human data to derive an occupational exposure limit (OEL) for n-propyl bromide. In addition, structure activity relationship within the homologous series of methyl, ethyl, and n-propyl bromide and an identical spectrum of effects caused by similar doses of 2-propyl bromide are used to increase the confidence of the analysis. The structure activity relationship was entirely consistent for acute and subchronic (neurologic, reproductive, and hematopoietic) toxicities and for mutagenic potency in that CH_3Br was more toxic than CH_3CH_2Br, which in turn was more toxic than $CH_3CH_2CH_2Br$ in every case in all species studied, including humans. Animals appeared to be similarly susceptible as, or slightly more susceptible than, humans to n-propyl bromide's toxicity. An OEL (60–90 ppm) was derived from a limited human study and supported by an across-the-toxic-spectrum comparison of animal and human data for both n-propyl and 2-propyl bromide. A carcinogenic classification was not deemed necessary at the recommended OEL based on very low mutagenic potency and the consistent structure activity relationship across the homologous series of these alkyl bromides.

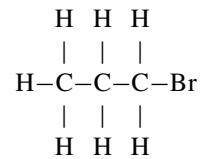
Keywords n-Propyl Bromide, Occupational Exposure Limit, Structure Activity

n-PROPYL BROMIDE

CAS: 106-94-5

1-Bromopropane, 1-Propyl bromide

C_3H_7Br



Chemical and Physical Properties

n-Propyl bromide is a colorless to light-yellow liquid with strong odor.

Chemical and physical properties include:[1–3]

Molecular weight: 123
Specific gravity: 1.3539 (20/4°C)
Melting point: −109.85°C
Boiling point: 71.0°C
Vapor pressure: 143 torr (25°C)
Refractive index: 1.4341
Solubility: 0.25g/100 ml water at 20°C; soluble in alcohol and ethyl ether
Conversion factors at 25°C, 760 torr: 1 ppm = 5.03 mg/m^3 and 1 mg/L = 198.8 ppm

MAJOR USES OR SOURCES OF OCCUPATIONAL EXPOSURE

n-Propyl bromide has been tried as an anesthetic but was without widespread use clinically. Since the reduction/banning of fluorohydrocarbons, it has been used increasingly as a replacement for them in cleaning solutions.

It is not known how many workers are currently exposed to n-propyl bromide but the number is increasing. The primary route of exposure is inhalation although dermal exposure may also contribute to total dose.

ANIMAL STUDIES

Acute

The acute intraperitoneal LD_{50} for n-propyl bromide was reported to be 2.5 g/kg in mice and 2.9 g/kg in rats.[3] The 30 minutes inhalation LC_{50} for n-propyl bromide in rats was determined to be 253 g/m^3 (50,394 ppm)[4] whereas the 4 hours LC_{50} was found to be 35 g/m^3 (6,972 ppm).[5] Thus, n-propyl bromide exhibits a clear c × t relationship under conditions of continuous exposure. Assuming a breathing rate of 200 L air per 24 hours, a body weight of 0.25 kg, and 100 percent absorption, this inhalation dose translates to 4.25 g/kg in terms of an oral dose. In good agreement with this calculation is an acute oral toxicity study indicating that the oral LD_{50} of n-propyl bromide in rats was greater than 2.0 g/kg.[6] An acute dermal LD_{50} study showed that n-propyl bromide was not toxic at 2.0 g/kg[7] to rats, which was to be expected based on the acute inhalation and oral toxicity because fluxes of dermally well-absorbed chemicals seldom exceed the lower mg/cm^2/hr range. Therefore, since the rate of elimination is faster than the rate of absorption through the skin only a fraction of the oral and inhalation peak concentration will be attained.

n-Propyl bromide is acutely less toxic than its lower homologues, ethyl bromide[8] and much less toxic than methyl bromide.[9] Acute toxicity in animals with all three chemicals is due to damage to the lungs resulting in edema and emphysema, which has also been reported in humans lethally intoxicated with methyl and ethyl bromide.[8,9]

Subchronic

Subchronic studies demonstrated that prolonged exposure of rats to n-propyl bromide caused neurotoxicity, reproductive/developmental toxicity, changes in hematologic parameters and perhaps slight liver toxicity. A 28-day inhalation study[10] in rats conducted under GLP conditions (6 hrs/day for 5 days/week) at nominal concentrations of 0, 2 mg/L (400 ppm), 5 mg/L (1,000 ppm), and 8 mg/L (1,600 ppm) demonstrated that severe toxicity occurred at the two higher doses in the form of low erythrocyte count, hemoglobin concentration, and hematocrit (including death at the highest dose). Atrophic changes in the male reproductive system were also ascribed to the n-propyl bromide treatment. Microscopic findings of vacuolization of white and gray matter in the central nervous system (CNS) and decreased brain weight were reported for all doses in this study, and therefore an NOEL could not be derived.

A 13-week inhalation study[11] examined the toxicity of n-propyl bromide also in rats at nominal concentrations of 0, 0.5 mg/L (100 ppm), 1 mg/L (200 ppm), 2 mg/L (400 ppm), and 3 mg/L (600 ppm). This study reported none of the lesions observed in the 28-day study. However, vacuolization of the liver and liver enlargement were observed at the two highest doses and a stated NOEL of 1 mg/L (200 ppm) was estimated for this effect.

Since changes were not seen in any hematologic parameters nor were any lesions reported in reproductive organs and since such effects were seen in the 28-day study at 800 and 1,600 ppm only, it is apparent that the NOEL for the hematologic and perhaps some reproductive effects of n-propyl bromide is about 400–600 ppm, which is also supported by a lack of consistent changes in the hematopoietic system below 800 ppm in the Ichihara et al. study.[12] The lack of vacuolization in the central nervous system even at 600 ppm in the 13-week study when contrasted with the findings of CNS vacuolization at 400 ppm in the 28-day study cannot be easily reconciled, although this could occur through adaptation. Nevertheless, this leaves us with the conclusion that the most sensitive endpoint of subchronic toxicity of n-propyl bromide is most likely neurotoxicity.

A third subchronic inhalation study conducted at 0, 200, 400, and 800 ppm for 8 hours per day every day of the week (7 days) for 12 weeks can be used to resolve the dose issue in n-propyl bromide's neurotoxicity.[13] This study also did not find vacuolization in the CNS even at 800 ppm (12-week study) compared to vacuolization at 400 ppm in the 28-day study, which provides further support for the validity of the assumption of an adaptive response. Nevertheless, this study confirmed the severe neurotoxicity of n-propyl bromide both in the CNS and in peripheral nerves (walking status, forelimb and hind limb grip strength, electrophysiological examination of tail nerve). According to the results of this study the most sensitive functional neurologic effect of n-propyl bromide is decreased hind limb grip strength with an LOEL of 200 ppm at 4 weeks into dosing. This study also demonstrates that adaptation is occurring because this effect is not observable with the same dose at later time points.

The structure activity comparison is also consistent for the homologous series of methyl-, ethyl- and n-propyl bromide with regard to their subchronic toxicity. All three compounds have been shown to cause neurotoxicity, reproductive toxicity, and impairment of the hematopoietic system.[8,9] The rank order of relative subchronic potency, both in terms of dose and time, is the same as that of acute toxicity: $CH_3Br > CH_3CH_2Br > CH_3CH_2CH_2Br$. For example, a five-day exposure to 200 ppm of methyl bromide for 6 hours per day caused a transient decrease in testicular nonprotein sulfhydryl content in rats during 3 days after cessation of dosing and plasma testosterone levels were suppressed during the same period of time,[14] whereas 200 ppm was a NOEL after 13 weeks of 5 times per week 6 hours daily exposure to n-propyl bromide indicating that it is much less potent in causing testicular effects than is methyl bromide.

Chronic/Carcinogenic

There are no chronic studies available on n-propyl bromide, nor has a carcinogenicity bioassay been conducted with this compound. However, carcinogenicity studies have been conducted in mice[15] with methyl bromide and in both mice and rats with ethyl bromide.[16] Methyl bromide's bioassay was negative in that at 33 ppm there was no evidence of carcinogenicity and at 100 ppm a large percentage of the animals died by 20 weeks and dosing was therefore discontinued for this group.

Since none of the high dose group animals developed cancer, it can be concluded that no residual effects of methyl bromide remained. Ethyl bromide was studied at 0, 100, 200, and 400 ppm (6 hrs per day, 5 days per week) for 2 years in a cancer bioassay using the same doses in rats and mice. The results were by and large equivocal except for uterine cancer, which was significantly elevated in mice at the highest dose (400 ppm) administered. The overall conclusion from these studies in conjunction with the clear mutagenicity response to both agents is that these two homologues of n-propyl bromide may be very weak carcinogens at overtly toxic doses and that the relative potency of ethyl bromide in terms of chronic toxicity is much lower than that of methyl bromide.

The lack of genetic toxicity of n-propyl bromide in all but one test performed is also in agreement with the structure activity analysis for acute and subchronic toxicities showing that $CH_3Br > CH_3CH_2Br > CH_3CH_2CH_2Br$ for genotoxicity. Therefore, it can be expected with confidence that if a carcinogenicity bioassay were to be conducted with n-propyl bromide at levels used in the ethyl bromide bioassay the outcome would be negative. Thus, even in the absence of a chronic bioassay it is clear that carcinogenicity is not an issue with n-propyl bromide because it could be only a very high dose effect or it would be not demonstrable. In agreement with this view is the finding that n-propyl bromide was found to be mutagenic only at cytotoxic doses, whereas the same tests were negative at non-cytotoxic doses (see section on Genotoxicity).

Reproductive/Developmental

There are two large-scale reproductive/developmental studies on n-propyl bromide in rats. The first was a range-finding experiment,[17] and the second a state-of-the-art reproductive toxicity study.[18] Nominal concentrations in the first study were 0, 100, 200, 600, and 1000 ppm, which was adjusted to 0, 100, 250, 500, and 750 ppm in the second study. It is clear that n-propyl bromide is a reproductive toxicant, since fertility in the highest dose group of the F_0 generation was reduced to zero and a statistically clear decrease was observed at 500 ppm in both generations. However, there were no apparent adverse developmental effects as judged from balanopreputial separation and vaginal patency.

Fertility indices were not significantly affected at 100 and 250 ppm in either the F_0 or F_1 generation. Histopathological changes (decreased number of corpora lutea, increased number of follicular cysts, and interstitial hyperplasia) in the ovaries correlated with infertility. The most sensitive endpoint of reproductive toxicity appeared to be an extended estrous cycle length at 250 ppm (F_1 females) and reduced weight of the epidydimis and prostate (F_0 males). Thus, this study provided an LOEL of 250 ppm and an NOEL of 100 ppm for the reproductive toxicity of n-propyl bromide in rats. LOELs in adult males ranged from 400–600 ppm depending on the endpoint and length of exposure. Since rats in the two generation study were exposed to n-propyl bromide in utero, during lactation, and for several weeks thereafter, pups do not seem to be more sensitive or perhaps only slightly so pre-, peri-, and postnatally than adults.

It is interesting to note that this study also showed evidence of liver enlargement at higher doses in agreement with the 13-week inhalation study and confirmatory evidence also for decreased brain weight in some of the higher dose groups as was reported in the 28-day inhalation study.

The overall conclusion from the animal data is that the most sensitive endpoint of toxicity of n-propyl bromide is peripheral/central neurotoxicity followed by reproductive toxicity, liver toxicity, hematopoietic toxicity, and CNS pathology with the possibility of cardiac and kidney effects at nearly lethal doses.

GENOTOXICITY STUDIES

The genotoxic potential of n-propyl bromide was tested on five *Salmonella typhimurium* strains: TA 1535, TA 1537, TA 1538, TA 9, and TA 100, both with and without metabolic activation. n-Propyl bromide was not genotoxic in any of the tests with or without metabolic activation.[19] Under the experimental conditions of a micronucleus test n-propyl bromide did not cause damage to chromosomes or the mitotic apparatus of bone marrow cells in mice at doses of 600 and 800 mg/kg/day in males and females, respectively.[20] Mutagenicity of n-propyl bromide was also tested in L 51784 mouse lymphoma cells for the potential to induce mutations at the thymidine kinase locus. The first test was negative with or without metabolic activation and there was lack of cytotoxicity. The second test was positive, especially without metabolic activation but the presence of cytotoxicity was noted. Another equivocal study allows us to illustrate the relative potency of 2-propyl bromide as a mutagen.[21] It took cytotoxic doses of 2,500–5,000 μg/plate of 2-propyl bromide to induce 300–450 revertants in the Ames test. In the same test system (TA 100) 0.15 μg/plate of ethyl bromide induced about 2,000 revertants,[16] indicating that 2-propyl bromide in this test system is at least 16,000 times less potent as a mutagen than ethyl bromide.

These findings are in agreement with structure activity relationships for decreasing genotoxicity in the homologous series $CH_3Br > CH_3CH_2Br > CH_3CH_2CH_2Br$. It is evident that n-propyl bromide is an extremely weak genotoxic agent and any such activity is most likely the result of cytotoxicity.

PHARMACOKINETIC/METABOLISM STUDIES

There are no studies reporting on the pharmacokinetics (plasma profile) of n-propyl bromide. Data on absorption, distribution, and excretion are also scant. However, one good study was published by Jones and Walsh,[22] which allows us to fill in the gaps with some limited confirmatory evidence from other publications.[23–25] Absorption, as is expected of such a small amphophilic molecule, is rapid by all routes of exposure (dermal, oral, inhalation) as this is also known for its structural analogues.[8,9]

About 42 percent and 56 percent of an i.p. injected dose was exhaled as the unchanged parent compound, by 1 and 2 hours after dosing, respectively. This implies a very swift absorption. Assuming rapid equilibration between blood and exhaled air, its half-life can be estimated to be about 1.3 hours.[21] n-Propyl bromide is probably distributed into total body water in the toxicologically relevant dose range because its water solubility is 0.25 g/100 ml. The non-exhaled part of the dose is mainly metabolized to three mercapturic acids and excreted with urine.

According to an in vitro study by Tachizawa et al.[23] by far the most important metabolite produced by hepatic microsomes is S-propyl glutathione, which then is converted by well-understood processes into the corresponding mercapturic acid. Part of the dose may bind to nonprotein sulfhydryl groups (e.g., glutathione) in other tissues such as the testes[14] and thereby cause toxicity indirectly. The reversibility half-life of this effect is also relatively short (estimated at 2 to 4 days from Hurtt and Working[14]).

Hydrolysis to propanol appears to be a negligible pathway of metabolism since only 1.4 percent of dose was exhaled as CO_2 but after administration of n-propanol, CO_2 is the major pathway of biotransformation/elimination.

In conclusion, n-propyl bromide is rapidly eliminated from the systemic circulation by exhalation and metabolic detoxification to mercapturic acids, which are rapidly cleared through the kidneys.

HUMAN STUDIES

Hematopoietic and reproductive toxicity of 2-propyl bromide has been reported in workers of a South Korean electronics factory.[26–28] Of 25 women, 16 had elevated FSH levels (and some also had elevated LH levels) and low estradiol levels, with most of them having had hot flashes, which is consistent with a diagnosis of secondary amenorrhea. Mild anemia and mild leukopenia were present in most female workers. Pancytopenia in 2 female workers was associated with hypoplastic (15–25% cellularity) marrow (bone biopsy). Prothrombin time, and kidney and liver function tests were normal in these workers. Among male workers azoospermia and oligospermia were reported. All workers complained of headache and/or dizziness. Ovarian failure was also reported in 16 women using solvent #5200 composed mainly of 2-propyl bromide.[29] No hematopoietic effects were reported in this study. The hematopoietic and reproductive effects are consistent with the animal database in that the reproductive effects seem to occur at lower doses.

The studies of Kim and associates[26–28] reported the concentration of 2-propyl bromide in the tactile switch assembly room at 12.4 ± 3.1 ppm. Short-term exposure levels were monitored inside a fume hood in the workplace and reported at 4,171 ppm.[27]

"Through the interview with tactile switch assembling workers, we were informed that they had believed the new solvents had little toxicity and had often put their heads inside the hoods of cleaning baths or had dipped their bare hands into the solutions without using any personal protective devices."[27]

The study by Koh et al.[29] did not report any information on exposure conditions that could be used to estimate levels of 2-propyl bromide causing toxicity in humans.

Two other studies reported on propyl bromide–exposed workers. A Japanese study conducted in China found no adverse health effects in workers exposed up to 111 ppm (median 89 ppm) of 2-propyl bromide.[30] A health hazard evaluation (HHE) has been conducted by NIOSH at the Custom Products, Inc. facility in Mooresville, North Carolina, which used n-propyl bromide as a solvent. Of 70 employees, 46 completed the questionnaire and provided blood for a complete blood count.[31] For statistical analysis the workers were divided into a low exposure group (117 ppm), a medium exposure group (170 ppm), and a high exposure group (197 ppm). No adverse effects were found with the exception of a possible association of an increased incidence of headaches in the highest (197 ppm) exposure group.

It is important to note that 2-bromopropane exposure results in the same spectrum of effects (neurotoxicity, reproductive and hematopoietic toxicities) at very similar doses as reported for 1-bromopropane.[32–34]

OEL RECOMMENDATION

There are three well-documented endpoints of toxicity of n-propyl bromide: neurologic, reproductive, and hematopoietic effects. Among these, the hematopoietic effects occur at the highest dose. Hematopoietic effects were observed only in animals exposed to levels above 600 ppm. More importantly, the theory of toxicology[35,36] implies that peak exposure is the key parameter for this effect since damage to the stem cells at any step of differentiation requires up to 120 days for complete repair because the half-life of new erythrocyte production in humans is about 30 days.[37,38] Thus, even infrequent (less than once per month) exposure to about 4,000 ppm as reported in the Korean study[27] will inevitably lead to this serious effect, which was not observed in humans exposed to lower concentrations for much longer periods of time.[30,31] A lack of liver effect in humans as opposed to animals is also consistent with occasional high peak exposure rather than to a low 8 hours time-weighted average.

Reproductive effects seem to occur at lower doses since the animal NOEL for this effect was 100 ppm. Also, the prevalence of amenorrhea among females and reduced sperm motility among males was higher than the incidence of hematopoietic effects. Nevertheless, reproductive toxicity was not found among workers exposed to up to 111 ppm[30] of 2-propyl bromide and up to 190 ppm[31] of n-propyl bromide, showing that humans are as sensitive as or less sensitive than rats with regard to this endpoint of toxicity. Peak concentrations may also be more important for this endpoint of toxicity as indicated by a recovery half-life of 2 to 4 days in non-protein sulfhydryl content in rats treated with methyl bromide.[14]

This leaves us with subtle neurotoxicity as the most sensitive endpoint of n-propyl bromide exposure, which is also consistent with other halogenated solvents.[39] Headache seems to have been the lowest dose effect of propyl bromides in humans[26,27,31] which is consistent with the subtle neurotoxicity effect in rats (transiently decreased hind limb grip strength at 100 ppm). From this it is evident that rats have similar or somewhat higher sensitivity to n-propyl bromide than humans. The human NOEL for n-propyl bromide–induced headache is reported to be 170 ppm.[31] Since the size of the population in that study was small, the use of a safety factor of two should be applied to protect nearly all workers, and a safety factor of three would be appropriate to provide a larger margin of safety from this adverse effect. Therefore, the recommended OEL for n-propyl bromide should be in the range of 60 to 90 ppm.

A skin notation is also recommended based on principles of dermal absorption and structure activity relationship with methyl and ethyl bromide, both of which are well absorbed through the skin.

Although peak concentration is an important issue with n-propyl bromide–induced hematopoietic effects and perhaps also regarding reproductive toxicity, no such recommendation is needed because the definition of excursion according to the American Conference of Governmental Industrial Hygienists (ACGIH®) would provide protection from any of the effects related to peak exposure concentrations.

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Development of an occupational exposure limit for *n*-propylbromide using benchmark dose methods

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Abstract

This paper presents the development of an occupational exposure level (OEL) for *n*-propylbromide (nPB) using benchmark dose methods. nPB is a non-ozone depleting solvent, proposed under the Significant New Alternatives Policy (SNAP) for use as a precision vapor degreaser. OELs have generally been developed on the basis of a NOAEL or LOAEL and application of uncertainty factors; this paper represents a departure from historic methods. Six recently completed toxicological studies were critically reviewed to identify (1) toxicologically significant endpoints, (2) dose–response information on these endpoints, and (3) uncertainties and limitations associated with the studies. Dose–response data were compiled and entered into the USEPA's benchmark dose software for calculation of a benchmark dose (BMD) and a benchmark dose low (BMDL). Once values were estimated for all relevant studies, they were then incorporated into a weight-of-evidence approach to develop a single BMD and BMDL representative of nPB. This approach is similar to that recently taken by USEPA to develop their own recommended OEL for nPB. USEPA's approach is compared and contrasted with ours, particularly in relation to the application of uncertainty factors (UFs) to generate a final OEL. There are no published criteria for application of UFs in developing an OEL. Although USEPA recommends utilizing a UF of 9, based on intraspecies variability and pharmacokinetic differences between rats and humans, to meet the goal of protecting healthy adult in a workplace setting, no uncertainty factor was deemed necessary for nPB in this paper. Therefore, the BMDL was recommended as the OEL.
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Keywords: Benchmark dose; *n*-Propylbromide; Dose–response; Occupational exposure level; 1-Bromopropane

1. Introduction

n-Propylbromide (nPB or 1-bromopropane) is used as an industrial solvent and has been proposed as a substitute for ozone-depleting substances (ODSs; Enviro Tech SNAP Petition, SNAP Docket No. A-91-42 VI-D-138). nPB could gain widespread use as a non-ozone depleting solvent. Over 55 toxicological studies have been conducted on nPB, the majority in the last four years. Early information (published before 1998) was used by the U.S. Environmental Protection Agency (USEPA) in 1999 to recommend preliminary air concentrations ranging from 50 to 100 parts per million (ppm) as protective of workplace exposure (USEPA, 1999). The bulk of information compiled in the last four years has only recently been reviewed. Since this work was completed, a recommended OEL using the standard NOAEL/LOAEL approach has been published (Rozman and Doull, 2002). Subsequently, the USEPA has conducted their own benchmark dose modeling for nPB with the goal of recommending an OEL, using the available toxicological database (USEPA, 2003). However, the Occupational Safety and Health Administration (OSHA) has not recommended a permissible exposure limit (PEL). In 1999, OSHA recommended

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nPB for testing by the National Toxicology Program (OSHA, 1999). In their nomination, OSHA stated "there is a pressing need to pin down the 'true' NOAEL—even better, to use standard study designs and statistical methods to establish a 'benchmark dose.'" In response to this request, this paper identifies a recommended occupational exposure limit (OEL) for nPB using statistical benchmark dose methods. This work predated both the Rozman and Doull (2002) and USEPA (2003) studies.

This paper critically evaluates the toxicological database compiled for nPB, focusing on toxicity in humans. Using USEPA's benchmark dose software (BMDS) Version 1.3 (USEPA, 2001a), a weight-of-evidence (WOE) approach was applied to the toxicity data to develop a recommended OEL. To fulfill this purpose, the literature on nPB was critically reviewed, and benchmark dose low (BMDL) concentrations were identified for various endpoints from the studies using the USEPA software. From these data, a single endpoint was selected upon which to base the OEL, and the use of an uncertainty factor (UF) was evaluated based on the strength of the toxicological database. Finally, an OEL was developed, and compared with the values developed by USEPA and Rozman and Doull.

1.1. BMDL and the traditional approach to occupational exposure levels

Traditionally, OELs are developed by identifying the lowest dose without deleterious effects (no-observed adverse effect level; NOAEL) and dividing by a series of UFs. In the absence of a NOAEL, a lowest-observed adverse effect level (LOAEL) is used (Fig. 1). This approach depends entirely on the doses used in the critical study. It ignores responses at other dose levels, and does not attempt to interpolate response as a function of dose. Advantages of the BMD approach are discussed later in this paper.

The BMDL resulting from this approach is more accurate than a NOAEL or LOAEL. The BMDL is typically calculated using the upper 95% confidence limit on the dose–response curve (Fig. 2). As a result of using the entire dose–response curve, lower UFs can be applied to adjust the BMDL to an OEL. UFs may be entirely unnecessary, depending on the strength of the database. As stated by Klaassen et al. (1996), "proposed [uncertainty] values...can range from the same factors used for the NOAEL to lower values because of increased confidence in the response level and increased recognition of experimental variability caused by the use of a lower confidence bound on the dose." Because of these advantages, the BMD approach was used in this study.

The approach presented in this analysis is a hybrid, applying the USEPA approach for developing reference concentrations (RfCs) and application of UFs therein, to OEL development. However, the goal of OEL development is to protect workplace exposure, while the goal of an RfC is to protect environmental exposure. Because these goals are different, USEPA methods are necessarily modified. As stated by USEPA (1994) "due to their derivation methods, attendant assumptions, and intended application, they (OELs) represent risk management values, and this distinction with the RfC as a dose–response estimate must be emphasized." They further state "OELs are generally time-weighted average concentrations of airborne substances to which a healthy worker can be exposed during defined work periods and under specific work conditions throughout a working lifetime, without material impairment of health." This is different than RfCs, which are relevant to those of any age and health status and are aimed at protecting the most sensitive members of the population, assuming long-term continuous exposures. Use of a BMD adds to the necessity of adapting USEPA's methods. Furthermore, as discussed later in this paper, the types of reproductive and developmental data applicable to OEL and RfC development differ (i.e., parent and offspring data).

OSHA and the American Council of Governmental Industrial Hygienists (ACGIH) have not formally recommended criteria for the application of UFs to OEL development. The ACGIH develops threshold limit

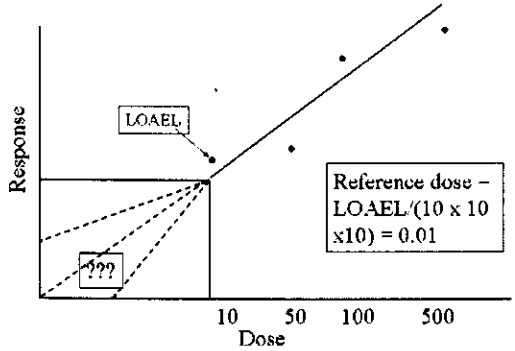

Fig. 1. Traditional approach example using NOAELs/LOAELs.

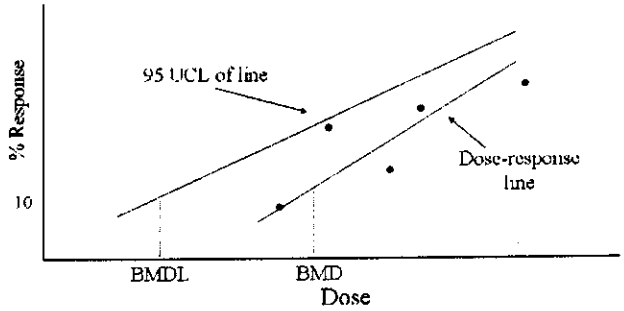

Fig. 2. Example using the benchmark dose approach.

nPB for testing by the National Toxicology Program (OSHA, 1999). In their nomination, OSHA stated "there is a pressing need to pin down the 'true' NOAEL—even better, to use standard study designs and statistical methods to establish a 'benchmark dose.'" In response to this request, this paper identifies a recommended occupational exposure limit (OEL) for nPB using statistical benchmark dose methods. This work predated both the Rozman and Doull (2002) and USEPA (2003) studies.

This paper critically evaluates the toxicological database compiled for nPB, focusing on toxicity in humans. Using USEPA's benchmark dose software (BMDS) Version 1.3 (USEPA, 2001a), a weight-of-evidence (WOE) approach was applied to the toxicity data to develop a recommended OEL. To fulfill this purpose, the literature on nPB was critically reviewed, and benchmark dose low (BMDL) concentrations were identified for various endpoints from the studies using the USEPA software. From these data, a single endpoint was selected upon which to base the OEL, and the use of an uncertainty factor (UF) was evaluated based on the strength of the toxicological database. Finally, an OEL was developed, and compared with the values developed by USEPA and Rozman and Doull.

1.1. BMDL and the traditional approach to occupational exposure levels

Traditionally, OELs are developed by identifying the lowest dose without deleterious effects (no-observed adverse effect level; NOAEL) and dividing by a series of UFs. In the absence of a NOAEL, a lowest-observed adverse effect level (LOAEL) is used (Fig. 1). This approach depends entirely on the doses used in the critical study. It ignores responses at other dose levels, and does not attempt to interpolate response as a function of dose. Advantages of the BMD approach are discussed later in this paper.

The BMDL resulting from this approach is more accurate than a NOAEL or LOAEL. The BMDL is typically calculated using the upper 95% confidence limit on the dose–response curve (Fig. 2). As a result of using the entire dose–response curve, lower UFs can be applied to adjust the BMDL to an OEL. UFs may be entirely unnecessary, depending on the strength of the database. As stated by Klaassen et al. (1996), "proposed [uncertainty] values...can range from the same factors used for the NOAEL to lower values because of increased confidence in the response level and increased recognition of experimental variability caused by the use of a lower confidence bound on the dose." Because of these advantages, the BMD approach was used in this study.

The approach presented in this analysis is a hybrid, applying the USEPA approach for developing reference concentrations (RfCs) and application of UFs therein, to OEL development. However, the goal of OEL development is to protect workplace exposure, while the goal of an RfC is to protect environmental exposure. Because these goals are different, USEPA methods are necessarily modified. As stated by USEPA (1994) "due to their derivation methods, attendant assumptions, and intended application, they (OELs) represent risk management values, and this distinction with the RfC as a dose–response estimate must be emphasized." They further state "OELs are generally time-weighted average concentrations of airborne substances to which a healthy worker can be exposed during defined work periods and under specific work conditions throughout a working lifetime, without material impairment of health." This is different than RfCs, which are relevant to those of any age and health status and are aimed at protecting the most sensitive members of the population, assuming long-term continuous exposures. Use of a BMD adds to the necessity of adapting USEPA's methods. Furthermore, as discussed later in this paper, the types of reproductive and developmental data applicable to OEL and RfC development differ (i.e., parent and offspring data).

OSHA and the American Council of Governmental Industrial Hygienists (ACGIH) have not formally recommended criteria for the application of UFs to OEL development. The ACGIH develops threshold limit

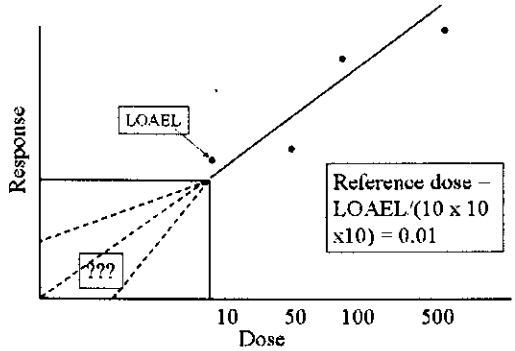

Fig. 1. Traditional approach example using NOAELs/LOAELs.

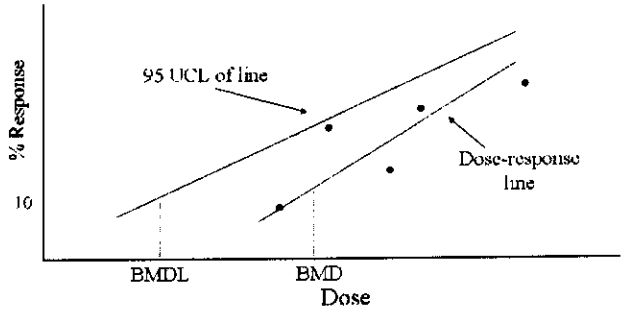

Fig. 2. Example using the benchmark dose approach.

values (TLVs), which have been historically used by OSHA to derive PELs. Based on a review of ACGIH TLVs, the ACGIH generally does not provide the rationale for the use of UFs. Also, OSHA does not typically provide such rationale. Therefore, USEPA criteria for application of UFs are also interpreted for use in this OEL development, as discussed later in this paper.

2. Summary of nPB toxicology

More than 50 toxicological studies have been conducted on nPB. The great majority of these studies were inhalation studies using laboratory rats. A brief overview of nPB toxicity, focusing on the inhalation exposure route, is provided below.

2.1. Toxicokinetics

There is sufficient evidence in both animals and humans that nPB is absorbed across the lung. However, blood–air partition coefficients measured for nPB in both the rat and human indicate a low potential for accumulation of nPB in the body (Clewell et al., 1998). The blood–air partition coefficient for humans is lower than in rats, indicating that relative inhalation absorption is likely higher in rats than humans. There is also sufficient evidence in laboratory animals that nPB is absorbed across the gut following oral administration; however the absorption efficiency through this route has not been measured.

nPB is primarily eliminated unchanged through the lungs in expired air. Once absorbed, nPB partitions predominantly into tissues rich in lipid (e.g., adipose tissue), with substantially lower levels in the liver, brain, and kidneys. nPB is not retained in the body; about 50% of an intraperitoneally absorbed dose is eliminated in expired air within 2h in rats (Jones and Walsh, 1979). The parent compound and metabolic products are excreted in the urine primarily as mercapturic acids (Clayton and Clayton, 1981; Jones and Walsh, 1979).

2.2. Toxicodynamics

n-Propylbromide is primarily metabolized through conjugation with glutathione, which results in the release of free bromine ions. In vitro nPB studies indicate that oxidation at the C2 and C3 positions occurs before conjugation of the alkyl group with glutathione (Jones and Walsh, 1979; Khan and O'Brien, 1991). Reactive intermediates have not been observed at detectable levels. The metabolic process is primarily through direct conjugation in a Phase II reaction. To a lesser extent, cytochrome P-450 appears to be involved in a Phase II reaction, which is then followed by conjugation with glutathione in Phase II. The same isoenzyme activity apparently catalyses the reaction in both humans and rats, but human enzyme activity is likely higher (Thier et al., 1999).

Because of the demonstrated presence of an epoxide during the metabolism of 2-bromopropane (and associated carcinogenic activity), the potential for an epoxide intermediate to be involved in nPB metabolism has been conjectured. The replacement of bromine with hydroxyl can occur through epoxidation, which leads to a short-lived reactive intermediate. Based on detected metabolites, it is clear that such a pathway, if present, is so minor that the risk of it significantly contributing to toxicity is negligible (Jones and Walsh, 1979). This is also supported by results of mutagenicity and carcinogenicity in vitro tests (EnviroMed, 1997), summarized later in this section.

Based on existing information and comparative toxicology gleaned from the critical studies reviewed in this report, it is possible that nPB toxicity is linked to saturation of the glutathione conjugation reaction. Micromolar concentrations of nPB have been shown to deplete glutathione (Khan and O'Brien, 1991). A low risk of toxicity may occur at doses below levels needed to saturate the pathway, but once that threshold is reached, toxicity occurs more frequently. Without knowledge of the quantitative reaction kinetics of nPB in vivo, it is difficult to relate a possible threshold dose at the target cells with a known air concentration of nPB. Data from a 90-day study in mice and rats by the National Toxicology Program, to be published in the near future, are expected to elucidate these points.

2.3. Acute inhalation exposure effects

nPB is an acute irritant, causing irritation to exposed eyes, skin, and respiratory and gastrointestinal tracts. Similar to halogenated solvents as a class, nPB has a depressant effect on the central nervous system (i.e., narcosis; Clayton and Clayton, 1981). Exposure may cause headache, dizziness, nausea, vomiting, or drowsiness and loss of consciousness (Enviro Tech; 2000). nPB is weakly narcotic compared to chloroform (Mueller, 1925). The 4-h 50% lethal concentration (LC_{50}) in rats exposed via nose-only inhalation is 6900 ppm, or 34,500 mg/m^3 (Elf Atochem, 1997). A whole-body 4-h inhalation LC_{50} in rats is 14,374 ppm (71,870 mg/m^3; Kim et al., 1999).

2.4. Longer-term effects

Several laboratory and clinical studies have been conducted on subchronic nPB exposure of animals and humans. The key animal studies, all based on inhalation exposure, are summarized below. Data from these studies were utilized to develop a BMD.

2.5. Four-week study

Rats were exposed to 1500 ppm (7500 mg/m^3) of nPB for 6 h per day, 5 days per week, for 4 weeks via whole-body inhalation (Ohnishi et al., 1999). Results indicated a statistically significant increased frequency of degeneration of the Purkinje cells in the cerebellum, in the fourth week. (Ohnishi et al., 1999).

2.6. Range-finding study

In a 28-day study by ClinTrials BioResearch (1997b), rats were exposed to nPB by whole-body inhalation. Rats were exposed for 6 h daily, 5 days per week, for 4 weeks in four dose groups: 0 (control), 400, 1000, and 1600 ppm. Toxicity was evident in the high-dose group, including mortality (about half of the animals), neurological signs (e.g., tremors, impaired gait, and hind limb weakness), and histopathological changes in the brain (cell vacuolization), spinal cord, and male reproductive system. Other effects on body weight gain, relative kidney weight, blood parameters (e.g., erythrocyte count), and sperm production were seen at multiple dose levels. Brain cell vacuolization may be reversible, and may be an artifact of how the tissues were prepared. Therefore, the toxicological significance of this effect has been questioned (Clewell et al., 1998). This effect has not been reproduced by others (see study summaries below) at similar exposure levels. However, because it is an indicator of central nervous system effects, this endpoint was further evaluated.

2.7. Ninety-day study

In a 90-day study by ClinTrials BioResearch (1997a), rats were exposed to nPB at 0, 100, 200, 400 or 600 ppm for 6 h per day, 5 days per week, for 13 weeks. Similar to the shorter studies previously discussed, this is a weekly exposure of 30 h. However, due to the longer study duration, total exposure was 390 h, or roughly three times the exposure in the 28-day study (ClinTrials BioResearch, 1997b). Fewer effects were noted in this longer-term study, likely due to the lower dose levels used. The only significant effect reported was slight to mild vacuolization in centrilobular liver cells in male animals exposed to 600 ppm, and male and female animals in the 400 ppm dose group. Changes were dose-dependent in the male but not the female. Hepatocyte vacuolization is reversible when chemical exposure ceases. This effect, therefore, is not necessarily adverse, especially at the relatively low levels of severity seen. None of the endpoints observed in the 28-day study were shown to be significant in this longer study, implying that exposure to concentrations in excess of 600 ppm may be necessary before such effects are observed.

2.8. Neurotoxicity study

In this study by Ichihara et al., male rats were exposed to nPB 8 h daily for 12 weeks to concentrations of 0, 200, 400, or 800 ppm via whole-body inhalation (Ichihara et al., 2000a). This is a weekly exposure of 56 h, totalling 672 h of exposure, almost twice the total exposure evaluated in the previously described studies. Also, exposure during this study was 7 days per week, so there was no recovery time for the exposed animals, unlike the previous studies. Therefore, it is not surprising that effects were observed at lower concentrations. The only effect reported at the low dose level (i.e., 200 ppm) was reduced hindlimb grip strength (Ichihara et al., 2000a). At the 400 ppm dose level, forelimb grip strength was also reduced, plasma creatinine phosphokinase (CPK) levels declined, and body weight was suppressed. At the high dose level, motor nerve conduction velocity and distal latency increased, indicating slower nerve conduction. Decreased cerebral weight and axonal swelling of the tibial nerve were also reported at 400 ppm.

2.9. Developmental and reproductive toxicity

Data from the three key studies discussed below were also utilized to develop a BMD for nPB.

2.10. Twelve-week study

In a study evaluating potential reproductive toxicity by Ichihara et al., male rats were exposed to nPB for 8 h daily for 12 weeks to 0, 200, 400, and 800 ppm by whole-body inhalation (Ichihara et al., 2000b). This is a weekly exposure of 56 h, and a total of 672 h of exposure over the study duration. Animals were exposed to almost twice the weekly dose compared to the 90-day study, and a greater maximum dose was administered (ClinTrials BioResearch, 1997a). The only effect seen at the low dose level (200 ppm) was a decrease in seminal vesicle weights. At the 400 ppm dose level, a decrease in number and percentage of motile sperm was reported, which was more pronounced at the 800 ppm dose level. Other effects on spermatogenesis were reported at the 800 ppm dose level. The authors concluded that the primary effect of nPB on the rat was inhibition of spermiation (Ichihara et al., 2000b).

2.11. Range-finding study

Huntingdon Life Sciences (1999) conducted this study to evaluate effects of inhaled nPB on the pregnant and lactating female rat and developing fetus and offspring. Fifty pregnant rats were exposed to 0, 100, 200, 600, and 1000 ppm nPB by whole-body inhalation for 6 h daily from implantation of the zygote through

weaning of F_1 pups. This represents a total of 31 days (or 186 h) of exposure for each F_0 animal. The F_1 pups were directly administered nPB on post-weaning days 1 through 7. Therefore, F_1 pups were exposed for 17 days through mother's milk, and an additional 7 days directly, totalling 24 days of exposure.

The only significant finding in the parent generation was an increase in relative liver and kidney weights in the 600 and 1000 ppm groups. In the F_1 generation, male pups in the high-dose group showed a significantly lower post-weaning body weight, and both males and females showed significant decreases in body weight gain post-weaning at the same dose level. In addition, dose-responsive decreases in serum glucose were seen in male pups at all dose levels, and gamma glutamyl transferase (GGT) levels for both male and female pups were statistically significantly increased at 1000 ppm, indicating potential hepatotoxicity. Finally, there was a statistically significant and dose-related increase in male pup relative adrenal gland weights at all doses. No effects on development or reproduction were identified by the authors.

2.12. Two-generation study

This comprehensive study by WIL Research Laboratories evaluated growth, mating, parturition, and lactation of the parental F_0 generation, and the following two generations in rats (F_1 and F_2). Development and survival of both F_1 and F_2 generations were also evaluated (WIL, 2001). The F_0 generation was exposed to nPB via whole-body inhalation 6 h daily for at least 70 days prior to mating, and daily throughout the breeding period and post-mating interval. Dose levels were 0, 100, 250, 500, and 750 ppm. This equates to a weekly exposure of 42 h, and a total of 420 h over this part of the exposure period. [Note that the Ichihara et al. (2000b) reproductive study used an 8-h daily exposure period, and the high dose level (800 ppm) was slightly higher than in the two-generation study.]

Beginning on postpartum day 22, F_1 pups were exposed to nPB identically to that used for the F_0 generation (WIL, 2001). In view of central nervous system pathology reported by others, comprehensive evaluation of both F_0 and F_1 animals included histopathological examination of many parts of the brain.

Key findings and comparison with endpoints reported in other studies are itemized below.

- There was complete infertility in the 750 ppm (F_0) group.
- Statistically significant reductions in sperm motility were seen in the 250 (F_1), 500 (F_0 and F_1), and 750 (F_0) ppm group males.
- A significant increase in abnormal sperm morphology was noted in the 500 (F_0 and F_1) and 750 ppm (F_0) group males.
- Decreased numbers of corpora lutea and an increased number of follicular and/or luteinized follicular cysts were observed in the 750 ppm group F_0 females. Interstitial hyperplasia, correlated with interrupted estrous cycles, was also observed in ovaries of the 500 ppm (F_1) and 750 (F_0) ppm group females.
- No histopathological changes in the brain, and no signs of central or peripheral nervous system effects were noted. The authors, therefore, questioned the relevance of changes in absolute brain weight observed in this study (WIL, 2001).
- Minimal to mild centrilobular hepatocyte vacuolization and increased plasma glycogen were noted. These changes were considered reversible and not adverse by the authors.

No significant effects were reported at the 100 ppm dose level in any generation. It should be noted that the exposure patterns in the studies discussed herein vary from typical workplace exposure patterns. For example, the majority of studies had an exposure pattern of 6 h daily over the exposure duration. This is a total of 42 h of exposure weekly, compared with a typical workplace setting of 8 h daily for 5 days each week (a total of 40 h of exposure weekly). Overall, however, total weekly exposures are very similar to those in a workplace setting. Therefore, no adjustments to exposure patterns were applied to these studies in OEL development.

2.13. Carcinogenicity

The USEPA, National Toxicology Program, and International Agency for Research on Cancer have not classified nPB with regard to potential human carcinogenicity. Both in vitro studies of human and animal cells and in vivo studies of laboratory animals have been conducted to evaluate potential mutagenicity and carcinogenicity of nPB (Elf Atochem, 1994–1996; EnviroMed, 1997). These findings indicate that in vitro results obtained from human liver cells are consistent with the relative toxicity of other solvents based on whole-animal toxicity testing, but that nPB has less inherent toxicity to humans than 1,1,1-trichloroethane (TCA). In addition, nPB clearly lacks the genotoxic (and hence, carcinogenic) potential of other halogenated solvents such as trichloroethylene (TCE), tetrachloroethylene (PCE), and 2-bromopropane. These findings are consistent with the assumption that any epoxide-forming metabolic intermediate is of negligible significance.

2.14. Occupationallepidemiological studies

A National Institute of Safety and Occupational Health study of 40 industrial workers indicated no

health effects, with concentrations in workplace air of up to 197 ppm (NIOSH, 1999). NIOSH is expected to publish results of other studies on nPB over the next two years.

A recent case report was published on health effects observed in three workers in a single facility using a solvent containing nPB in a spray gun (Ichihara et al., 2002). Based on the data presented, exposure concentrations are unknown but likely in excess of 150 ppm, and durations ranged from as little as two months to one year. The three female workers reported difficulty walking, dizziness, light-headedness, and headache, weakness and numbness in the legs, lower back and genitals, abnormal sensations in the legs, and difficulties with elimination of urine and stool. A staggering gait (ataxia) and decreases in vibration and temperature sensation were observed in the lower extremities of all three women. Physiological tests indicated no impairment to peripheral nerves or any CNS impacts. Based on this evidence, the authors concluded that nPB was likely the causative agent. The evidence is circumstantial at best because (1) no accurate dose levels were reported, (2) other potential causes were not adequately addressed, and (3) inadequate details were provided in the study to form causative conclusions. Moreover, the report did not state whether or not symptoms resolved when nPB exposure declined or stopped, and no follow-up study has been published.

A case report was published in 1999 describing a demyelinating condition predominantly affecting the lower extremities with CNS involvement in one worker exposed to a solvent containing nPB (Sclar, 1999) for up to two months. Based solely on comparison of these findings with the Ichihara et al. (2000a) neurological study in rats, where similar effects were seen at high concentrations (e.g., 800 ppm), the author postulated that nPB was the causative agent. No measures of exposure to nPB (e.g., biomarkers in urine) or other definitive tests were conducted to identify the causative agent, and possible confounding factors were not addressed. In the absence of exposure information, this case study does not provide useful information to address potential causes of the observed toxicity.

3. Benchmark dose methods

Historically, regulatory agencies used NOAELs and LOAELs in combination with UFs as the basis for developing exposure limits and critical toxicity values [e.g., PELs, RfCs, and reference doses (RfDs)]. However, there are many limitations with this approach (Crump, 1984; Gaylor, 1983; Leisenring and Ryan, 1992; USEPA, 1995). Some of the major limitations are listed below (USEPA, 2000):

- The NOAEL/LOAEL is highly dependent on dose selection since the NOAEL/LOAEL is limited to being one of the doses included in the study.
- The NOAEL/LOAEL is highly dependent on sample size, and does not account for the uncertainty in dose–response estimation due to study design.
- NOAELs/LOAELs do not correspond to consistent response levels for comparisons across studies, chemicals, or endpoints.
- The slope (or steepness) of the dose–response curve is not taken into account.
- A LOAEL cannot be used to derive a NOAEL if no NOAEL is defined in a study. Instead, an uncertainty factor of 10 is routinely assigned.
- A NOAEL is not an accurate estimate of a threshold (i.e., no-effect level).

The BMD approach eliminates many of these limitations, and was, therefore, used to develop an OEL for nPB. USEPA developed its BMDS to facilitate the application of BMD methods (USEPA, 2000). Research into model development began in 1995 (USEPA, 2001b). BMDS version 1.3, released in March of 2001, was used to conduct this analysis.

BMD methods are used within USEPA to develop RfDs and RfCs, which are in turn used to set environmental exposure standards for non-cancer human health effects. A stated goal of the BMD method is to "define a starting point of departure (POD) for the computation of a reference value (RfD or RfC) or slope factor that is more independent of study design" (USEPA, 2000). BMD methods involve fitting mathematical models to dose–response data and using results to select a BMD associated with a predetermined benchmark response (BMR). For example, a BMR could be a 10% decrease in relative organ weight, or a 10% increase in the incidence of a lesion or other endpoint. The BMR values used in this nPB analysis are consistent with recent USEPA practice. As stated by USEPA (2000), "the major aim of benchmark dose modeling is to model the dose–response data for adverse effects in the observable range (i.e., across the range of doses for which toxicity studies have reasonable power to detect effects) and then select a "benchmark dose" at the low end of the observable range to use as a 'point of departure' for deriving quantitative estimates below the range of observation."

A 10% response level is conventionally used for dichotomous endpoints (e.g., tumor formation) because it is at the low end of the observable range for many common study designs (USEPA, 2000). For continuous data (e.g., body weight gain), a variety of options can be used to identify a BMR. The convention utilized herein is to select a BMR equal to a change in the mean response equal to one control standard deviation from the control mean. This provides a standardized basis for comparison similar to the 10% response level for

dichotomous data, and generates an excess risk of approximately 10% for the proportion of study individuals either below the second percentile, or above the 98th percentile (depending on the direction of the adverse effect), relative to control individuals (USEPA, 2000). As a result, the BMR for continuous data differs for each endpoint and is a direct function of the variability of responses seen in the control animals.

In general, the BMDS utilizes models that express dose–response information as a function of dose, covariates (if applicable), and a set of value parameters that govern details of the shape of the curve. The models are fitted to a data set by identifying parameter values that adjust the predictions of the model for observed values of dose and covariates to be as close to the observed responses as possible. Such models are considered "nonlinear" because the response is not a linear combination of the parameters. They are more difficult than linear models to fit to data, and statistical inference is more approximate than with linear models. Nonlinear models do not necessarily have a biological interpretation. Criteria for final model selection are based almost exclusively on how well the model fits a given data set.

Applying the dose–response models using the BMDS involves four basic steps (USEPA, 2001b): (1) create a data set, (2) select the appropriate model based on the type of data evaluated (e.g., continuous or dichotomous), (3) specify the parameters associated with the model, and (4) run the model and review textual and graphic results. The BMDS provides results for each modeling run that includes a reiteration of the model formula and model run options, goodness-of-fit information, the BMD, and the estimate of the lower 95% confidence limit on the BMD, known as the BMDL. The focus of results discussed below is the BMDL, which is the value used as the POD for the computation of an OEL.

Goodness of fit is represented by a p value calculated by the BMDS. p Values measure the degree to which the observed dose and response data differ from the dose–response predictions. Small p values indicate that the actual data do not fit the model well. USEPA (2000) recommends use of a p value of 0.10 as the critical value for goodness of fit, instead of the typical value of 0.05 used for most statistical tests. They further advise that selecting the best model should include more analysis than solely using the model with the highest p value. For example, USEPA (2000) suggests that, after running the models for a given endpoint, the residuals from the model, data, and model graphs should be examined to ensure that the models adequately describe the data, especially at the low end of the dose–response curve. Then, a "best" model needs to be selected from among those retained. If the BMDL estimates for different models are within a factor of 3 they are considered indistinguishable, and the model with the lowest Akaike Information Criteria (AIC) value is selected to provide the BMDL. If the BMDLs are not within a factor of 3, USEPA (2000) recommends selecting the model with the lowest BMDL unless it appears to be an outlier. This approach was implemented for each endpoint and study combination identified for selecting a representative BMDL.

3.1. Endpoints considered for BMD analysis

The studies considered for quantitative evaluation included all multi-dose studies previously discussed: the 28- and 90-day studies (ClinTrials BioResearch, 1997a,b), the neurological study (Ichihara et al., 2000a), and the three reproductive/developmental studies (Huntingdon Life Sciences, 1999; Ichihara et al., 2000b; WIL, 2001). For each of these studies, endpoints were selected for BMD modeling on the basis of toxicological significance, relevance to humans, whether effects were test-related, evidence of a dose–response, statistical significance, and severity of effect. Additional guidance on interpretation of reproductive results was provided by USEPA (1996). A total of 60 endpoints across these six studies were evaluated for applicability to BMD modeling. Based on the nature of the significant endpoints, the following categories of endpoints were identified across the studies: (1) reproductive, (2) neurological, and (3) liver and blood.

In general, reproductive and neurological endpoints were the focus of the BMD analysis. Several endpoints in each category were excluded from quantitative analysis using the criteria discussed above. A subset of 38 endpoints from the six studies was evaluated using BMD modeling. These endpoints are shown in Table 1.

After conducting modeling for each of these 38 endpoints, 14 endpoints were eliminated from further consideration because no modeling results for these endpoints met the minimum criteria (e.g., p value for goodness-of-fit of at least 0.10). For each of the remaining 24 endpoints, where at least one model met minimum criteria, the model with the lowest AIC value was chosen to represent that endpoint, consistent with USEPA (2000) recommendations.

4. Results and discussion

BMDs and BMDLs for each of the 24 successfully modeled endpoints were identified and are presented in Table 2. A total of 10 reproductive endpoints across two generations was compiled, along with nine neurological and five liver and blood endpoints. There is a widespread range of values across endpoints, but the majority of values are in the range of 300–400 ppm. The lowest significant BMDL for each group of endpoints ranged from 156 to 263 ppm. Values below

Table 1
Endpoints evaluated using the benchmark dose modeling software

Critical effect	Study reference
Neurological endpoints	
Decreased forelimb grip strength in male rats	Ichihara et al. (2000a)
Decreased hindlimb grip strength in male rats	Ichihara et al. (2000a)
Decreased maximum motor nerve conduction velocity in male rats	Ichihara et al. (2000a)
Increased distal latency in male rats	Ichihara et al. (2000a)
Gray matter vacuolization in male rats	ClinTrials BioResearch (1997b)
Gray matter vacuolization in female rats	ClinTrials BioResearch (1997b)
White matter vacuolization in male rats	ClinTrials BioResearch (1997b)
White matter vacuolization in female rats	ClinTrials BioResearch (1997b)
Decreased plasma creatinine phosphokinase	Ichihara et al. (2000a)
Reproductive/developmental endpoints	
Parent generation (F_0) endpoints	
Fertility index (both sexes with identical results)	WIL (2001)
Increased number abnormal sperm	WIL (2001)
Reduced sperm motility	WIL (2001)
Decreased sperm count in the epididymis	WIL (2001)
Ovaries—reduced organ weight[a]	WIL (2001)
Decreased sperm count	Ichihara et al. (2000b)
Decreased testosterone level[a]	Ichihara et al. (2000b)
Decreased number of spermatozoa[a]	Ichihara et al. (2000b)
Decreased number of motile sperm	Ichihara et al. (2000b)
Increased percentage of tailless sperm	Ichihara et al. (2000b)
Increased percentage of sperm with abnormal heads	Ichihara et al. (2000b)
Increased number of degenerating spermatocytes per tubule[a]	Ichihara et al. (2000b)
Increased number of degenerating spermatocytes per 100 Sertoli nuclei[a]	Ichihara et al. (2000b)
Increased number of retained spermatids at basal region per tubule[a]	Ichihara et al. (2000b)
First generation (F_1) endpoints	
Increased number abnormal sperm[a]	WIL (2001)
Increased number unaccounted uterine implantation sites[a]	WIL (2001)
Decreased number viable pups per litter	WIL (2001)
Reduced sperm motility	WIL (2001)
Adrenals—increased relative organ weight[a]	Huntingdon Life Sciences (1999)
Decreased serum glucose levels (males)	Huntingdon Life Sciences (1999)
Increased serum γ-glutamyl transaminase (males)[a]	Huntingdon Life Sciences (1999)
Increased serum γ-glutamyl transaminase (females)[a]	Huntingdon Life Sciences (1999)
Second generation (F_2) endpoints	
Decreased number viable pups per litter	WIL (2001)
Liver and blood endpoints	
Liver—increased relative organ weight[a]	Huntingdon Life Sciences (1999)
Centrilobular hepatocyte vacuolization	ClinTrials BioResearch (1997a)
Decreased hematocrit level	ClinTrials BioResearch (1997a)
Decreased number of segmented neutrophils	ClinTrials BioResearch (1997a)
Decreased number of monocytes	ClinTrials BioResearch (1997a)
Decreased number of red blood cells[a]	ClinTrials BioResearch (1997a)
Decreased hemoglobin	ClinTrials BioResearch (1997a)

[a] No BMDS modeling results met minimum criteria for BMDL development.

156 ppm appear on Table 2, but are not considered significant BMDLs. Results and rationale for selection of significant BMDLs are separately discussed by type of endpoint below.

4.1. Reproductive endpoints

Reproductive endpoints are often the most sensitive endpoints of chemical toxicity, and provide important information regarding multi-generational effects of a chemical, including teratogenic, fetotoxic, and mutagenic effects. For nPB, reproductive endpoints were analyzed for the parent (F_0) generation in two different studies (Ichihara et al., 2000b; WIL, 2001), and the parent, first, and second generation of the same study (WIL, 2001). The only overlapping significant endpoint in both studies was sperm count in the F_0 rats. The BMDL was 232 ppm in the Ichihara et al. (2000b)

Table 2
Summary of BMD and BMDL estimates for *n*-propylbromide

Endpoint	Study reference	Benchmark dose (BMD; ppm)	Benchmark dose low (BMDL; ppm)
Reproductive			
I. Parent (F_0) generation			
Sperm count	Ichihara et al. (2000b)	380	232
Retained sperm in seminiferous tubules	Ichihara et al. (2000b)	194	103[a]
Sperm deformities	WIL (2001)	351	296
Sperm motility	WIL (2001)	343	**263**
Epididymal sperm count	WIL (2001)	717	585
Fertility index	WIL (2001)	448	356
II. First (F_1) generation			
Sperm motility	WIL (2001)	261	**156**
Litter viability	WIL (2001)	280	188
Plasma glucose level (males)	Huntingdon Life Sciences (1999)	554	333
III. Second (F_2) generation			
Litter viability	WIL (2001)	238	**169**
Neurological			
Forelimb strength	Ichihara et al. (2000a)	531	345
Hindlimb strength	Ichihara et al. (2000a)	286	**214**
Motor conduction velocity	Ichihara et al. (2000a)	632	369
Distal latency time	Ichihara et al. (2000a)	416	307
Plasma creatinine phosphokinase (CPK)	Ichihara et al. (2000a)	239	149[a]
Brain cell vacuolization:	ClinTrials BioResearch (1997a)		
Grey matter (females)		1178	985
White matter (females)		1535	969
Grey matter (males)		922	728
White matter (males)		285	146[a]
Liver and blood			
Centrilobular vacuolization (males)	ClinTrials BioResearch (1997b)	345	226[a]
Number of segmented neutrophils (females)	ClinTrials BioResearch (1997a)	1520	1175
Number of monophils (females)	ClinTrials BioResearch (1997a)	1545	1327
Hematocrit (females)	ClinTrials BioResearch (1997a)	642	401
Hemoglobin (females)	ClinTrials BioResearch (1997a)	631	**399**

Bold values represent recommended BMDL for each type of endpoint. *Abbreviations used:* BMD, benchmark dose; BMDL, benchmark dose low; ppm, parts per million.
[a] Not considered a significant BMDL.

study and 585 ppm in the WIL (2001) study (Table 2). The only other significant endpoint successfully modeled in the Ichihara et al. (2000b) study was the number of retained spermatids in the seminiferous tubules of F_0 rats. The BMDL associated with that endpoint was 103 ppm, the lowest of any of the 24 endpoints included in Table 2. This effect was not specifically evaluated by WIL (2001), although several other measures of spermatogonia function were quantified. This endpoint was not statistically significant at the 200 ppm dose level, but was significant at the 400 and 800 ppm dose levels. The resulting BMDL was below the lowest dose tested, and also below a dose level where no effects were reported (i.e., 200 ppm). The BMDL estimated using the retained spermatid endpoint in the Ichihara et al. (2000b) study was not considered appropriate for consideration because it was estimated to be below the NOAEL, and no supporting studies have been conducted to confirm this possible effect. Therefore, this endpoint was excluded from further evaluation. In their independent BMD analysis, USEPA (2003) also excluded this endpoint from quantitative evaluation.

Reviewing modeling results presented in Table 2, the lowest BMDL obtained for the F_0 generation from the WIL (2001) study was 263 ppm, for a decrease in sperm motility. This was slightly lower than the value based on sperm deformities, and substantially less than values for fertility index and other reproductive endpoints. This BMDL of 263 ppm is recommended as the BMDL representing reproductive endpoints in the parent generation for consideration in developing an OEL. Although the BMDL of 232 ppm for the Ichihara et al. (2000b) sperm count endpoint (Table 2) is lower than this value, the BMDL of 263 ppm is the lowest consistently reproduced value among those evaluated for the parent generation, particularly when compared to an average of the sperm count BMDLs of 232 and 585 ppm.

For the first (or F_1) generation of offspring, three reproductive endpoints were successfully modeled (Table 2). Sperm motility generated the lowest BMDL (156 ppm); the BMDL of 188 ppm, based on litter viability, was slightly higher (WIL, 2001). The BMDL for sperm motility was about 100 ppm lower in the F_1 generation than in the parent generation (i.e., 263 ppm; Table 2). This lowest value of 156 ppm is recommended as the BMDL representing reproductive endpoints in the F_1 generation for consideration in developing an OEL (Table 2).

As shown in Table 2, only one endpoint, litter viability, was successfully modeled for the second (or F_2) generation. The BMDL resulting from this endpoint was 169 ppm, which is consistent with the litter viability BMDL estimated for the F_1 generation (188 ppm). Therefore, this value of 169 ppm is recommended as the BMDL representing reproductive endpoints in the F_2 generation for consideration in developing an OEL, as shown in Table 2.

As previously discussed, the goals of protective occupational and environmental exposure levels are substantially different. Consequently, the type of data evaluated for each application also differ. The following text provides a discussion of these different applications.

The goal of this analysis is to develop a safe exposure level for the workplace. Therefore, the parent generation provides the most relevant values upon which to base an OEL. Additionally, since the presence of pregnant women and nursing mothers in the workplace could lead to fetal exposure, OELs are also intended to protect the fetus and breastfed infant under typical working conditions. However, exposure of rodent F_1 offspring in the two-generation study (WIL, 2001) continued from weaning into adulthood. Given the existing information, it is not possible to separate out impacts to the F_1 generation caused in utero and during suckling versus those caused during independent exposure of pups. This reduces the direct relevance of the results observed in the F_1 generation of this study for OEL development. Such impacts seen in adult F_1 or F_2 generation animals are relevant when discussing environmental exposure. Environmental exposure is expected to occur in all environments over several generations and involve both parents and their offspring. Such exposure is expected to be relatively constant (e.g., up to 24 h daily for residents) compared to adult workplace exposure (i.e., 8 h daily for 5 days per week).

For impacts in adult F_1 or F_2 generation animals such as those documented by WIL (2001) to be directly relevant to a workplace scenario, it would be necessary for both human parents to be exposed to nPB long-term in a workplace environment, conceive while employed there, and continue to work there throughout pregnancy and nursing following delivery. To be consistent with the exposure profile of the two-generation study, their children would then also need to be exposed from weaning (age 1–2 years) to adulthood and subsequent conception of the F_2 generation. This scenario is highly unlikely to occur in the workplace. By contrast to the environmental setting, results based on adult F_1 generation impacts (under conditions applied by WIL, 2001) and F_2 generations (under any conditions) should, therefore, receive less weight for occupational settings than results from the parent generation. Although adult F_1 and F_2 animal data are clearly applicable to RfC development, they are not directly applicable to OEL development. This is supported by USEPA (1994), "OELs are generally time-weighted average concentrations of airborne substances to which a healthy worker can be exposed during defined work periods and under specific work conditions throughout a working lifetime, without material impairment of health."

4.2. Neurological endpoints

Neurological endpoints were evaluated in two subchronic studies (ClinTrials BioResearch, 1997b, Ichihara et al., 2000a). The BMDLs based on the Ichihara et al. (2000a) study ranged from 149 to 369 ppm, as shown in Table 2. The four significant endpoints from the 28-day study (ClinTrials BioResearch, 1997b) were vacuolization of either gray or white matter in the brain in rats of each sex. Three of the four BMDLs from this study ranged from 725 to 1000 ppm. The fourth BMDL, corresponding to white matter vacuolization in males, was 146 ppm (Table 2). This appears to be an outlier, considering the abundance of evidence suggesting that the sexes are similar in their sensitivity to this chemical. In addition, brain cell vacuolization was not confirmed as an endpoint by the two-generation study (WIL, 2001). Only one male survived in the high-dose group studied by Ichihara et al. (2000a), which further decreases confidence in the BMDL based on brain cell vacuolization in male rats. In fact, as the authors stated in their report on the two-generation study, the toxicological significance of vacuolization in neural tissue is questionable because it is reversible once exposure stops (WIL, 2001). Also as previously noted, this endpoint may be an artifact of how the tissues were fixed. Therefore, the brain cell vacuolization-based BMDLs were not further evaluated. Given the lower BMDLs corresponding to other neurological endpoints (except for the discounted outlying result), this exclusion has no effect on the OEL.

As shown in Table 2, the lowest BMDL of 149 ppm from the Ichihara et al. (2000a) study corresponds to reduced plasma CPK, which is an enzyme used in muscle contraction. The second lowest BMDL derived from this study was 214 ppm, which corresponds to hindlimb strength in rats. Although reduced plasma CPK may be a biomarker for neuromuscular toxicity, it was not

specifically measured in any other critical study. Moreover, the goodness-of-fit p value associated with the model used to develop this BMDL was only 0.104, which marginally exceeds the threshold value of 0.100. This indicates that the model is not robust for the data set associated with this endpoint, and that the BMDL is uncertain. Therefore, reduced CPK was not used to represent nPB neurotoxicity. Instead, the second lowest BMDL of 214ppm for hindlimb strength is recommended to represent neurological endpoints for consideration in OEL development, as shown in Table 2. The associated goodness of fit p value for this endpoint was 0.60, which is much more robust.

4.3. Liver and blood endpoints

Liver and blood endpoints include measures of blood components (i.e., number of different types of white and red blood cells, and hematocrit and hemoglobin levels) and centrilobular vacuolization of liver cells. The latter was seen in the 90-day study (ClinTrials BioResearch, 1997a) while the blood endpoints were observed in the 28-day study (ClinTrials BioResearch, 1997b). The lowest BMDL for this group of endpoints was 226ppm for centrilobular vacuolization, the only relevant endpoint from the 90-day study. BMDLs from the 28-day study ranged from 400 to 1325ppm. The authors stated that centrilobular vacuolization was considered reversible and not adverse (ClinTrials BioResearch, 1997a). Therefore, this is not a toxicologically significant endpoint, and was not further evaluated. Instead, the second lowest BMDL of 399ppm, for reduced hemoglobin in female rats, is recommended to represent liver and blood endpoints for consideration in developing an OEL, as shown in Table 2.

4.4. Summary of BMDLs

The BMDLs recommended for each of the five groups of endpoints are shown in bold type in Table 2. These values are summarized below:

• Reproductive, parent generation (sperm motility)	263ppm
• Reproductive, F_1 generation (sperm motility)	156ppm
• Reproductive, F_2 generation (litter viability)	169ppm
• Neurological (hindlimb strength)	214ppm
• Liver and blood (hemoglobin)	399ppm.

These five BMDLs are very similar, and differ by a factor of approximately 2. They incorporate endpoints from three different organ systems, and encompass three generations of test animals. The lowest of these BMDLs is 156ppm. This value is for sperm motility in the F_1 generation, which was also a significant endpoint in the parent generation. Due to the reproducibility of this endpoint, the rigorous study protocol and thorough documentation (WIL, 2001), and the consistent pattern of toxicity seen with regard to BMDL values, the BMDL of 156ppm is recommended to represent the toxicity of nPB for purposes of developing an OEL. Because this is based on an endpoint in the F_1 generation, this BMDL should be considered conservative for occupational exposure, in light of the preceding discussion. In their independent BMDL analysis, USEPA (2003) questioned whether data from the F_1 generation were applicable to derivation of a workplace exposure limit, particularly in relation to the potential mechanisms by which nPB exerts its effects on the reproductive system. They stated that the available data do not rule out the possibility that the effects on the F_1 generation occurred as a result of effects on parental germ cells or effects mediated by changes to the endocrine system. However, they concluded that, in view of the lack of mechanistic data on potential *trans*-generational effects of nPB, that use of data from the F_1 generation was appropriate and protective.

These results are remarkably similar to those developed by USEPA in their independent analysis of the nPB database. They used decreased sperm motility in F_0 and F_1 males from the WIL (2001) study, and liver cell vacuolization in male and female rats from the ClinTrials BioResearch (1997a) 90-day study. Their resulting recommended BMDL was 169ppm, based on the same sperm motility endpoint we used to generate our recommended BMDL. This equated to 177ppm after dosimetry adjustments. Therefore, in essence the only difference between the OEL recommended in this paper and that recommended by USEPA is in the use of uncertainty factors. This is further discussed below.

4.5. Uncertainty factors

As discussed in Section 1, neither the ACGIH nor OSHA has published guidance on the application of UFs in setting a workplace exposure level. The USEPA offers some guidance for the use of UFs, which are used to downwardly adjust a NOAEL or LOAEL to a RfC or RfD. However, this is applicable to environmental, not workplace exposure. The following discussion provides an adaptation of USEPA's approach. USEPA (1994) clearly states that there are differences in development of RfCs and OELs. They state "the evaluation of toxicity data by agencies deriving OELs may differ from that of EPA with respect to weight-of-evidence classification, application of UFs, and other issues...the use of OELs is established to protect the average healthy worker (ages 18–65 years) against the adverse effects of inhaled pollutants to which they are exposed only a fraction of a

day (i.e., during a typical 8-h work shift). Inhalation reference concentrations, however, are relevant to those of any age and health status and are aimed at protecting the most sensitive members of the population, assuming long-term continuous exposures." While a healthy worker population will have individual variation, such variability is incorporated into the BMD approach by accounting for individual variability in response across the tested animals. The assumption that must be met in order for an uncertainty factor to be used to adjust a BMDL based on individual variability in a healthy population is that the individual variability in that population is wider than that in test animals. There is no inherent rationale to make this assumption. Nevertheless, USEPA used an uncertainty factor of 3 to account for sensitive individuals in their OEL derivation.

Historically in developing RfCs and RfDs, the USEPA uses separate UFs, each of which may be up to 10, to account for each of the following criteria when using the NOAEL/LOAEL method: (1) protection of sensitive individuals within the receptor population, (2) extrapolation of toxicity data from animals to humans, (3) extrapolation of subchronic toxicity data to chronic exposure durations, and (4) extrapolation from a lowest-observed adverse effect level (LOAEL) to a no-observed adverse effect level (NOAEL) to assess toxicity. A modifying factor (MF), generally no higher than 3, is typically also used to account for other considerations such as perceived adequacy of the scientific data. The UFs and the MFs for a given chemical are then multiplied together to provide a total UF, which is then used to derive a chronic RfD. The higher the total UF, the greater the degree of uncertainty and conservativism in the resultant RfD. Given the statement from USEPA that application of UFs differs between RfCs and OELs, each criterion is discussed below for its applicability to an OEL for nPB.

4.6. Extrapolation From LOAEL to NOAEL

Use of the BMD approach negates the need for an UF-related to LOAEL to NOAEL extrapolation (Barnes et al., 1995). Since USEPA also used the BMD approach, they did not apply an uncertainty factor for this extrapolation.

4.7. Protection of sensitive individuals

Workplace exposure typically does not involve sensitive individuals. ACGIH TLVs and OSHA PELs are based on exposure of healthy adult workers, and rarely employ a UF protecting sensitive individuals. Neither agency typically provides information regarding the use of UFs in establishing OELs. Use of an OEL based on F_1 generation data (156 ppm) is adequate to address potential fetal exposure through pregnant workers, particularly when different human child and F_1 pup exposures are considered.

Data for nPB are available for both animals and humans. In vitro bioassays are available for both human and animal cell cultures (EnviroMed, 1997; Elf Atochem, 1994, 1995). For humans, liver hepatocytes were used for the bioassays, while mouse lymphoma and bone marrow cells were used in separate animal bioassays (without metabolic activation). Comparison of these bioassays indicates that effects are seen at similar levels. These results are supported by the inhalation toxicity studies of rats and mice. In addition, the BMD approach incorporates individual variability because it considers all data across individuals for a given endpoint and study, and develops a dose–response curve encompassing individual variability of responses. Taken together, this weight-of-evidence implies that a UF is neither necessary nor warranted for nPB for protection of sensitive individuals. As previously stated, USEPA used an uncertainty factor of 3 for this extrapolation.

4.8. Extrapolation of toxicity data from animals to humans

Historically, the USEPA has used an animal-to-human UF of 3 for inhalation-based values when deriving RfCs (Barnes et al., 1995). This UF has typically been employed to account for differences across species, and always assumes that a chemical can be more toxic in humans than laboratory animals. In vitro bioassays of nPB have been conducted in both human and animals cells, demonstrating that effects are seen at similar levels. Moreover, in vitro data on human cells correlate well with the BMDLs developed from animal studies. For example, nPB was toxic in human in vitro bioassays at only the highest dose tested (500 ppm in solution, which is essentially the concentration at the target cells in an in vitro study. To reach a 500 ppm level at a target cell in vivo, a much higher air concentration would be required because much less than 100% of an air concentration will reach a target cell; EnviroMed, 1997). The range of significant BMDLs derived from animal data was 156–1328 ppm in air, with a mean BMDL across all 24 endpoints of 448 ppm. This implies that human and animal responses first occur at similar concentrations, which is also supported by the available information on occupational exposure by humans (Ichihara et al., 2002; NIOSH, 1999). No effects have been reported in NIOSH studies on volunteers exposed to nPB at concentrations up to 170 ppm (NIOSH, 1999). No exposure levels were measured by Ichihara et al. (2002) during the time the workers reported symptoms. Air measurements after the affected women left the plant, and ventilation of fume hoods was repaired, indicated that concentrations ranged from 60 to 261 ppm. The authors stated that the actual exposure concentrations during the

period when the affected workers were engaged at the plant were likely much higher, since no ventilation was operating in the building.

USEPA used an uncertainty factor of 3 for this extrapolation, based on their conclusion that there are not data to compare the pharmacodynamics between rodents and humans, despite the information presented above.

An OEL developed for workplace exposure precludes children from being regularly exposed. Although fetuses could be exposed, data from the two-generation study (WIL, 2001) indicate that the developing fetus is not substantially more sensitive to nPB than the mother. Use of a UF of 3 adds unnecessary conservatism to the overall OEL estimate, especially considering the proposed OEL is based on an F_1 generation endpoint not expected to be encountered in actual practice. The BMDL of 156 ppm essentially incorporates a UF of 2 compared with the BMDL for the same endpoint in the more relevant F_0 generation (263 ppm/2 = 131.5 ppm).

An alternate approach would base the OEL on the lowest BMDL of the F_0 generation. Since existing data indicate that human and animal responses to nPB occur at similar concentrations, if a UF were to be used, it should be lower than 3, and no more than 2. Applying this factor to the lowest relevant F_0 generation endpoint, 214 ppm for hindlimb strength in the Ichihara et al. (2000a) neurological study, results in an OEL of 107 ppm.

4.9. Extrapolation from subchronic to chronic exposure duration

For nPB, there are several long-term studies as well as shorter-term subchronic and acute studies. Because long-term studies have been conducted, and the BMD is primarily based on chronic studies, there is no need to incorporate a UF for this extrapolation. Further, comparing the subchronic- and chronic-based BMDLs indicates that use of such a UF is not warranted for this chemical. For example, the range of BMDLs developed from the 28-day study (ClinTrials BioResearch, 1997b), 146–1328 ppm, is similar to those developed from the two-generation reproduction study (WIL, 2001), which range from 156 to 785 ppm. This implies that duration of exposure is not a key factor in nPB toxicity. Instead, the data indicate that the peak air concentration and frequency of exposure (which governs the body's ability to recover between exposures) are the most important factors in determining if toxicity may result.

The recommended BMDL for use in developing an OEL is based on the decline in sperm motility in male rats in the first generation of the two-generation study (WIL, 2001). The BMDL associated with this endpoint is 156 ppm. For the reasons discussed above, a UF is not warranted, as the BMDL of 156 ppm reflects impacts on the F_1 generation and essentially incorporates an uncertainty factor of 2 from the same endpoint in the F_0 generation. Actual human workplace exposures are unlikely to replicate those of the F_1 generation, where both parents would be exposed to nPB at work full-time, and their children would be exposed daily until adulthood. Therefore, an OEL of 156 ppm is sufficiently protective of worker health. USEPA (2003) did not incorporate an uncertainty factor for this extrapolation.

Using the traditional NOAEL/LOAEL approach and evaluating the same studies discussed herein, a NOAEL of 170 ppm corresponding to headache in humans has been identified (considered a precursor to neurotoxicity; Rozman and Doull, 2002; NIOSH, 1999). This is very close to the recommended BMDL of 156 ppm in this paper. A UF of no greater than 2 was recommended to account for the slope of the dose–response curve, leading to a recommended OEL of 90 ppm based on headaches in humans (Rozman and Doull, 2002). Even with the lack of individual variability incorporated into a NOAEL, these authors concluded that a factor of 2 would "protect nearly all workers" based on the following assumptions:

- Neurotoxicity is the most sensitive endpoint of exposure.
- Headache is a low-dose precursor effect for other neurotoxicity effects in humans (Rozman and Doull, 2002).
- The steepness of the dose–response curve for anesthesia indicates that a factor of 2 will encompass virtually every individual in any realistic population size.
- Rats have similar or higher sensitivity to nPB than humans.

If this approach were used with the lowest F_0 BMDL for neurotoxicity (i.e., 214 ppm; Ichihara et al., 2000a), a UF of two would result in an OEL of 107 ppm, close to the value recommended using the NOAEL/LOAEL approach (Rozman and Doull, 2002). In either event, an OEL of no less than 90 ppm is supported by both approaches.

Overall, USEPA (2003) used an uncertainty factor of 9 to lower their BMDL of 169 ppm to a recommended OEL of 18 ppm (which they suggested could be adjusted to 25 ppm). This is the only difference between the 25 ppm recommended by USEPA and the 156 ppm recommended in this paper. At most, an uncertainty factor of no more than 2 is relevant for this chemical, setting the lower bound of an OEL at 78 ppm, or three times that recommended by USEPA.

5. Conclusion

A relatively large toxicological data base is available for nPB. For purposes of developing an OEL for nPB,

over 60 endpoints were considered across six studies and spanning three generations of test animals. A total of 38 of these endpoints were identified for BMD modeling, and BMDL estimates corresponding to various dose–response models were compiled for 24 of these separate endpoints. Reproductive, neurological, blood, and liver endpoints were quantitatively evaluated. A high variability in the significant BMDLs across endpoints was observed. However, the low end of the range of significant BMDLs associated with each group of endpoints was similar across endpoints. These values ranged from 156 to 263 ppm. Consistent with USEPA, the lowest BMDL of this group, 156 ppm, was used to develop an OEL. This BMDL was derived from data on decreased sperm motility in F_1 generation rats provided in the two-generation reproductive study (WIL, 2001). This endpoint is relevant to humans, represents a sensitive endpoint (i.e., reproduction), is supported by results of animal and human in vitro bioassay results, and is protective based on available occupational data. If the OEL were based on the most sensitive F_0 endpoint observed for nPB, the resulting BMDL would be 214 ppm, for neurological effects in rats (Ichihara et al., 2000a).

Methods recommended by USEPA for application of UFs were modified for OEL development, as opposed to environmental exposure levels. Due to the large toxicology data base, which encompasses varying stages of the life cycle (e.g., neonatal and reproductive), varying exposure periods (from acute to chronic), and studies on several rat strains and some human data, an uncertainty factor is not necessary to protect adult workers. Conversely, USEPA used an uncertainty factor of 9 to derive their recommended OEL of 25 ppm. Uncertainty factors are used to address lack of knowledge regarding the relative sensitivity of a chemical in humans versus animals; there is information on nPB that negates this uncertainty. Acceptable OELs based on this and other studies evaluating the entire nPB data base range from 90 to 214 ppm, incorporating UFs of 1 or 2. The recommended OEL for nPB from this study is 156 ppm, which is near the midpoint of this range.

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SLR Memorandum

To: Rich Morford, EnviroTech International

From: Mark Stelljes

Date: 9/26/2005

Re: Arsenic as a Potential Confounding Factor in Human Occupational Exposure to nPB

The information summarized in this memorandum was presented during a symposium on n-propylbromide (nPB) held on September 14, 2005 at the North American Congress of Clinical Toxicology 2005 meeting in Orlando, Florida. During the symposium, a summary of several human medical cases was presented in which the affected workers were occupationally exposed to high concentrations of nPB (greater than 100 ppm) in the spray adhesive sector in North Carolina. An important report was made by Dr. Lawrence Raymond of the Carolinas Medical Center, who was one of the treating physicians for the affected workers. High levels of urinary arsenic (average of 242 micrograms per liter; ug/L) were present in the affected workers in the absence of any known source of arsenic. According to the presenters, the drinking water, diet, and soil were tested and not shown to contain elevated levels of arsenic, and hobbies were similarly ruled out as potential sources. However, although no evidence of arsenic was found in the workplace, the presenters acknowledged a historical common work practice in the industry of adding arsenic to the glue to prevent rot and mildew. The presenters concluded by calling arsenic a "confounding factor" in their assessment.

Typical arsenic levels in urine are below 10 ug/L, while levels above 100 ug/L are referred to as "excessive exposure" in *Casarett & Doull's Toxicology* (Klaassen, C.D., Editor, fifth edition, 1996). These elevated urinary arsenic levels were measured between two and three weeks after the workers presented with their illnesses. Since the half-life of arsenic in the body is about 3 days, approximately 6 half-lives elapsed between the time the workers stopped working and their urinary arsenic levels were measured. Since urinary levels of arsenic are the best indicator of recent exposure, this implies that the urinary levels were much higher while the workers were still on the job.

This may be a key statement because arsenic toxicity has been known to cause some of the same symptoms as reported by the workers exposed to nPB. A typical noncancer syndrome associated with arsenic includes neurotoxicity of both the peripheral and central nervous systems. It typically begins with sensory changes, numbness, and tenderness followed by

muscle weakness. Peripheral neuropathy can progress, leading to demyelination and motor dysfunction, which is similar to that seen in the case studies discussed during the symposium.

This makes any determination of chemical causality of the workers' toxic syndrome suspect, since effects could be due in part or in whole by arsenic. Therefore, these reports should not be granted much, if any, weight to support an analysis of the toxicology of n propyl bromide.

SLR Memorandum

To: Rich Morford, EnviroTech International

From: Mark Stelljes

Date: 9/26/2005

Re: Mechanistic Hypothesis for n-Propylbromide and Ramifications for Occupational Exposure Limit in the United States

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Introduction

This Technical Memorandum (TM) presents a synthesis of the current scientific understanding of the toxic mechanism for n-propylbromide (nPB) based on its extensive toxicological database, including the recently completed kinetics and disposition studies conducted on behalf of the National Toxicology Program (NTP; RTI, 2005).

The chemical nPB is known to have neurotoxicity based on laboratory rat and human occupational studies (Ichihara et al., 2000b, 2002, 2004b, Honma, et al., 2003). Data on rats suggest that nPB also exhibits reproductive toxicity, but the specific toxic mechanism and site of action, as well as differential species sensitivities, are not well understood.

This TM does not summarize information already documented in other memoranda and reports. Rather, it proposes a hypothesis of how the body and nPB interact, and discusses the application of this understanding in setting applicable workplace exposure levels for the chemical in the United States (US). Although not all toxicological studies on nPB are mentioned herein, those relevant to reproductive toxicity in rodents or humans are cited and discussed, as are toxicokinetic studies.

The ultimate objective of this work is to establish a "safe" occupational exposure level for workers. Toward this end, the toxicological database was evaluated to identify appropriate uncertainty factors (UFs) for use in extrapolating animal data to the human worker population.

This Technical Memorandum is organized as follows:

- Regulatory Overview
- Technical Issues
  - Concept Overview
    - Reproductive Toxicology
    - Metabolism and Structure-Activity Relationships
  - Overview of Reproductive Toxicity Potential of nPB in Rats and Mice
  - Update of nPB Metabolism
  - Species Sensitivity to nPB
    - Cytochrome P450 CYP21
    - 1,3-Butadiene
    - TCE
    - Glutathione
    - Human Data
- Discussion
  - Metabolic Pathways
  - Kinetics of nPB in Rats and Mice
  - Unifying Mechanistic Hypothesis
  - Weight of Evidence for Reproductive Toxicity Potential of nPB in Humans
- Conclusions and Recommendations
- Citations.

Regulatory Context

The conclusions reached regarding nPB toxicity have regulatory ramifications in the US. SLR initially suggested an occupational exposure level (OEL) of 156 milligrams per kilogram (mg/kg) for nPB. This recommendation has since been published in a peer-reviewed journal (Stelljes and Wood, 2004). Subsequently, the US Environmental Protection Agency (USEPA, 2003) recommended an OEL of 20 mg/kg, even though they selected the

same endpoint and essentially the same benchmark dose as did SLR in their analysis. The difference in recommendations resulted from the application of different UFs. SLR recommended a total UF of 1, while USEPA recommended a value of 9 (a factor of 3 each for intraspecies variability and animal to human extrapolation). The kinetics and other available data discussed herein will provide USEPA with the information necessary to revise their recommended OEL.

Technical Issues

Following an overview of key concepts, which provides the reader with pertinent background, this section presents specific information on and analyses of the reproductive toxicity potential, metabolism and kinetics, and species sensitivity for nPB.

Throughout this paper, many references are cited that primarily address the following topics:

- nPB toxicology
- Cytochrome P450
- Glutathione

These include studies generated by a single Japanese laboratory (Ichihara et al., 2000a, 2004a; Li et al., 2004; Wang et al., 2003, 2004; Yamada et al., 2003), other Japanese researchers (Tachizawa et al., 1982; Kawai et al., 2001; Ishidao et al., 2002), US research (Barnsley et al., 1966; Hymer and Cheever, 2004; Jones and Walsh, 1979; Khan and O'Brien, 1991, Rozman and Doull, 2002; RTI, 2005; Stelljes and Wood, 2004), and human case studies (Sclar, 1999; Ichihara, 2002; Beck and Caravati, 2003; Majersik et al., 2004; Ichihara, 2004b). Research on other chemicals (e.g., isopropylbromide, dibromochloropropane, trichloroethylene) and enzyme systems is also cited and discussed as relevant. These include studies on cytochrome P450 (Botto et al., 1994; Ding and Kaminsky, 2003; Dybing et al., 1990; Guengerich, 1991; Healy et al., 1999; Jiang et al., 1998; Lipscomb et al., 1997, 1998; Nakajima et al., 1993; Nishimura et al., 2003; Seaton et al., 1995; Snawder and Lipscomb, 2000) and glutathione (Forkert et al., 2002, 2003; Gandy et al., 1990, 1992; and Igarashi et al., 1983), especially in relation to chemicals with structural and/or metabolic similarities with nPB. As will be shown, these two enzyme systems are key in the metabolism of nPB and in understanding the potency of this chemical relative to different species.

Concept Overview

The following conceptual overview of technical issues provides discussions of reproductive toxicology, metabolism, and structure-activity relationships.

Reproductive Toxicology

Humans have a relatively low sperm count among mammals. The number of sperm per ejaculate is only about 2 to 4 times above a level at which fertility can be impaired in humans (Spielmann, 1997) but up to 1,000 times that level in rats. Due to this difference, a rat can have epididymis sperm counts reduced by 90 percent without infertility occurring, but a human likely cannot.

Normal human male fertility is defined as semen sperm density greater than 20 million/milliliter, sperm motility greater than 40 percent, and normal sperm morphology greater than 14 percent (Forkert et al., 2003). Chemicals can primarily affect reproductive ability in males through either perturbation of spermatogenesis with targets within the testis, or indirectly by interfering with hormonal stimulation or changes in blood supply (Spielmann, 1997). Dr. Spielmann, active in the Centre for Validation of Alternative Methods for Toxicity Testing (headquartered in Ispra, Italy), discusses the value of *in vitro* studies of reproductive tissues, and states that toxicokinetic studies are essential for interpreting results from reproductive studies and extrapolating them to a whole animal situation.

Brominated chemicals have long been known to be reproductive toxins. The first such chemical with widespread use, dibromochloropropane (DBCP), left many male workers sterile before these effects became known in the 1970s (Kumar, 2004). Since then, other brominated compounds have also been reported to be reproductively toxic to human males, including ethylene dibromide (Kumar, 2004) and 2-bromopropane (Kim et al., 1996, 1999).

Mechanisms underlying reproductive toxicity are usually complex. Effects may be either induced directly by a chemical on the reproductive organs, or indirectly through alteration of hormonal regulation. The overall function of the reproductive system is governed by the nervous system and hormones produced in the endocrine system. This neuroendocrine axis in males includes the central nervous system, pituitary gland, and the testis. For example, chemicals that damage Leydig cells within the testis can reduce secretion of testosterone, which in turn affects Sertoli cell function and spermatogenesis. To date, most reproductive toxicants are assumed to act directly on the testis, but this has not been well studied or documented for most chemicals (Kumar, 2004).

Using results from reproductive studies in animals to extrapolate the potential for reproductive toxicity to occur in humans is difficult. A study conducted by the U.S. National Toxicology Program evaluated fifty 13-week studies focusing on reproductive toxicity in rats

and mice (Morrissey et al., 1988). Twenty-five studies each on rats and mice were evaluated. They found that the most statistically powerful endpoints were sperm motility and male reproductive organ weights (testis, epididymis, and cauda epididymis). Sperm head morphology was considered a useful sensitive endpoint as well. Overall, rats seemed to be affected at slightly lower concentrations than mice. In females, estrus cycle disruption is often cited as a basis for identifying a chemical as potentially toxic to reproduction. However, results presented by Morrissey et al. (1988) indicated that that the stages of the estrus cycle are so variable that they are not useful in assessing potential reproductive toxicity. Therefore, estrus cycle effects were not included in this discussion. Instead, the discussion focuses on the most powerful endpoints, particularly sperm motility.

Metabolism and Structure-Activity Relationships

There are two general types of metabolic reactions, referred to as Phase 1 and Phase 2 reactions. Phase 1 reactions typically increase the water solubility of a chemical by the addition of a polar reactive group (e.g., alcohol or other oxygen-containing group). Sometimes this activates the potential toxicity of a chemical by making it more reactive (e.g., chloroform), but for most chemicals it reduces or eliminates the toxicological activity (e.g., methoxychlor). Phase 2 reactions, also known as conjugation reactions, add an endogenous substance to the chemical (e.g., glutathione), which both inactivates the chemical and enhances its elimination from the body.

Both types of reactions require the presence of enzymes. The most common type of enzymes that catalyze Phase 1 reactions are known as mixed function oxidases (MFOs). Because the activity of these enzymes depends on the presence of a subcellular enzyme known as cytochrome P450, they are also referred to as "cytochrome P450 MFOs" (CYP is often used as an acronym). There are many different enzymes comprising the MFO group, and these different enzymes catalyze reactions for different types of chemicals. Current information indicates that at least 38 different P450 enzymes are present in mammalian cells (Guengerich, 1991), and the distribution and activity of these enzymes differ by organ within an organism, and across species. Up to 15 different P450 enzymes are present in the human liver (Klaassen, 1996). One specific type of P450 is referred to as CYP2E1; this enzyme catalyzes Phase 1 reactions for many halogenated compounds, including trichloroethylene (TCE), chloroform, dibromoethane, vinyl chloride, and vinyl bromide (Lieber, 1997). Current data strongly suggest that this subgroup also catalyzes Phase 1 reactions for nPB (RTI, 2005).

Regarding Phase 2 reactions, two of the most common enzymes required are glutathione-S-transferase, which catalyzes the addition of glutathione to the target compound, and UDP glucuronyl transferase (UDP). Glutathione is a derivative of the amino acid cysteine. UDP catalyzes the addition of glucuronic acid, a derivative of glucose, to the target compound. A typical metabolic process for a target compound is addition of a hydroxyl group (-OH) to a compound in Phase 1 through MFO reactions, and then conjugation with either glucuronic acid or glutathione by reaction with the hydroxyl group.

Most metabolic activities of both types occur in the liver. Other tissues (e.g., lung, nasal mucosa, esophagus, kidney, brain, adrenal, placenta, testis, ovary, skin, aorta, blood platelets, small intestine) also contain these types of enzymes (Healy et al., 1999; Ding and Kaminsky, 2003, Nishimura et al., 2003), but, P450 enzymes are less abundant in these other organs across essentially all mammals. Also, because the distribution of P450 subgroups varies between organs, and some subgroups are absent in some organs, the types (and rates) of reactions often differ from those in the liver. Therefore, to understand the relative metabolism of a chemical across species, enzyme activity in both the liver and in any target organs needs to be considered. As stated by Ding and Kaminsky (2003),

"Each tissue has a unique profile of CYP enzymes that, by and large, determine the sensitivity of that organ to a given xenobiotic compound. Although most CYPs expressed in extrahepatic tissues are also present in the liver...at least some of them may be regulated differently in different tissues, therefore leading to a tissue-selective response to chemical exposure. Furthermore, some CYPs are expressed preferentially in extrahepatic tissues, which may lead to unique extrahepatic metabolites and tissue-specific consequences in cellular toxicity and organ pathology. Because of the well-known specific differences in biotransformation, a detailed characterization of the expressed CYP enzymes in human target tissues is crucial for a more accurate prediction of human risk".

Therefore, this issue is examined later in this paper. Structure-activity relationships (SARs) depend on this same knowledge, since relying on the known metabolism of one compound to predict metabolism of another compound depends not only on the structure of the target chemical, but also on knowledge of its metabolism, and the degree to which metabolism can be predicted by another chemical with similar structure.
The following sections provide literature reviews pertinent to reproductive toxicity, including SARs, and metabolism of nPB.

Overview of Reproductive Toxicity Potential of nPB in Rats and Mice

Metabolism of nPB is complex, but in general is dominated by two distinct enzyme systems, P450 and glutathione. P450 metabolism produces several intermediate products. According to Research Triangle Institute (RTI, 2005), the primary intermediate in both rats and mice is 1-bromo-2-propanol. In subsequent, Phase 2 reactions, the intermediates react, with the assistance of glutathione transferase enzymes, to covalently bind with glutathione or glucuronide (representing a minor pathway in rats). These conjugated products are then excreted through the urine, often in the form of mercapturic acids.

Direct conjugation of nPB with glutathione can also occur in both rats and mice, bypassing the P450 Phase 1 reactions. Four glutathione-conjugated metabolites have been identified in rat and mouse urine by RTI (2005; Table 1). At an inhalation dose level of 800 ppm, the most abundant of these in rats is N-acetyl-S-propylcysteine (APC), comprising 37% of the total excreted metabolites. N-acetyl-S-(2-hydroxypropyl)cysteine (AHPC; 16%), N-acetyl-S-(2-oxopropyl)cysteine (AOPC; 12%), 1-bromo-2-propanol-O-glucuronide (BPG; 9%), and N-acetyl-S-propylcysteine-S-oxide (APCO; 5%) are next in abundance in rats. In mice, the most abundant metabolite is AHPC. All of these except APC and BPG are mercapturic acids (representing a more water-soluble form of glutathione). Similarly, BPG is a more water-soluble form of the metabolite, enhancing excretion. APC and APCO are metabolites that result from bypassing the Phase 1 reaction with P450 and instead directly bind to nPB through the enzymatic removal of bromine. In mice, all of these metabolites are produced except BPG, but in much different proportions (Table 1). Most of the oxidation occurs at the C2 position, which results in a more water-soluble but also somewhat more reactive intermediate (1-bromo-2-propanol).

In the rat and the mouse, this intermediate then undergoes additional metabolism to form several different products. One of these products is the glucuronide conjugate (BPG), and a second is a glutathione conjugate (AOPC). These two metabolites are found in both rats and mice. Additional pathways lead to other oxidation products. One of these latter metabolic pathways includes an intermediate hypothesized to be bromoacetone (in both rats and mice; RTI, 2005). Strong circumstantial evidence from the results of an experiment where mice were pretreated with a P450 inhibitor (1-aminobenzotriazole; ABT) supports this hypothesis (RTI, 2005). This pathway is minor in mice compared with rats.

Bromoacetone is a reactive free radical, and could represent an activation reaction (i.e., the reaction results in a toxic product). Bromoacetone is rapidly bound by glutathione to produce APC. RTI did not speculate on which enzyme system catalyzes that activation reaction. The duration of this free radical is short, since it has not been detected in either urine or rat liver homogenates. Nevertheless, this free radical may be responsible for some

of the toxicity produced by nPB. This statement is supported by the results obtained by RTI, which indicate rats appear to be more sensitive to nPB than mice. They certainly have a lower metabolic capacity, since their response was affected by dose levels above 70 parts per million (ppm) in air, while mice were not affected by dose levels up to 800 ppm (RTI, 2005). If one assumes that metabolic capacity is related to toxicity (and it usually is), then the species with the higher metabolic capacity should be less sensitive to toxicity (assuming metabolism is a detoxication). This is consistent with the idea that mice are substantially less sensitive than rats, and also with the idea that the relative amount of bromoacetone formed and available to bind with macromolecules (e.g., proteins) may be linked to this differential sensitivity. A summary of proposed nPB metabolism in the rat and mouse is shown on Figures 1 and 2, respectively.

The amount of bromoacetone available for binding should be dependent both on the rate at which it is produced and the rate at which it is bound by glutathione. If the glutathione metabolic pathway were saturated, then the amount of this reactive metabolite would increase, leading to increased likelihood of toxicity. The glutathione pathway in the rat appears to become saturated at intravenous dose levels between 20 and 100 milligrams per kilogram (mg/kg). This pathway was not saturated in the mouse at 100 mg/kg, the highest tested dose (RTI, 2005).

The second oxidative pathway in the rat results in the formation of alpha-bromohydrin (ABH; 3-bromo-1,2-propanediol). This metabolite was not identified in mouse urine. Although a minor product, this chemical has been implicated in the inhibition of boar sperm motility (Jones and Gillan, 1996). This represents a second potentially toxic metabolite produced by the rat. This provides further evidence that the rat is more sensitive to the reproductive toxicity of nPB.

In humans, the parent compound (nPB), APC, and bromide ion have been reported in the urine (Ichihara, 2004a; Kawai, 2001).

Based on these data, a key to understanding the differential species sensitivity to nPB toxicity appears to lie in the relative rates of bioactivation and detoxication reactions within the liver and target organs. The MFO-based CYP2E1 reactions are bioactivation reactions. In the rat, there are more ways in which these reactions can occur, leading to a greater degree of bioactivation than in the mouse. The glutathione and glucuronide-based reactions are detoxifying reactions that render the chemical inactive and enhance excretion. The reaction rate for glutathione binding in the mouse is much higher than in the rat, indicating that the mouse detoxifies nPB much more rapidly (Table 2). In addition, metabolic saturation occurs

in the rat at lower doses than in the mouse, further implying that the mouse is more resistant to nPB toxicity than the rat (Figure 3).

Structure-Activity Relationship of nPB with Other Reproductive Toxicants

Information on the SAR of nPB and other reproductive toxicants is relevant to the discussion of appropriate uncertainty factors to apply in developing an OEL for nPB. The most relevant anti-fertility agents for comparing with nPB are those that are structurally similar. This includes iPB, which differs only in the position of the bromine – carbon bond. 2-BP has been shown to be a reproductive toxicant in animals, and has been implicated in several occupational studies (NTP, 2002, Kim et al., 1996, 1999; Koh et al., 1998; Park et al., 1999; Ichihara et al., 1999). In addition, several SAR studies on halogenated propanes have evaluated both nPB and iPB (Lag et al., 1991, 1994; Saito-Suzuki et al., 1982).

The SAR discussion demonstrates that there is essentially no relationship between nPB and iPB with regard to metabolism, likely toxic mechanism, or site of action. Therefore, the high toxicity of iPB should not imply that nPB is equally toxic.

Site and Mechanism of Action

The site of action of iPB in the male rat reproductive system is the Leydig cell (Ichihara, 2000a), but effects on Sertoli cell structure have also been reported (NTP, 2002). NTP (2002) identified a no-observed adverse effect level (NOAEL) for reproductive toxicity of 100 mg/kg in rats based on a literature review. The mechanism of action for reproductive toxicity of iPB has not yet been identified. However, recent studies have tentatively concluded that both the site and mechanism of action of iPB and nPB differ in rats.

For example, Ichihara (2000a) first implied that the toxic action of nPB was inhibition of spermiation, while the toxic action of iPB is impairment of spermatogonia. The authors state "the histopathological changes in the testis induced by nPB are much different from those by 2-bromopropane [iPB]...1-bromopropane [nPB] does not have the severe toxicity toward spermatogonia which 2-bromopropane has."

Wu et al. (2001) provided evidence for a mechanism of action for iPB involving induction of DNA damage and impairment of the functional antioxidant cellular defense in Leydig cells, as well as enhancing lipid peroxidation. DNA damage and/or lipid peroxidation have not been reported in the literature for nPB, further implying that the mechanism and sites of action are different between these two chemicals.

In a more recent study, Yamada et al. (2003) state "1-bromopropane is less toxic to spermatogonia when compared with 2-bromopropane...the underlying mechanism of the toxic effects of 1-bromopropane on the reproductive system is different from those of 2-bromopropane in rats." Focusing on female rat reproductive toxicity, these authors go on to say "in contrast to the...findings on 2-bromopropane, 1-bromopropane seems to mainly alter the maturation of follicles and is less toxic to follicles at early stages." Finally, they provide the following summary:

"The...differences between the toxic effects of 1-bromopropane and 2-bromopropane on female reproductive organs seem to parallel the differences in the actions of the two isomers on the male reproductive system. Previous studies showed that long-term exposure to 2-bromopropane resulted in reductions in the numbers of all types of spermatogenic cells (Ichihara et al., 1997) and that acute or subacute exposure impaired spermatogenesis (Omura et al., 1999), followed by apoptosis of spermatocytes (Yu et al., 2001). On the other hand, 1-bromopropane had little effect on spermatogonia, spermatocytes, and round spermatid (Ichihara et al., 2000a), and only a mild effect on weight gain of seminal vesicles and a failure of spermiation in seminiferous tubules in male rats (Ichihara et al., 2000a). Considered together, these results indicate that 1-bromopropane has adverse effects on both male and female reproductive organs, although the mechanisms of these effects are different from those of 2-bromopropane."

Yamada et al. (2003) suggest that ovarian effects of nPB may be "indirect through the disruption of hormonal regulation following central nervous system impairment." This statement directly contradicts one of the key criteria for classifying a chemical as a Category 2 reproductive toxicant, which is that direct effects on reproductive organs should result from exposure. The nervous system is a known target of nPB toxicity, and other published data support the idea that the nervous system is the most sensitive target organ of nPB exposure (Rozman and Doull, 2002). They concluded that neuroproteins are affected by nPB, and at lower dose levels than those resulting in reduced sperm motility, which is regarded as the most sensitive reproductive endpoint for nPB toxicity (Stelljes and Wood, 2004; Rozman and Doull, 2002; USEPA, 2003). This suggests that effects on the testis, and also on sperm motility, may be secondary to effects on non-reproductive tissue.

This conclusion is further supported by the recent studies by Wang et al. (2004), Ichihara et al. (2004a), and Li et al. (2004). Wang et al. (2004) focused on evaluating potential damage to specific proteins found both in the nervous system and the testis. A second study (Ichihara, et al., 2004a) showed that glutathione-specific metabolites are present in neurofilaments obtained from the spinal cord of male rats, and that the level of the metabolites was related to dose. This documents that the nervous system is a direct target

organ for nPB toxicity, and support previous studies by Wang et al. (2003) indicating that biochemical changes occur in rat neurons due to glutathione depletion.

Li et al. (2004) conducted a study on male rats to compare the mechanism of male reproductive toxicity between nPB and iPB at the gene expression level. They found that 37 genes were suppressed by nPB only, including sex hormone synthesis genes, while 119 genes were suppressed by iPB only, including proto-oncogenes and cell cycle checkpoint genes. As the authors point out, "this difference of altered gene profiles might reflect a difference in toxic mechanism between 1-BP and 2-BP, when taken together with previous studies suggesting that 1-BP disrupts the endocrine balance while 2-BP disrupts undifferentiated cells."

These results strongly imply that the mechanism of action differs between the two chemicals. While iPB directly affects development and maturation of sperm cells (clearly a direct effect on the testis), nPB disrupts endocrine balance. This disruption of endocrine balance then secondarily affects testicular function with regard to sperm development and function. These examples demonstrate both a site and mechanism of action for iPB that are clearly different from those of nPB. Therefore, reproductive effects due to iPB cannot be extrapolated to nPB despite their structural similarities.

SAR analyses have also been conducted on other chemicals, focusing on the positioning of halogen atoms in halogenated propanes (Lag et al., 1991; Saito-Suzuki et al., 1982). Saito-Suzuki et al. (1982) demonstrated that, while DBCP and 1,2,3-tribromopropane both induced dominant lethal mutations in the early spermatid stage in male rats, nPB had a negative response. The authors concluded that bromine or chlorine presence on both carbon atoms 2 and 3 were required for dominant lethal mutations, and that 2 of the 3 halogen atoms should be bromine. They hypothesized that metabolism of DBCP and 1,2,3-tribromopropane included formation of halogenated epoxides (e.g., epibromohydrin). Later, Lag et al. (1991) supported this conclusion in a study evaluating the effect of bromine positioning in the induction of testicular toxicity by halogenated propanes. They noted a wide variation in the extent of target organ toxicity across several halogenated propanes, and that the type, number, and position of the halogens affected activity. They stated that "halogen substituents at all three carbons are also essential for toxic activity", and that the availability of a good leaving group in the C2-position (e.g., a halogen atom) would promote formation of a reactive metabolite from glutathione conjugation. nPB does not have a good leaving group in the C2-position, while iPB does (i.e., bromine).

The other line of evidence typically used in SAR is metabolism. As will be clearly shown below, the metabolism between iPB and nPB are substantially different, verifying that use of SARs for reproductive toxicity is not warranted for nPB.

Update of nPB Metabolism

Several papers present information on the metabolism of nPB and iPB, and the newly completed study from RTI (2005) provides detailed information on nPB metabolism. For SARs to be appropriate for use in evaluating nPB, the two chemicals should have similar metabolism. The first comparative study on the metabolism of nPB and iPB was published by Barnsley et al. (1966). In that article, the authors demonstrated that metabolism was different between the two chemicals in male rats. While nPB metabolism led to formation of n-propylmercapturic acid metabolites (purportedly through reaction with glutathione), these mercapturates were not produced at detectable levels through iPB metabolism. Barnsley et al. (1966) also found that epoxides were formed in the metabolic processes of iPB, but not in nPB metabolism. Given the comparative studies summarized above by Saito-Suzuki et al. (1982) and Lag et al. (1991), it should be expected that the metabolism of these two chemicals must be different.

In 1979, a metabolic scheme was proposed for nPB by Jones and Walsh (1979). They supported the results obtained by Barnsley (1966), and demonstrated that nPB is metabolized through conjugation with glutathione, with oxidation at the C2 and C3 positions occurring before conjugation of the alkyl group. Khan and O'Brien (1991) provided further evidence for this conclusion by demonstrating that glutathione can be depleted through exposure to nPB in vitro. Oxidation cannot proceed at the C2 position of iPB because that is the location of the bromine atom. These studies further support the conclusion that metabolism, and generation of potentially reactive metabolites, is different between iPB and nPB.

N-acetyl-S-propylcysteine, the primary metabolite of nPB reported by Jones and Walsh (1979), has also been found in the urine of rats in recent studies (Ichihara, 2004a; RTI, 2005). The metabolites identified in humans following iPB exposure include isopropyl alcohol and acetone; no propylcysteine metabolites have been identified in humans following iPB exposure (Kawai et al., 1997). This demonstrates that the differences between iPB and nPB metabolism observed in rats are also relevant to humans.

As discussed earlier, the new data from RTI (2005) indicate that both cytochrome P450 and glutathione are involved in nPB metabolism. Oxidative metabolism is much more important for iPB due to its different placement of bromine in the molecule. The specific mixed function oxidase enzyme involved in nPB metabolism (and likely iPB as well) is CYP2E1. This enzyme is present in the Leydig cells of male rats, but apparently not in other cell types

in the testis. These findings support the conclusion that iPB can exert toxicity directly on Leydig cells (Wu et al., 2001) while nPB does not. Oxidative metabolism of iPB in the testis can bioactivate iPB and lead to the spectrum of toxicity reported in the testis. By contrast, nPB is primarily metabolized through glutathione, particularly at higher doses, and oxidative metabolism does not lead to generation of similar reactive intermediates via P450. Different metabolic pathways are mirrored in the different toxic actions of nPB and iPB.

Based on this discussion, differences in metabolism between nPB and iPB preclude meaningful evaluation of potential reproductive toxicity of nPB based on chemical relationships with iPB and DBCP.

The following key points can be gleaned from new report by RTI (2005) in relation to SARs:

- The RTI (2005) study is the first rigorous study of kinetics conducted on nPB in any species
- It is also the first study where a second species has been evaluated (both rats and mice were included)
- Mice are substantially less sensitive to nPB than are rats (at least fivefold more resistant)
- Metabolism is dose-dependent in the rat, but not in the mouse
- Metabolic processes differ between the two species.

Species sensitivity to nPB

A wide body of data is available on the distribution and activity of various P450 enzymes and glutathione in rats, mice, and humans, but rarely have all three species been evaluated in a single study with the same chemicals. An overview of this information is provided as a framework for evaluating the relative sensitivity of these species to nPB toxicity. Information from the existing database will then be compared with the nPB kinetic data compiled for rats and mice by RTI (2004).

Cytochrome P450 - CYP2E1

This cytochrome is most abundant in the liver (Klaassen, 1996; Nishimura et al., 2003). Until recently, it had not been identified in mammalian reproductive organs, presumably due to its relatively low abundance and activity, which had been below the sensitivity of detection techniques. CYP2E1 was identified in the rat testis in 1998 (Jiang et al., 1998), and in the mouse testis in 1999 (Healy et al., 1999). More recently, this cytochrome was detected

in human and monkey testis and epididymis (Forkert et al., 2003). Based on information compiled as part of the human genome project, genes responsible for the expression of CYP2E1 are found in many human organs. Normalized expression of the CYP2E1 distribution across organs from this project (Bioinformatic Harvester, 2005) is summarized below:

Tissue	Normalized Expression (%)
Liver	71.1
Thymus	18.4
Lung	2.2
Others	2.1
Brain	1.6
Ovary	1.6
Bone	1.1
Muscle	0.62
Testis	0.53
Uterus	0.44

This table shows that the liver has about 150 times higher expression of CYP2E1 than the testis in humans. Also, we know that CYP2E1 is polymorphic in humans (i.e., subgroups have been shown to have different activity and distribution than others). This is especially important for CYP2E1 because of its unique capacity to activate xenobiotics (at least 85 different chemicals; Lieber, 1997). Much of this information on humans was gleaned from studies of alcoholics after it was determined that CYP2E1 was implicated in the accelerated metabolism and tolerance to alcohol in heavy drinkers. Therefore, use of alcohol may impact the activity of this cytochrome. For example, it is known that CYP2E1 activates carbon tetrachloride (CCl_4) to an active intermediate in the periportal regions of the liver, and that alcohol pretreatment stimulates CCl_4 toxicity in those same regions (Hasumura, Teschke, and Lieber, 1974). This likely complicates evaluation of human case studies involving nPB, since historical or recent alcohol use might impact the metabolism of nPB.

Another factor influencing cytochrome activity is diabetes. CYP2E1 levels are elevated in diabetics, particularly those who do not respond to insulin (Botto et al., 1994). A 6- to 20-fold variability in human CYP2E1 activity has been described that is apparently not related to alcohol intake (Lieber, 1997). This likely incorporates both polymorphism as well as "environmental" factors. An independent study using a different technique found an 11-fold variation in CYP2E1 human liver content, with a mean content of 52.2 picomoles per milligram (pmol/mg) of liver tissue, representing about 12% of total CYP content in the liver) and a normal distribution across all samples (Snawder and Lipscomb, 2000). (Activity was 1.06 nanomoles per minute per milligram protein (nmol/min-mg) for chlorzoxazone,

which is preferentially metabolized by CYP2E1.) In rodents, both rats and mice have approximately equal amounts of cytochrome P450 in their livers, but male mice have more CYP2E1 in the liver than do male rats (Nakajima et al., 1993).

Studies from the human genome project indicate that, within the testis, CYP2E1 expression is highest in round spermatids, and is lowest in pachytene spermatocytes (those in a specific stage of meiotic cell division; Bioinformatic Harvester, 2005). Expression of this cytochrome was also reported in human Sertoli cells. In mice, results of one study indicate that CYP2E1 may only be present in the Leydig cells within the testis (Healy et al., 1999). Tissue specificity has not been evaluated for CYP2E1 in the rat testis (Jiang, et al., 1998).

The literature was reviewed to identify relevant studies in which tissue-specific activity of CYP2E1 was measured in humans, rats, and/or mice for a specific chemical. This information is summarized below. Multiple species studies were found on two compounds, TCE and 1,3-butadiene (BD). These are two- and four-carbon compounds; TCE contains three chlorine atoms while BD contains carbon double bonds. Both chemicals are bioactivated by CYP2E1 through oxidation into reactive intermediates, both of which are putatively identified as the source of their potential carcinogenic activity.

1,3-Butadiene

For 1,3-butadiene, oxidation by CYP2E1 was studied in mice, rats, and humans by Seaton et al. (1995). Pharmacological kinetic constants (K_m and V_{max}) were measured in liver microsome homogenates. The K_m, also known as the Michaelis-Menton equilibrium constant, is the concentration of a chemical at which the metabolic process occurs at half the maximum rate. To normalize this constant for chemicals with different molecular weights, this constant is typically expressed in molar concentrations (1 mole of a chemical is equal to the molecular weight in grams). This value is a function of the steepness of the kinetic curve for the chemical. The steeper the curve, the less difference there is between concentrations associated with equilibrium and maximum reaction rates. K_m is referred to as an "equilibrium" constant because at this concentration, the amount of circulating chemical is equal to the amount metabolized. Below the K_m, more of a chemical is circulating than metabolized. V_{max} is defined as the maximum reaction rate for a given process, and is typically expressed as a rate in units of moles of a chemical metabolized per milligram of protein per minute (mol/mg-min). This rate represents the maximum speed at which the chemical can be metabolized through a specific reaction, regardless of dose.

Mean results obtained for pharmacological kinetic constants for 1,3-butadiene oxidation by CYP2E1 at a dose of 80 micromolar (uM) are summarized below (from Seaton, et al., 1995):

Parameter	Units	Human	Mouse	Rat
K_m	mM	0.50	0.14	0.15
V_{max}	nmol/mg-min	0.92	1.3	0.41

The concentrations of CYP2E1 (in pmol/mg protein) in human, mouse, and rat liver microsomes were 70.5, 96, and 35.8, respectively. The ratio of V_{max} to K_m, also referred to as the intrinsic metabolic clearance, provides in this case an indication of the relative rate of bioactivation across species. When similar units are used, and individual ratios are used as the basis for the calculation (rather than the averages across all individuals shown above), these ratios are 1295, 157, and 230 for the mouse, rat, and human. This indicates that bioactivation, in this case metabolic reactivity of CYP2E1, is more than tenfold greater in the mouse than in the rat, and about five times greater in the mouse than in humans. Humans have slightly higher reactivity in this instance than do rats, but by less than a factor of two. The range of these ratios in mice was 2.4 to 61 times greater than ratios measured in individual humans. This indicates that, , humans will produce less of the reactive metabolite than would a mouse, even when incorporating the high interindividual variability factor of 25 observed in these ratios from humans. Therefore, humans are also expected to be less sensitive to the carcinogenicity of 1,3-butadiene than mice.

These findings indicate that more of the reactive intermediate would be produced in mice than in rats or humans following exposure to butadiene, particularly at low exposure concentrations (e.g., those below the K_m). They also support toxicological evidence that mice are more sensitive to the carcinogenic effects of butadiene than rats. Following this Phase 1 reaction, binding with glutathione can occur, which provides a protective role. This will be more fully discussed later.

TCE

TCE, which is bioactivated through oxidation by CYP2E1, has been studied in mice and rats (Nakajima et al., 1993), and in mice, rats, and humans (Lipscomb et al., 1997, 1998; Forkert et al., 2002, 2003). Initial data from Nakajima et al. (1993) indicated that male mice have more CYP2E1 than male rats in their livers, and that this cytochrome is responsible for the metabolism of TCE in both species. Studied in vitro using liver microsome preparations, male mice demonstrated 2 to 4 times higher metabolic oxidation of TCE than male rats (although other cytochrome activity in mice may contribute to this difference).

Lipscomb et al. extended this research by measuring TCE oxidation metabolism through CYP2E1 activity, and identifying K_m and V_{max} constants in mice, rats, and humans. In the first study Lipscomb et al. (1997) found variability of these rate constants in human liver cells, and reported that variability ranged by less than a factor of ten across 23 individuals. This is significant considering the wide range of individuals used in the study. Subject ages ranged from 22 to 63 and ethnicity included Caucasian, Asian, Filipino, and Hispanic. Both males and females were included, about a third of the subjects smoked, and most were at least social alcohol users. Trends observed indicated that K_m values were significantly lower in females than males, although these differences were not observed with regard to V_{max}. Saturation of metabolism was seen in all analyses. Lipscomb et al. (1997) provide the following conclusions:

- Metabolism by CYP2E1 is a crucial step in TCE bioactivation in humans (confirming similarity to rats and mice)
- Maximal metabolic rates (V_{max}) by human liver microsomes vary less than ten-fold
- K_m values in human liver microsomes vary up to a factor of four
- Human microsomes differ both in their affinity and capacity to metabolize TCE; the degree of CYP2E1 expression is the overriding factor
- Quantifiable species-dependent differences in bioactivation, and identification of factors contributing to interindividual differences, assist in extrapolating rodent toxicity data to humans.

Subsequent to this work, Lipscomb et al. (1997) measured kinetic parameters for this same bioactivation reaction in human, rat, and mouse microsomes. In part, this was to evaluate if different metabolism between these two species could be responsible for the observation that liver carcinomas can be caused by TCE in mice, but not in rats.

Parameter	Units	Human	Mouse	Rat
K_m	uM	24.6	35.4	55.5
V_{max}	nmol/mg-min	1.44	5.43	4.83

These results indicate that TCE microsomal metabolism is highest in the mouse, slightly lower in the rat, and much lower in humans. K_m values were also evaluated at different ranges of TCE concentrations in an attempt to identify if different CYP enzymes were involved in this metabolic activity in any of these three species. Results demonstrated this to be true in the rat (since K_m values of the rat corresponding to high, medium, and low affinity were derived based on dose), but not in the mouse or human. TCE metabolism in rats appears to become saturated at 2,000 mg/kg, but not in mice. Intrinsic clearance values were estimated as 0.153, 0.087, and 0.058 ml/min-mg protein for the mouse, rat, and human,

respectively. This indicates that humans have the lowest ability to clear TCE from the body through metabolism with CYP2E1. For example, the authors demonstrate that at a concentration of 15 uM (about 2 milligrams per liter [mg/L] or 370 parts per million [ppm]), the metabolic rate in humans (545 pmol/min-mg) is about half the rate in rats (1,026 pmol/min-mg), and about one-third of the rate in mice (1,614 pmol/min-mg). All of these data support Lipscomb et al.'s (1997), conclusion that the mouse is best able to metabolize TCE. Since this metabolism represents bioactivation, this suggests that the mouse forms more reactive metabolites and should be more sensitive to the toxic effects of TCE. This supports the observation that liver tumors develop in mice, but not rats, following TCE exposure.

To evaluate the potential reproductive toxicity associated with TCE, metabolic and kinetic studies on mice and humans were subsequently conducted using reproductive tissues (e.g., testis) by Forkert et al. (2002, 2003). Earlier work demonstrated the presence of CYP2E1 in rat and mouse testis. Forkert et al. (2002) identified the relative amounts of this cytochrome in mouse reproductive organs, and found that about twice as much is present in the epididymis than the testis. In the mouse testis, CYP2E1 was localized in the Leydig cells, consistent with the findings of Healy et al. (1999). The relative abundance of CYP2E1 in the epididymis provides support that TCE (at the high concentration of 1000 ppm used in the study) can affect development and maturation of spermatozoa, which occur in the epididymis. Levels of CYP2E1 in rat testis (Jiang et al., 1998) were lower than those reported here. Although humans were not included in the study by Forkert et al. (2002), the time course of metabolite production and excretion in mice was consistent with that seen in humans. However, this time course differed in rats. This suggests that humans are more similar to mice than rats with regard to TCE metabolism associated with CYP2E1.

Forkert et al. (2003) conducted a follow-up study on humans. Seminal fluid was obtained from the infertile workers, who had been occupationally exposed to TCE for at least two years prior to study initiation, following inhalation exposure to 1000 ppm TCE for 1 to 4 weeks. Samples contained TCE and metabolites, indicating that CYP2E1 activity can directly metabolize TCE in reproductive tissues. In addition, reproductive tissues from anonymous donors were analyzed to evaluate the amount and distribution of CYP2E1. Results indicate that, like mice, CYP2E1 is more abundant in the epididymis than the testis, and the cytochrome present in the testis was limited to Leydig cells. *In vitro* studies on the epididymis and testis of mice indicate that metabolite production was much higher in the epididymis than the testis, and cellular damage was observed in the epididymis (but not the testis). Forkert et al. (2003) offered the following additional conclusions:

- Generation of CYP2E1-mediated metabolites play a role in reproductive toxicity
- Cellular distribution of CYP2E1 in human male reproductive tissues is similar to mice
- Metabolic disposition of TCE in humans seems to be similar to that in mice, indicating that the mouse model is appropriate for investigating effects and mechanisms of TCE-induced toxicity in the male reproductive system.

These studies provide valuable information for evaluating the toxicological database of nPB as it relates to male reproductive toxicity, particularly with regard to identifying the most appropriate animal model upon which to base extrapolations to humans. However, since nPB is primarily metabolized by two processes, this only provides part of the story. Similar information was researched with regard to glutathione, and this is summarized below. This is followed by a synthesis of the information from both types of metabolic processes with regard to nPB.

Glutathione

Glutathione (often abbreviated as GSH) plays a major role in detoxification of harmful chemicals (Klaassen, 1996). Unlike cytochrome P450 reactions, almost all glutathione reactions with chemicals serve to detoxify chemicals. Exceptions include reactions with some haloalkanes containing multiple halogen atoms, often on adjacent carbon atoms, which can form episulfonium ions that bind to macromolecules (e.g., dibromoethane, dichloromethane). No episulfonium ions are formed from metabolism of nPB (RTI, 2005). A useful review article by Lomaestro and Malone (1995) indicates over 8,000 papers on glutathione were published during a recent five-year period. As they state, glutathione is considered to be the most prevalent and important intracellular nonprotein compound in mammalian cells, as well as the most abundant low molecular weight peptide. GSH is present in millimolar concentrations in human cells, but only in trace amounts in blood plasma and most body fluids. The primary source of GSH in plasma is the liver. Glutathione is involved with many metabolic functions, including DNA synthesis and repair, protein and prostaglandin synthesis, amino acid transport, enzyme activation, prevention of oxidative cell damage, immune system functionality, and metabolism of toxicants. It is this latter role that is the focus of this discussion.

Given its importance and abundance, it may be surprising that GSH can be depleted through various processes. Since GSH is a combination of three amino acids, fasting can deplete GSH levels. Other ways in which GSH can be depleted include inhibition of synthesis, exposure to oxidative stress, and binding to chemicals. The capacity for GSH synthesis is

insufficient to maintain GSH concentrations when tissues are exposed to certain chemicals or their metabolites (Lomaestro and Malone, 1995). For example, studies have shown that many chemicals (e.g., acetaminophen, bromobenzene, menadione), including nPB, can deplete intracellular GSH (Khan and O'Brien, 1991). Depletion of GSH can lead to enhanced toxicity, as evidenced by the liver toxicity of acetaminophen in situations where the dose exceeds the ability of GSH to detoxify the reactive metabolite produced through Phase 1 reactions.

Similar to the cytochromes, glutathione reactivity and binding is generally affected by the presence of enzymes, most typically glutathione-S-transferases, which are comprised of different classes. However, unlike the cytochromes, the conjugation of exogenous chemicals with glutathione is catalyzed by all classes of glutathione-S-transferases. These enzymes can be induced in rodents, but it is not clear if this also occurs in humans. Humans and rats contain different classes and compositions of these transferases (Klaassen, 1996).

A literature review was conducted to evaluate species and tissue differences in glutathione in an effort to identify the relative level of detoxification afforded by GSH with regard to xenobiotics in general, and nPB in particular. Most information was available for the liver, but some studies focused on reproductive tissues.

In an early study (Igarashi et al., 1983), GSH levels in the liver were shown to be similar in rats and mice (7.1 and 7.8 mM, respectively). However, mice are much more sensitive to liver toxicity from acetaminophen than are rats, despite this similarity in GSH levels. The authors demonstrated that this may be due to differential activity of enzyme activity, including glutathione-S-transferases. Rats became much more susceptible to toxicity after 48 hours of fasting, but mice did not. This was associated with greater depletion of GSH levels in rats than in mice following fasting. The authors did not expound further on these data.

Gandy et al. (1990, 1992) studied GSH with regard to rat reproductive toxicity. The authors state that all constituents of the GSH detoxication system are present in male rats, and hypothesize that reduction of epididymis or testicular GSH-dependent protective mechanisms may lower the threshold for reproductive toxicity (the authors specifically focused on mutagenicity in germ cells; Gandy et al., 1990). Gandy et al. (1990) used methyl iodide, which is known to deplete GSH in reproductive tissues, for their analysis in male rats, which included measuring baseline levels of GSH in various organs. They found that the liver contained the highest amounts of GSH on a normalized wet-weight basis (2,900 mg/kg), but also found quite high levels of GSH in several reproductive organs, including the vas deferens (2,700 mg/kg) and epididymis (1,400 mg/kg). The testis and prostate had lower

levels of GSH (750 mg/kg in each organ), and the seminal vesicles had the lowest amount (500 mg/kg). Although the kidney is considered to be an organ rich in GSH, in this study the authors found lower amounts in the kidney (700 mg/kg) than in any reproductive organ other than the seminal vesicle. This strongly suggests that the male reproductive tract is capable of extensive detoxication through GSH activity.

Exposure to methyl iodide at up to 100 mg/kg via intraperitoneal injection depleted GSH in several organs, most notably in the liver (98% depletion) and epididymis (63% depletion). GSH in the testis was only significantly depleted at the 1-hour time point following dosing (22% depletion relative to control rats). The depletion in the testis was slower and occurred to a lesser extent relative to the epididymis and liver. The authors suggested that the testis was protected in part through the blood-testis barrier. However, more recent data indicates that partitioning of small alkyl halides (e.g., TCE, nPB) into the testis is similar to the blood (Gargas et al., 1989; RTI, 2005). The epididymis, which is outside the blood-testis barrier, has much higher levels of GSH than the testis. It is logical to assume that this higher level of GSH is in part present to detoxify the greater amount and diversity of chemicals reaching the epididymis than the testis. This explains why the liver and epididymis were both similarly affected after exposure to methyl iodide, but the testis was relatively unaffected.

In a follow-up study, Gandy et al. (1992) pretreated male rats with N-acetylcysteine, which increases tissue GSH levels, and then treated them with ethyl methanesulfonate, a chemical known to cause lethal mutations that is detoxified through conjugation with glutathione. This study evaluated. Their results demonstrated that the glutathione pathway affords protection against lethal mutations, which is direct evidence that elevated GSH levels can provide additional protection from germ cell-based mutations. In an additional analysis, rats were pretreated with phorone, which depleted liver GSH but not GSH in the reproductive tract. This evaluates the protection afforded by GSH in the reproductive tract alone. Results demonstrated little protection afforded by these liver-GSH-depleted rats. This led Gandy et al. (1992) to conclude that "GSH reserves in the male reproductive tract [of the rat] are insufficient to protect developing spermatozoa from damage...in the absence of hepatic GSH". Therefore, it appears that the majority of protection afforded by GSH is due to glutathione activity in the liver. This indicates that analysis of plasma-based GSH in kinetic studies should enable an understanding of the potential for a chemical to impact reproductive tissues in the absence of specific data from these tissues.

As an example of GSH-related toxicity specific to male reproduction, a study on the testicular metabolism and toxicity of dibromochloropropane (DBCP) was conducted in rats (Dybing et al., 1990) after DBCP was observed to cause testicular necrosis (note that this a

different type of toxicity than observed for nPB). In this study, several halogenated propanes were evaluated for their ability to cause testicular necrosis in the rat, and this ability was related to the relative *in vitro* induction of testicular DNA damage. The authors found that the type, number, and location of halogen atoms on the molecule all affected activity, with the highest potency associated with chemicals containing vicinal bromine atoms. Importantly, no testicular necrotic activity or DNA damage was reported for propanes with fewer than three halogen atoms (e.g., dibromopropane). Dybing et al. (1990) found that isolated rat testicular cells can covert DBCP to a DNA-damaging metabolite, indicating that bioactivation can occur in the testis. Binding of this metabolite with GSH was also observed in testicular cells, demonstrating that this Phase 2 reaction can occur in the testis. However, consistent with findings of Gandy et al. (1992), the amount of GSH present in testicular cells is insufficient to fully protect against toxicity from the reactive metabolite in the absence of liver GSH. For DBCP, the reactive metabolite is an episulfonium ion, which has not been reported for nPB. As stated earlier, generation of episulfonium ions is an exception to the rule that GSH reactions are protective. Therefore, DBCP reactions with GSH are actually bioactivation reactions, whereas nPB reactions with GSH are detoxifying reactions. This is another reason for the lack of relevance for SAR with regard to DBCP and nPB. The primary value of Dybing et al.'s (1990) study with regard to nPB is the evidence it provides that direct conjugation of a parent compound with GSH can occur directly in the testis, in addition to the liver.

Human Data

Human data are scarce with regard to nPB toxicity, and are limited to a few case studies involving occupational exposure (Sclar, 1999; Ichihara et al., 2002; Beck and Caravati, 2003; Majersik et al., 2004). The Beck and Caravati (2003) and Majersik et al. (2004) studies evaluated the same human data. In all three of these case studies, neurological symptoms were reported following at least 3 months of exposure, but air concentrations during exposure were not measured, making interpretations of causality difficult.

Air concentrations were estimated after the affected workers presented to the doctors for the cases involving three workers in North Carolina (Ichihara et al., 2002) and three workers in Utah using personal monitors, which do not afford much precision. All of these workers were using nPB as a spray adhesive in unventilated buildings. Concentrations estimated in the Utah study four days later, after air exchange was implemented, averaged about 130 ppm, with some concentrations as high as 176 ppm. Therefore, it is likely that actual exposure concentrations during the time the affected workers were engaged in their activities were substantially higher than these estimates.

Both males (Sclar, 1999, Beck and Caravati, 2003; Majersik et al., 2004) and females (Ichihara et al., 2002; Majersik et al., 2004) were included in the case studies. Symptoms included numbness and weakness of the extremities (all three studies), and some central nervous system (CNS)-based effects (e.g., dizziness) in the latter two studies (i.e., effects on both peripheral and central nervous systems). The only report of any reproductive symptoms was irregular periods in two of the three affected female workers from one study (Ichihara et al., 2002). These findings imply that the primary effects of nPB from human occupational exposure are neurological. However, sperm motility was not measured in the affected male workers, and fertility was not evaluated in any of the studies.

In another study, Ichihara et al., (2004) evaluated exposure levels and health status in 24 female and 13 male workers in China. This study was the only human study in which both urine and blood samples were collected and analyzed. The worker exposure durations ranged from 1 month to ten years, their ages at the time of the study ranged between 25 and 60, and time weighted average nPB concentrations ranged from 0.6 to 170 ppm. The four workers with the longest exposure durations (six years or more) were estimated to be exposed to time weighted average concentrations between 25 and 107 ppm. Prior to 1996, this facility used 2-bromopropane and some of the same employees were historically exposed to that solvent as well. The most common symptom reported by the workers was sore throat (i.e., irritation of mucus membranes), which was common to exposures to both solvents. Dizziness, light-headedness, headache, and feeling intoxicated were the most common neurological symptoms reported. As stated by the authors,

> "the present neurological or mucous-irritating symptoms may not be specific to 1-bromopropane exposure but could be also caused by 2-bromopropane. This argument is based on the fact that the frequencies of almost all symptoms did not differ from those of the 1996 investigation, when 2-bromopropane was the main product, although the frequency of headache rather decreased significantly...the present study, as well as NIOSH studies and our case report [Ichihara et al., 2002], suggested that neurological- or mucosal irritation-related symptoms could be caused by 1-bromopropane exposure although their specificity is uncertain."

The authors conclude by saying "there were no severe chronic symptoms suggestive of neurological damage in workers exposed to less than 170 ppm." The authors found the parent chemical, nPB, in the urine of workers, and concluded that the level of nPB in urine correlated well with individual exposure levels.

This study supports the previous statement that the workers affected in the Sclar (1999), North Carolina (Ichihara, 2002), and Utah (Beck and Caravati, 2003; Majersik et al., 2004) case studies were exposed regularly to concentrations in excess of 200 ppm. Since neurological symptoms first appear in rats at concentrations in excess of 150 ppm, this implies that humans are not particularly susceptible to the neurological effects of nPB, even incorporating individual variability across males and females in a workplace setting.

Discussion

How does all of this information presented on CYP and GSH relate to nPB, and how can it be applied to develop an appropriate occupational exposure level for nPB in the US?

First, metabolic pathways for nPB proposed for the rat and mouse are summarized, followed by a discussion of the basis for these pathways and differences between the two species. This is then followed by kinetic modeling conducted by RTI, and interpretations of that modeling for use in establishing the relative toxicity of nPB to humans.

Metabolic Pathways

The metabolic pathways for nPB in rats and mice, gleaned from the kinetics and disposition studies conducted by RTI (2005), are summarized in Figures 1 and 2, respectively.

The following metabolites were identified in both mice and rat urine:

- N-acetyl-S-propylcysteine
- N-acetyl-S-(2-hydroxy)-propylcysteine
- N-acetyl-S-propylcysteine S-oxide
- 1-Bromo-2-propanol-O-glucuronide
- N-acetyl-S-(2-oxopropyl)cysteine
- N-acetyl-S-(2-oxopropyl)cysteine-S-oxide.

The key intermediate produced from CYP2E1 metabolism is 1-bromo-2-propanol in both rats and mice. This then further reacts with GSH or is glucuronidated, which eliminates the activity of the compound. RTI stated that direct conjugation of part nPB may be a minor pathway relative to oxidative metabolism at exposures similar to those in the workplace. However, N-acetyl-S-propylcysteine, which is formed from direct conjugation of nPB with glutathione, has been reported in occupationally-exposed humans. Since information on human metabolites is not available for different exposure levels, it is not known if the percentage of a dose directly conjugated by GSH in humans changes based on exposure

level. Rats produce several oxidative metabolites, while mice produce only one. Bromoacetone, a reactive metabolite produced through further reaction of 1-bromo-2-propanol with P450, appears to be a much more abundant metabolite in rats than mice. Alpha-bromohydrin, shown to form in vitro in the rat and mouse, is also produced from oxidative metabolism. This reactive metabolite, implicated in boar sperm toxicity, is a major metabolite in rats but a minor one in mice.

Based on data compiled by RTI (2004), the K_m for male rats and mice are 1.64 and 39.9 uM, respectively. Assuming total absorption of inhaled nPB, this equates to air concentrations of 40 and 975 ppm for rats and mice, respectively. At concentrations below the K_m, metabolism is essentially perfusion-based. In this situation, liver activity is high enough to completely extract the chemical from the blood and metabolize it, which keeps blood levels from increasing to any appreciable extent. At concentrations above the K_m, metabolism is directly affected by dose because the liver activity is not high enough to completely extract and metabolize the chemical from the blood. Therefore, circulating levels of the chemical increase, metabolic clearance drops, and more parent compounds circulates to extrahepatic organs. This phenomenon underscores the primary difference between rats and mice. All dose levels in mice, except for 2700 ppm, are below the K_m, and no saturation is seen at these dose levels. Circulating nPB levels remain low over the 70 to 800 ppm dose range, and increasing the dose does not lead to elevated levels in reproductive or other organs. However, at the 2,700 ppm dose level, the mouse begins to show reduced metabolic clearance, which leads to higher levels of nPB available for other target tissues. By contrast, all dose levels are above the K_m in rats, indicating that liver metabolism is not sufficient to extract all nPB from the blood. As a result, more of the chemical reaches potential target sites, and a higher burden is placed on extrahepatic metabolism.

As we saw previously, glutathione levels in reproductive organs are insufficient to protect against reactive metabolites formed through reactions with CYP2E1. Therefore, metabolic saturation occurs and levels of potentially toxic metabolites build up throughout the organs in which nPB is distributed.

RTI (2005) used different pharmacokinetic models for rats and mice to generate their estimates of V_{max} and K_m. For the rat, both CYP2E1 and glutathione activity were included in the model, while for the mouse, only CYP2E1 activity was included. This does not imply, as RTI states, that glutathione is only important in metabolizing nPB in the rat. However, it does imply that glutathione levels in the rat are not sufficient to protect against buildup of potentially reactive intermediates across all dose levels, although they are sufficient in the mouse (except at the highest dose level). This observation is supported by the RTI

intravenous dosing data, which showed a difference in kinetics for rats between the 5 and 20 mg/kg dose levels. Similar kinetics data were not compiled for mice; pharmacokinetic studies were only conducted on rats.

For example, plasma bromide levels were 3.4 times greater in rats following the 20 mg/kg dose than after the 5 mg/kg dose, and estimated clearance dropped from 2,648 milliliters per hour (ml/hr) for the 5 mg/kg dose to 1,869 ml/hr for the 20 mg/kg dose. This led to much greater distribution of nPB following the 20 mg/kg dose (775 ml/kg versus 1,619 ml/kg, respectively). 28% of the 5 mg/kg dose was metabolized and 37% of the higher dose was metabolized. Despite these differences, clearance was still rapid as indicated by the estimate that 85% of the dose was eliminated within 2.5 hours.

Additional comparison can be made based on disposition studies done on rats and mice at dose levels of 5, 20, and 100 mg/kg. In male mice, the percent of the dose remaining in the liver, testis, and blood after 48 hours following exposure declined slightly as the dose increased (liver from 0.432 to 0.138 to 0.086; testis from 0.006 to 0.005 to 0.004; blood from 0.093, 0.076, 0.051%), demonstrating that accumulation due to reduced clearance was not occurring at any of the dose levels. These data also indicate that about 50% of these dose levels were metabolized, higher than that seen in rats (about 19%, 17%, and 11% for 5, 20, and 100 mg/kg doses).

Unlike the mouse, testis nPB levels in the rat remained constant at both 5 and 20 mg/kg dose levels (0.022%). These levels are 4 to 6 times the relative amount measured in mouse testis. However, in the rat liver the relative percent of the dose in total tissues dropped markedly as dose levels increased (1.15% to 0.68% to 0.23%, respectively). Blood levels of nPB in the 20 mg/kg dose were twice that after the 5 mg/kg dose (0.331% to 0.58%, respectively), consistent with the kinetic discussion provided above with regard to K_m. Testis and blood data were not available for the 100 mg/kg dose.

Inhibition intravenous studies on rats at 25 mg/kg provide further support for the importance of CYP2E1 and glutathione in nPB metabolism. One group of rats was pretreated with buthionine-sulfoximine (BSO), which is typically used to inhibit GSH synthesis, while a second group of rats was pretreated with ABT, which is used to inhibit MFO activity, including CYP2E1.

ABT-pretreated rats had a higher percentage of the nPB dose eliminated as parent compound (76% compared with about 50% for untreated or BSO-pretreated), but a lower percentage exhaled as CO_2 (4% compared with about 18% in the other groups) and lower percentage

excreted in urine (9.8% vs. about 14% in other groups). BSO-pretreatment halved the percent of the tissue dose retained in the liver (from 0.6 to 0.33%), but this effect was much more pronounced in the ABT-pretreated rats (0.071%, or a nine fold reduction). This reduction in liver levels implies that MFO inhibition was the causative factor. The reduction in MFO-mediated metabolism would also explain the lower amounts excreted in urine and exhaled as CO_2. The authors stated that, for a 20 mg/kg intravenous dose of nPB, MFO-mediated metabolism was three times that of GSH-mediated metabolism (30% oxidized compared to 10% conjugated). Since less reactive metabolites are produced in the absence of MFO activity, less nPB (and metabolites) is retained in liver tissue. In rats, RTI (2005) concluded that the relative importance of GSH increases with the dose, and at a dose level of 200 mg/kg nPB, essentially all metabolism is GSH-mediated. This is likely not true for mice, since saturation of metabolic pathways is not evident at similar dose levels. It is possible that the same effects would be seen in mice, but only at much higher concentrations. The 25 mg/kg dose level may be insufficient to completely deplete GSH stores in tissues, which would be consistent with the results reported by RTI (2005). If exposure were repeated, or was done at a higher concentration, greater impacts may have been seen with regard to conjugation-based metabolite formation.

Finally, ABT-pretreated rats had only a single metabolite detected in urine (N-acetyl-S-propylcysteine), which corresponded to the most abundant metabolite in the untreated rats (but represented only about 20% of total metabolites at the 20 mg/kg dose). In contrast, untreated rats had 10 metabolites in urine. The percentage of total metabolites represented by NASP increased in the 100 mg/kg rats to about 85%, or near that seen in the ABT-pretreated rats. Similar results were observed in the rat urine sample from the 800 ppm inhalation study. BSO-pretreated rats had the same five primary metabolites as did the untreated rats, but the relative amounts of these metabolites were somewhat different than in the untreated animals.

One additional experiment conducted by RTI (2005) confirmed that CYP2E1 is the MFO enzyme responsible for oxidative metabolism of nPB. In this study, CYP2E1-deficient mice (referred to as CYP2E1(-/-) mice) were exposed to 600 ppm nPB for 6 hours, and metabolites were identified in urine. N-acetyl-S-2-hydroxypropyl-cysteine, 2-hydroxy-1-bromopropane-O-glucuronide, and N-acetyl-S-propylcysteine were all detected in urine from these mice, but the two metabolites that require MFO in Phase 1 (N-acetyl-S-2-hydroxypropyl-cysteine and 1-bromo-2-propanol-O-glucuronide) were reduced by 38 and 64%, respectively, relative to normal mice. Conversely, the metabolite formed through direct conjugation with glutathione, N-acetyl-S-propylcysteine, was increased by 190% relative to normal mice. This demonstrates conclusively that CYP2E1 is the primary MFO enzyme involved with nPB

metabolism, but also indicates that others must also be involved to a minor extent since the MFO-based metabolites were still produced by these modified mice.

The metabolic profile changed in rats based on dose, while it remained the same in mice. For example, the relative amount of NASP was about the same for all dose levels tested in mice, while it increased dramatically for rats at the 100 mg/kg dose level relative to the 5 and 20 mg/kg dose levels. This provides evidence that the CYP2E1 metabolic pathway in rats may become saturated at fairly low concentrations, resulting in more direct conjugation with GSH. This also implies that mice have a higher capacity for nPB metabolism than rats.

Kinetics of nPB in Rats and Mice

Kinetics parameters in both rats and mice were estimated from the gas uptake studies, not from measurements of plasma concentrations following intravenous injection. The model used to calculate the kinetic parameters K_m and V_{max} (as well as the glutathione conjugation constant and half-life) was based on the work of Filser et al. (1995), which focused on volatile organic compounds (VOCs) such as styrene and ethylene oxide. This two-compartment model with physiological gas uptake was used instead of physiologically-based toxicokinetic modeling. This type of model assumes an organism is a single homogeneous compartment. For our purposes, where testis-specific metabolism is critical, such a model is not helpful.

Filser et al. (1995) states that their model allows quantification of invasion, accumulation, excretion, and biotransformation. It can also be used to calculate tissue concentrations at steady state if partition coefficients between tissues and air are known (these were estimated by RTI [2004]). Inhalation and exhalation clearances are independently measured, which can lead to generation of more accurate constants for these clearances. However, this does not extend to urinary clearance, which is more relevant for interpretation of the intravenous dosing studies conducted by RTI.

As stated by Filser et al. (1995), the benefits of the two-compartment model as opposed to a physiologically-based toxicokinetic model are:

- Few variables are involved, making calculations simpler
- Experimentally it is easy to apply to gas uptake studies.

However, disadvantages of this model relative to physiologically-based toxicokinetic models (as stated by the authors) include:

- Redistribution and metabolism in multiple organs cannot be distinguished.
- Understanding of tissue-specific concentrations are impossible
- Prediction of species-specific kinetics from in vitro data cannot be made.

Also, Filser et al. (1995) indicate that physiological models allow incorporation of physiologically and biochemically relevant mechanisms, which allows in-depth elucidation of toxicokinetic processes.

Based on this discussion, the kinetic parameters and modeling conducted by RTI (2005) may be useful in estimating the oxidative metabolism parameters for the entire animal, but they are not useful in delineating what occurs in the testis as opposed to the liver or other organs. Therefore, intrinsic clearance could not be estimated from the data because the K_m and V_{max} values are based on gas uptake, not on intravenous-based kinetics like both the TCE and 1,3-butadiene examples discussed above. Nevertheless, the results from RTI were further interpreted to the extent possible, as discussed below.

Rat studies by RTI (2005) indicate K_m in males is much higher than that of females (estimated values from RTI suggest K_m in males is 24 times higher than in females), while V_{max} is about 50% higher in males (0.227 mg/kg-hr) than females (0.143 mg/kg-hr). In addition, the glutathione conjugation constant in males is about twice that in females. If true, this suggests female metabolism becomes saturated at substantially lower concentrations than in males. This could lend support to the human studies indicating females appear more sensitive to neurotoxicity of inhaled nPB than males. It appears from the data presented that the oxidative pathway may become saturated in rats between 240 and 800 ppm.

These studies indicate that the percent of a dose metabolized in rats drops rapidly at the 2,700 ppm level (less than 50%) compared with all lower dose levels. This is at odds with the information obtained from their intravenous studies, which showed only 28 and 37% of the dose metabolized at 5 and 20 mg/kg, respectively. In the latter case, the percent of dose metabolized increased with dose, while in the gas uptake study the percent of dose metabolized was inversely proportional to dose. The intravenous dose represents a single injection, while the gas uptake studies evaluated inhalation exposures over a 6-hr period. This may provide an explanation for the differences observed. GSH levels in the liver were lowered about 80% in the gas uptake studies in both sexes, regardless of the air concentration. Therefore, once dose levels are reached that saturate the MFO system, it is plausible that significant amounts of unmetabolized nPB may remain in the rats for some time (the half-life was 5 times greater in rats pretreated with ABT). This would result in

higher levels of nPB reaching target organs such as the CNS and testis. It has already been demonstrated through work with other compounds that metabolism can occur directly in these organs, but insufficient amounts of GSH are available to bind to reactive metabolites formed in these tissues.

Mouse studies indicate no differences between males and females at gas uptake dose levels of 70 or 240 ppm. At the two higher dose levels, some of the sex differences observed in rats also begin appearing in mice, but the differences are much smaller in mice. K_m in males and females are similar (but much higher than in rats), although V_{max} is estimated by RTI (2005) to be about 50% higher in males (0.329 mg/kg-hr) than females (0.234 mg/kg-hr). This is essentially the same ratio calculated in rats. V_{max} is greater in mice than in rats, regardless of sex. Contrasting with the rat however, the glutathione conjugation constant in males is about four times lower than that in females. Therefore, sex-based metabolic differences do not appear significant in mice. It appears from the data presented that the oxidative pathway may become saturated in mice between 800 and 2,700 ppm.

Since mice appear to be able to metabolize higher doses of nPB through the liver than the rat, it is plausible to assume that higher doses would be necessary in the mouse to lead to accumulation of unmetabolized nPB in target organs (e.g., CNS and testis). Since the glutathione conjugation constants are much higher in mice than rats, it is also likely that any reactive intermediates formed in mice would be bound up by glutathione more rapidly than in rats. This affords the mouse greater protection than rats.

Development of firm conclusions regarding nPB kinetics is hampered by the lack of appropriate toxicity studies in mice, which would be helpful in validating the statements made above. If the arguments presented are true, then sperm motility and CNS effects in mice should only begin to occur at higher concentrations than in rats. Given the results of the intravenous dosing studies, rats appear to have metabolic impacts from dose levels of 20 and 100 mg/kg. Therefore, internal blood levels in rats between 5 and 20 mg/kg may be associated with metabolic pathway saturation. For mice, this did not occur at the highest tested intravenous dose, or 100 mg/kg. This implies at least a tenfold level difference between the two species in metabolic capacity. This is qualitatively supported by the gas uptake results, where rats appear to have metabolic changes at about 500 ppm (the midpoint between the 240 and 800 ppm dose levels) while mice do not have noticeable changes in the kinetic curves until dose levels exceed 1,000 ppm (and possibly as high as 2,500 ppm).

Unifying Mechanistic Hypothesis

Wang et al. (2004) theorized that the neurological and reproductive effects of nPB could have a common basis through impacts on neurospecific proteins. An earlier study (Wang et al., 2003) measured changes to gamma-enolase (a neuron-specific protein) in the rat CNS following 12-week daily inhalation exposures to nPB at 200, 400, and 800 ppm. Their results showed dose-dependent decreases in gamma-enolase levels in the cerebrum at 400 and 800 ppm dose levels. The authors suggested that this decrease is due to involvement of biochemical changes in neurons. They also reported depletion of glutathione at the 800 ppm dose level in several regions within the CNS (cerebrum, cerebellum, and brainstem). The authors concluded that glutathione depletion may be the underlying mechanism of neurotoxicity of nPB, and that this depletion leads to a decline in creatinine kinase (CK) in the CNS (this endpoint was also measured). In turn, the decline in CK can adversely impact the levels of adenosine triphosphate (ATP) in affected neurons, which can lead to toxicity.

Wang et al. (2004) did a similar analysis at the same dose levels, but focused on gamma-enolase and alpha-enolase levels in the testis and epididymis of male rats. Sperm count was not affected at any dose level, but sperm motility was significantly decreased at 800 ppm. Gamma-enolase levels were significantly increased at all dose levels in the epididymis (but not in the testis), while alpha-enolase levels were increased in the testis (but not in the epididymis) at dose levels of 400 and 800 ppm. While the information provided was not sufficient to postulate on a mechanism for these changes, they nevertheless demonstrate that impacts to neuron-specific proteins occur following exposure to nPB in both the CNS and reproductive tissues. This suggests that there may indeed be a single mechanistic basis for nPB toxicity, and that this mechanism affects neurological proteins. In turn, these neurological effects at the biochemical level impact proper functioning of the epididymis (and possibly the testis) in spermatogenesis.

Weight of Evidence for Reproductive Toxicity Potential of nPB in Humans

Based on the extensive information on nPB and other compounds presented in this memorandum on rats and mice, combined with the available data on humans, the following points can be made that focus on the potential for reproductive toxicity of nPB in humans.

With regard to metabolic processes:

- Mice tend to metabolize chemicals at a faster rate than do rats.
- Both mice and rats tend to metabolize chemicals at a faster rat than do humans.

With regard to anatomy and physiology:

- In the epididymis, more CYP2E1 is present in the mouse than the rat.
- CYP2E1 is more abundant in the epididymis than in the testis of humans.
- CYP2E1 in human testis is limited to Leydig cells.
- The cellular distribution of CYP2E1 in male reproductive tissues is similar in mice and humans.
- GSH levels in the liver were shown to be similar in rats and mice.
- GSH is present in the testis and epididymis of mice; more is present in the epididymis.

With regard to other structurally similar brominated compounds:

- iPB affects Leydig cells, where CYP2E1 is present. Leydig cells have not been shown to be affected by nPB.
- iPB mechanism of action involves induction of DNA damage and impairment of the functional antioxidant cellular defense in Leydig cells, and enhances lipid peroxidation. DNA damage and/or lipid peroxidation have not been reported in the literature for nPB.
- The histopathological changes in the testis induced by nPB are much different from those by iPB. nPB does not have the severe toxicity toward spermatogonia exhibited by iPB.
- Differences in altered gene profiles might reflect a difference in toxic mechanism between 1-BP and 2-BP, suggesting that nPB disrupts the endocrine balance while iPB disrupts undifferentiated cells.
- Metabolism of DBCP and 1,2,3-tribromopropane includes formation of halogenated epoxides (e.g., epibromohydrin). SAR work by Lag et al. (1991) indicates that the availability of a good leaving group in the C2-position would promote formation of a reactive metabolite from glutathione conjugation. nPB does not have a good leaving group in the C2-position, while iPB and DBCP do (i.e., bromine, chlorine).
- DBCP metabolism includes formation of a reactive episulfonium metabolite, which is not formed in the metabolism of nPB.
- DBCP reactions with GSH are actually bioactivation reactions, whereas nPB reactions with GSH are detoxifying reactions.

With regard to other chemicals metabolized through a combination of CYP2E1 and GSH:

- CYP2E1 activity for 1,3-butadiene is more than ten-fold greater in the mouse than in the rat, and about five times greater in the mouse than in humans. Therefore, humans generate fewer metabolites from this chemical than do mice or rats.
- TCE metabolism by CYP2E1 is highest in the mouse, slightly lower in the rat, and much lower in humans. Therefore, humans generate fewer metabolites from this chemical than do mice or rats.
- TCE metabolism in the rat becomes saturated at lower levels than in mice.
- CYP2E1 activity can directly metabolize TCE in reproductive tissues in mice and rats.
- TCE metabolites can directly bind with GSH in reproductive tissues in mice and rats.
- K_m values for TCE were significantly lower in liver cells from human females than those from human males, although these differences were not observed for V_{max}.
- Metabolic disposition of TCE in humans seems to be similar to that in mice, and indicates that the mouse model is appropriate for investigation effects and mechanisms of TCE-induced toxicity in the male reproductive system.
- GSH is depleted more in rats than in mice following methyl iodide exposure.
- For methyl iodide, the majority of protection afforded by GSH is due to activity from glutathione in the liver.

With regard to nPB:

- Metabolic processes differ between rats and mice.
- Metabolism is dose-dependent in the rat, but not in the mouse.
- Mice are substantially less sensitive to nPB than are rats (at least fivefold more resistant).
- Rats form more types of reactive metabolites from nPB CYP2E1 metabolism than do mice.
- K_m values for nPB in female rats are much lower than that in male rats; V_{max} is about 50% higher in males than females.
- K_m values for nPB in mice are similar in males and females (but much higher than in rats).
- V_{max} values for nPB in mice are higher in males than females.
- Data on humans generally indicate that females are more sensitive to nPB than are males, and neurological impacts are most frequently reported.
- Concentrations of nPB up to 170 ppm in the workplace have not been associated with neurological impact in humans.
- Reproductive effects have not been reported in human clinical or occupational studies.

This substantial body of information strongly implies that humans are not more sensitive to toxic effects of nPB than rats or mice, and are most likely less sensitive than rats. This information should be considered when identifying appropriate uncertainty factors for an OEL. TCE metabolism closely mirrors that of nPB in contrasting between rats and mice. The primary difference is that CYP2E1 metabolism of TCE leads to metabolites that are much more toxic than those from CYP2E1 metabolism of nPB.

Conclusions

Information presented in this memorandum suggests that the mechanism of action for nPB is based on effects on neuroproteins both within the nervous and reproductive systems. In turn, these neurological effects at the biochemical level impact proper functioning of the epididymis (and possibly the testis) in spermatogenesis. Therefore, the mechanism of action is not specific to the reproductive system, but rather is most specific to the neurological system.

Information presented herein indicates that the site of action for nPB may be intracellular neuroproteins, possibly within the mitochondria, and that these are affected both in the nervous system and reproductive organs, particularly the epididymis. Sites of action in the testis, spermatogonia, or Leydig cells have not been identified. Therefore, the site of action does not appear to be specific or localized to the reproductive tissues, but again is most specific to neurologically-related loci.

The SAR discussion demonstrates that there is essentially no relationship between nPB and other brominated compounds with reproductive toxicity, including iPB and DBCP, with regard to metabolism, likely toxic mechanism, or site of action.

Lastly, despite several case reports of humans occupationally exposed over several months to ten years at concentrations up to 170 ppm (and likely higher in some cases), only neurological toxicity has been reported. Data available for other similarly metabolized chemicals with reproductive toxicity, such as TCE, strongly imply that humans are less sensitive to the toxic effects due to slower metabolism of the parent chemical to reactive metabolites than rats or mice.

Uncertainty Factors

With this understanding, a recommendation for an overall uncertainty factor (UF) to convert the toxicity data in rodents to one that can be used as an occupational exposure limit in humans can be made. This is discussed below.

Neither the American College of Governmental Industrial Hygienicists (ACGIH) nor the Occupational Safety and Health Administration (OSHA) has published guidance on the application of UFs in setting a workplace exposure level. The USEPA offers some guidance for the use of UFs, which are used to downwardly adjust a no-observed adverse effect level (NOAEL) or low-observed adverse effect level (LOAEL) to a reference concentration (RfC) or a reference dose (RfD). However, this is applicable to environmental, not workplace exposure.

Historically in developing RfCs and RfDs, the USEPA uses separate UFs, each of which may be up to 10, to account for each of the following criteria when using the NOAEL/LOAEL method: (1) protection of sensitive individuals within the receptor population, (2) extrapolation of toxicity data from animals to humans, (3) extrapolation of subchronic toxicity data to chronic exposure durations, and (4) extrapolation from a lowest-observed adverse effect level (LOAEL) to a no-observed adverse effect level (NOAEL) to assess toxicity. A modifying factor (MF), generally no higher than 3, is typically also used to account for other considerations such as perceived adequacy of the scientific data. The UFs and the MFs for a given chemical are then multiplied together to provide a total UF, which is then used to derive a chronic RfD. The higher the total UF, the greater the degree of uncertainty and conservativism in the resultant RfD.

USEPA has recommended using an overall UF of 9 to downwardly adjust the identified NOAEL of 168 ppm (for reproductive effects) to 18 ppm (USEPA, 2003). This includes a factor of 3 for protection of sensitive individuals within a population, and a factor of 3 for interspecies extrapolation.

USEPA (1994) clearly states that there are differences in development of RfCs and OELs. They state "the evaluation of toxicity data by agencies deriving OELs may differ from that of EPA with respect to weight-of-evidence classification, application of UFs, and other issues...the use of OELs is established to protect the average healthy worker (ages 18 to 65 years) against the adverse effects of inhaled pollutants to which they are exposed only a fraction of a day (i.e., during a typical 8-h work shift). Inhalation reference concentrations, however, are relevant to those of any age and health status and are aimed at protecting the most sensitive members of the population, assuming long-term continuous exposures". Given the statement from USEPA that application of UFs differs between RfCs and OELs,

the two criteria for which UFs were applied are further discussed below with regard to their relevance in identifying an OEL for nPB.

Extrapolation of Toxicity Data from Animals to Humans

Historically, the USEPA has used an animal-to-human UF of 3 for inhalation-based values when deriving RfCs (Barnes *et al.*, 1995). This UF has typically been employed to account for differences across species, and always assumes that a chemical can be more toxic in humans than laboratory animals. USEPA used an uncertainty factor of 3 for this extrapolation, based on their conclusion that there are not data to compare the pharmacodynamics between rodents and humans. While this may have been true when written in 2003, recent research (RTI, 2005) has now addressed this data gap.

The toxicological information presented herein indicates that humans will generate toxic metabolites at a lower rate than rats or mice, and therefore should be less sensitive to nPB than either of these species. Even though humans have a lower margin of safety than rats or mice with regard to sperm motility in general, the available animal and human data on nPB support the interpretation that humans are not more sensitive to nPB than either rats or mice. Therefore, for this chemical actual data should preclude the need for a UF for this extrapolation.

Protection of Sensitive Individuals

Workplace exposure typically does not involve sensitive individuals. ACGIH TLVs and OSHA PELs are based on exposure of healthy adult workers, and rarely employ a UF protecting sensitive individuals, even though some workers may be pregnant and would be defined as "sensitive receptors" in a risk assessment. Neither agency typically provides information regarding the use of UFs in establishing OELs. USEPA used an uncertainty factor of 3 to account for sensitive individuals in their OEL derivation.

While a healthy worker population will have individual variation, such variability is not expected to be wider than that in test animals. Human data on TCE collected from a random sample of workers demonstrated a range of enzyme activity involved in nPB metabolism of less than a factor of ten, similar to test animals (Lipscomb et al., 1997). This implies that sensitive humans are no more sensitive than sensitive rats or mice.
An OEL developed for workplace exposure precludes children from being regularly exposed. Although fetuses could be exposed, data from the two-generation study (WIL, 2001) indicate that the developing fetus is not substantially more sensitive to nPB than the mother. Use of an OEL based on F_1 generation data, as was done by both USEPA (2003) and Stelljes and

Wood (2004) is adequate to address potential fetal exposure through pregnant workers, particularly when different human child and F_1 pup exposures are considered, without the need for an additional uncertainty factor.

The concentration recommended by USEPA (2003) and Stelljes and Wood (2004) for use in developing an OEL is based on the decline in sperm motility in male rats in the first generation of the 2-generation study (WIL, 2001). The BMDL associated with this endpoint is 156 ppm, and reflects impacts on the F_1 generation. This concentration essentially incorporates a UF of 2 compared with the value for the same endpoint in the more relevant F_0 generation (263 ppm / 2 = 131.5 ppm). Actual human workplace exposures are unlikely to replicate those of the F_1 generation, where both parents would be exposed to nPB at work full-time, and their children would be exposed daily until adulthood.

A UF of no greater than 2 was recommended by others to account for the slope of the dose-response curve for nPB using headaches in humans as an endpoint and precursor to other effects (Rozman and Doull, 2002). These authors concluded that a factor of 2 would "protect nearly all workers" based on the following assumptions:

- Neurotoxicity is the most sensitive endpoint of exposure in humans
- Headache is a low-dose precursor effect for other neurotoxicity effects in humans (Doull and Rozman, 2002)
- The steepness of the dose-response curve for anesthesia indicates that a factor of 2 will encompass virtually every individual in any realistic population size
- Rats have similar or higher sensitivity to nPB than humans.

These assumptions have been supported by the data discussed in this paper.

Recommendations

At most, the overall toxicological database indicates that an uncertainty factor of no more than two is relevant for nPB, rather than the UF of nine used by USEPA (2003).

Much of the most relevant data used to reach this recommendation was not available when USEPA published their OEL recommendation in 2003. Considering the new information provided herein, the relevance of UFs for developing an OEL for nPB should be reevaluated. We consider the database sufficiently robust to recommend an overall UF of one or two for this chemical.

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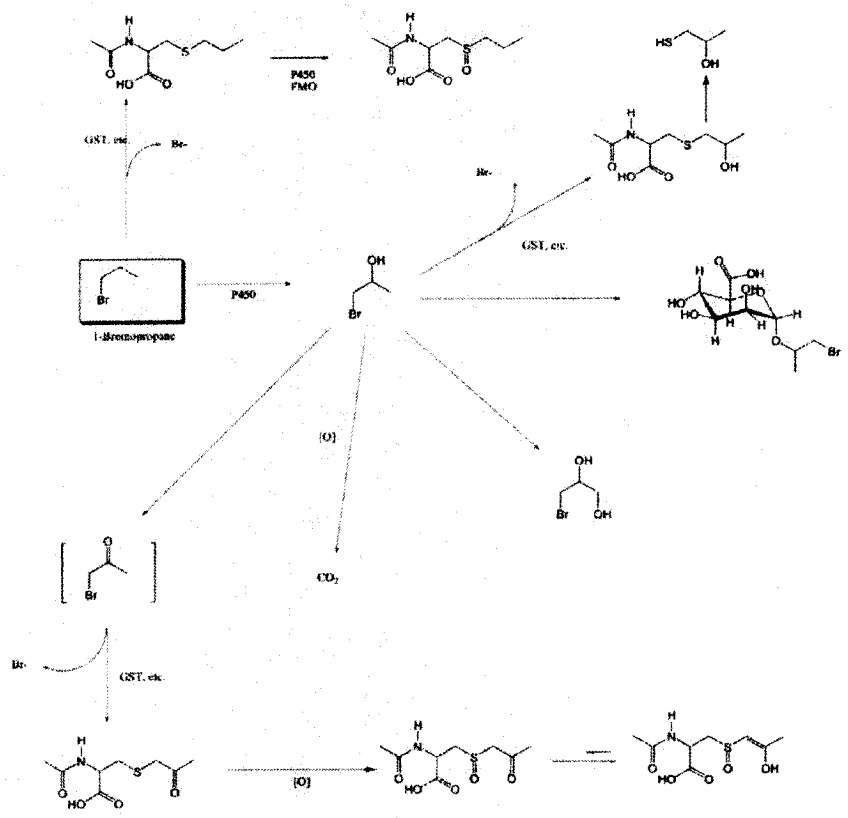


Figure 1. Proposed Metabolism of 1-Bromopropane in Rats (from RTI, 2005). Blue lines represent predominant pathways; red line predominates at high doses.

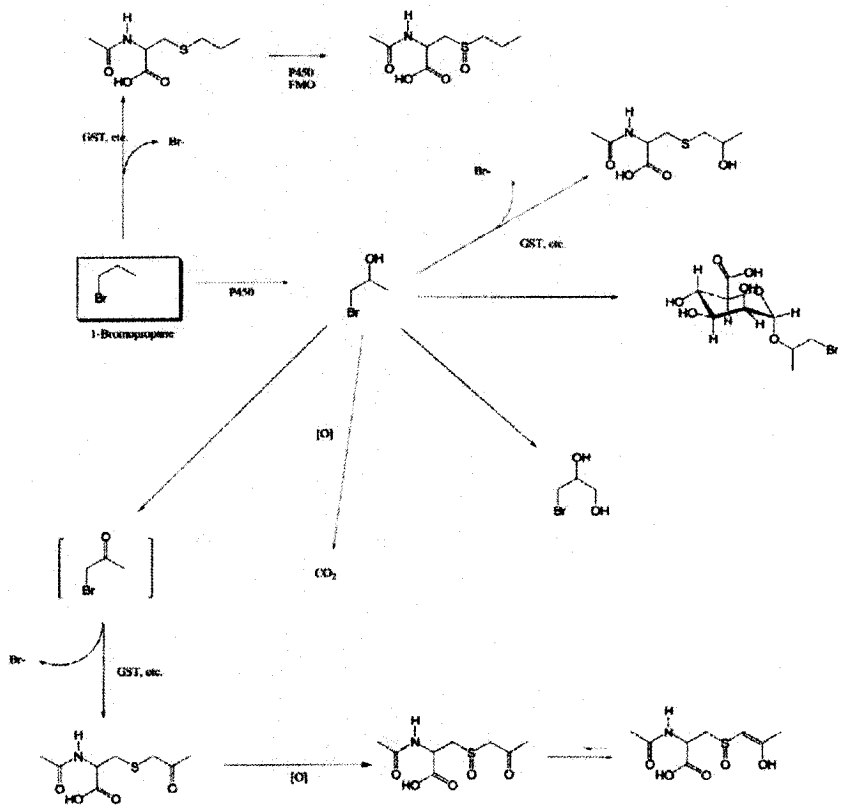
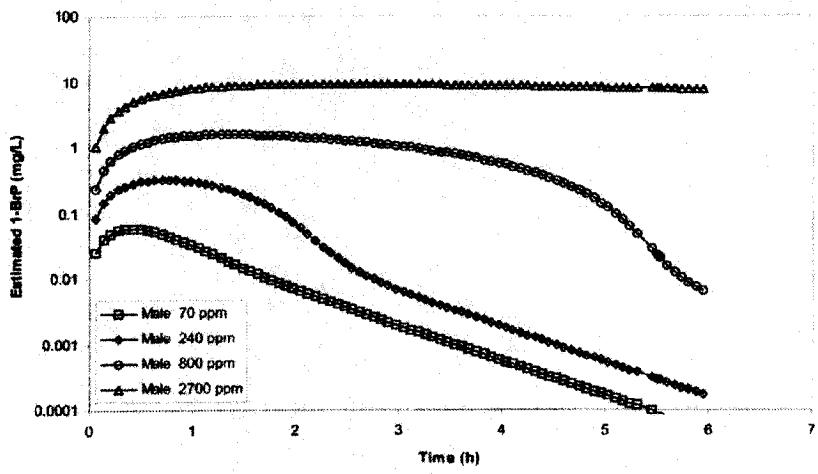
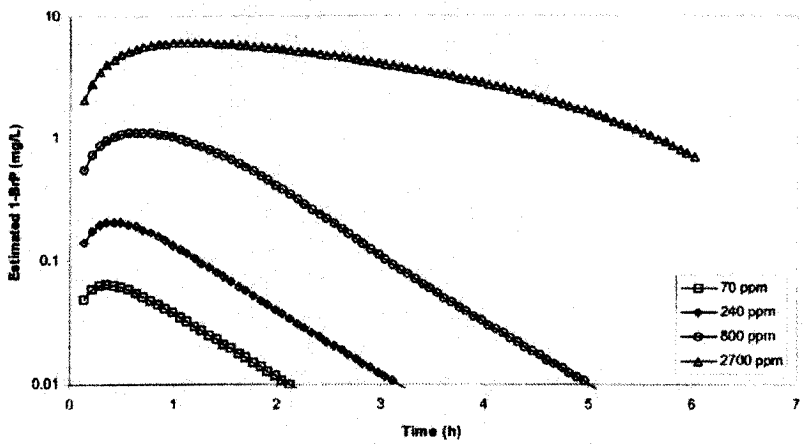


Figure 2. Proposed Metabolism of 1-Bromopropane in Mice (from RTI, 2005). Blue lines represent predominant pathways.



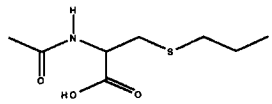
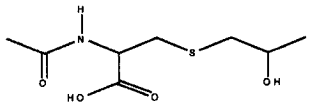
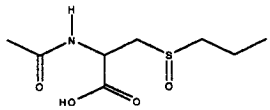
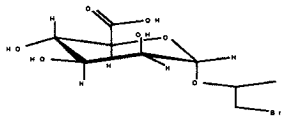
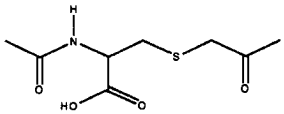
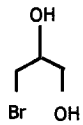


* Whole body 1-BrP levels were estimated using a 2 compartment model based on the work of Filser et al. (1995) with estimated kinetic parameters.

Figure 3. Body Levels of nPB in rats (top panel) and mice (lower panel) after inhalation exposures to different dose levels (from RTI, 2005).

Table 1.

Urinary Metabolites of nPB Detected in Mouse and Rat Urine

			Relative Abundance[a]	
Acronym	**Metabolite[b]**	**Chemical Structure**	**Rat[c]**	**Mouse[d]**
APC	N-acetyl-S-propylcysteine		37	Primary
AHPC	N-acetyl-S-(2-hydroxy)-propylcysteine		16	Highest
APCO	N-acetyl-S-propylcysteine S-oxide		5	Secondary
BPG	2-hydroxy-1-bromopropane-*O*-glucuronide		9	Primary
APS	N-acetyl-S-(2-oxopropyl)cysteine		12	Secondary
ABH	alpha-bromohydrin		"Major"	Minor

Notes:

-- = Not present.

Footnotes:

[a] As measured in urine following 6-hr nPB inhalation at 800 ppm.

[b] Three additional trace metabolites were detected in rats, but no identifications were provided by RTI (2005).

[c] Percent of administered dose.

[d] Relative peak sizes from urinary GC data for intravenous doses of 20 and 100 mg/kg, and inhalation dose of 800 ppm.

Table 2.

Estimated Metabolic Rate Constants in Mice and Rats Following Gas Uptake Inhalation[a]

Parameter	Units	Rats		Mice	
		Males	Females	Males	Females
Vmax	mg/hr-kg	0.227	0.143	0.329	0.234
Km	mg/L	0.215	0.009	5.22	5.90
Kgst	hr^{-1}	0.00011	0.00005	5.97	24
$T_{1/2}$ (70 ppm)	hr	0.5	1.0	0.7	0.4
$T_{1/2}$ (240 ppm)	hr	0.6	1.0	0.6	0.7
$T_{1/2}$ (800 ppm)	hr	1.1	2.0	0.9	0.7
$T_{1/2}$ (2700 ppm)	hr	2.4	6.1	3.8	1.9

Abbreviations:

mg = milligrams; hr = hours; kg = kilogram, L = liters; V_{max} = maximum P450 reaction rate;
'K_m = Michaelis-Menton constant; K_{gst} = glutathione conjugation constant;
$T_{1/2}$ = half-life of nPB in the body.

Footnotes:

[a] Calculated by RTI (2005) using model by Filser et al. (1995).

Opinion on the Potential Carcinogenicity of 1-Bromopropane Based on the Preliminary Results of the 2008 NTP Rat Bioassay

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Opinion on the Potential Carcinogenicity of 1-Bromopropane

Based on the Preliminary Results of the 2008 NTP Rat Bioassay

In July, 2008, the National Toxicology Program released the pathology tables, growth and survival curves for the Fischer F344 rat (NTP 2008a) associated with the Technical Report on a study in which Fischer 344 rats and B6C3F1 mice were administered various concentrations of 1-bromopropane by inhalation for 2 years. Upon the release of these data, ENVIRO Tech International, Inc. contracted with ENVIRON International Corporation, in conjunction with Dr. Harvey Clewell of The Hamner Institutes for Health Sciences, to provide an opinion on the potential for the US Environmental Protection Agency (USEPA) to classify 1-bromopropane as a possible or likely human carcinogen.

In considering the potential for USEPA to classify 1-bromopropane as a carcinogen, there are several types of data analyses and comparisons that must be considered. These include not only the statistical evaluation of the pathology endpoints evaluated in the bioassay, which provides a comparison to the corresponding control animals, but also comparison of the pathology incidence of historical controls for the endpoints of interest. Consideration of any precedents where the USEPA considered similar endpoints in the development of cancer potency factors is also critical, as well as how the new cancer guidelines (USEPA 2005) and the human relevance framework described in these guidelines might be used in determining the potential relevance to human health of selected endpoints observed in chronic animal bioassays.

In evaluating the neoplastic endpoints noted in the pathology tables for 1-bromopropane, the incidence of a limited number of endpoints significantly increased with increased dose (positive trend) or demonstrated pair-wise significance (Table 1). These were limited to various combinations of lesions of the skin in male and female rats, pancreatic adenomas in male rats, and benign tumors (adenoma) of the colon in female rats.

In consideration of the skin tumors, the largest incidence of lesions observed was from a combination of a number of tumor types including basal or squamous cell carcinoma, carcinoma, basosquamous tumors (malignant or benign), basal cell adenoma, adenoma, papilloma, squamous papilloma, keratoacanthoma, and trichoepithelioma. Of these tumors, only the incidence of keratoacanthoma was statistically significantly increased by both trend analysis and pairwise comparison.

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The standard protocol for an NTP inhalation bioassay involves the animals being exposed to the compound of interest in whole body inhalation chambers. Because frequent symptoms noted in workers using 1-bromopropane are nose, throat, and eye irritation (Ichihara et al. 2004), an initial mode-of-action hypothesis would be that the observed skin tumors are a result of the irritant potential of NPB and possibly not an endpoint that would be relied upon by the USEPA to assess carcinogenic potential. If this were the case, those animals with skin tumors would be expected to have signs of skin irritation.

A significant dose-related increase in the incidence of mild to marked chronic inflammation of the skin (1/50, 4/50, 5/50, 14/50) was observed in male rats. However, comparison of the animals noted to have a skin tumor and those with inflammation of the skin (Table 2) suggests that inflammation or irritation of the skin is not likely a mode of action for the observed skin tumors, since most of the animals with skin tumors were not diagnosed to have chronic inflammation of the skin.

It is possible that the tumors observed in the skin of rats following inhalation exposure to 1-bromopropane are the result of the dermal absorption of 1-bromopropane into the skin and the subsequent metabolism to a reactive intermediate. If this were the case, it is possible that the mode of action for these skin tumors may not be relevant to humans, because of differences in metabolism in the skin across species. However, further investigation would be required to establish such as mode of action.

While there is no precedent for the USEPA to use skin tumors in assessing the potential carcinogenicity of a compound following inhalation exposure, the NTP has used similar tumors in the assessment of the evidence of carcinogenicity of a compound following inhalation exposure. In the technical report for chloroethane (NTP 1989), the presence of similar benign and malignant neoplasms of the skin in male F344 rats observed following inhalation exposure resulted in the categorization of *equivocal evidence of carcinogenic activity*. As with 1-bromopropane, the incidence of the individual skin lesions was small, with only a combination of tumor types (trichoepithelioma, sebaceous gland adenoma, or basal cell carcinoma) achieving statistical significance (0/50 in controls, 5/50 in treated). The NTP's definition of this category is that there are marginal increases in neoplasms that may be chemically related. While this category does not suggest strong carcinogenic potential, the NTP did find it sufficient to suggest equivocal, rather than no, carcinogenic activity of chloroethane.

One of the external peer reviewers for the NTP (1989) chloroethane technical report recommended that the conclusion for male rats be changed to no evidence of carcinogenic activity; however, the recommendation was not accepted by the panel. One justification for consideration of these tumors was that the combined incidence was outside the range of values for historical controls. The current NTP historical male F344 control incidence for the skin tumor combination reported for 1-bromopropane following inhalation exposure to compounds is 7.7±4.4% (NTP 2008b). Therefore, it could be

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concluded that the incidence in the highest treated group is greater than historical controls.

One critical determinant of whether the USEPA may use the skin tumor incidence for classification of the carcinogenic potential of 1-bromopropane will be the conclusions and recommendations made by the Pathology Working Group for the NTP and the external Peer Review Panel.

Pancreatic adenomas (a benign tumor) in male rats, while statistically significant by both pairwise and trend analysis, do not appear to progress, as there is a negative trend for carcinomas with increasing dose. The incidence of another benign tumor, adenoma of the colon, increased with increasing dose of 1-bromopropane in female rats, achieving statistical pairwise significance at the high dose. Although benign tumors do not represent the same potential health risk to humans as malignant tumors, according to the USEPA (2005) Cancer Guidelines:

> "Observation of only benign neoplasia may or may not have significance for evaluation under these cancer guidelines. Benign tumors that are not observed to progress to malignancy are assessed on a case-by-case basis. There is a range of possibilities for their overall significance. They may deserve attention because they are serious health problems even though they are not malignant; for instance, benign tumors may be a health risk because of their effect on the function of a target tissue such as the brain. They may be significant indicators of the need for further testing of an agent if they are observed in a short- term test protocol, or such an observation may add to the overall weight of evidence if the same agent causes malignancies in a long-term study. Knowledge of the mode of action associated with a benign tumor response may aid in the interpretation of other tumor responses associated with the same agent. In other cases, observation of a benign tumor response alone may have no significant health hazard implications when other sources of evidence show no suggestion of carcinogenicity."

Therefore, for both of these tumor types, it would be important to establish that they either develop by a mode of action specific to the animal or would not be expected to result in serious health problems.

No quantitative inhalation assessments since the development of the latest Cancer Guidelines (USEPA 2005) are available on IRIS using benign tumors, specifically adenomas. However, the available assessment for 1,3-dichloropropene (USEPA 2000) is conducted based on the incidence of bronchioalveolar adenomas in male mice. The documentation indicates that:

> 'The critical study for assessment of cancer inhalation potency is the study by Lomax et al. (1989) in which rats and mice were exposed to up to 272 mg/m3 1,3-

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dichloropropene vapors for 6 hours/day, 5 days/week for 2 years. This is a well-designed and well-conducted bioassay that followed standard guidelines. Epoxidized soybean oil was the stabilizing agent in the formulation of 1,3-dichloropropene, which eliminated possible confounding effects of epichlorohydrin. Lomax et al. (1989) is the only available 2-year inhalation bioassay. Confidence in this study is supported by the results of a 90-day subchronic study (Stott et al., 1988), which are consistent with the Lomax et al. (1989) bioassay findings.

The only neoplastic response observed in any species or sex was an increased incidence of bronchioalveolar adenomas with late onset, in male mice in the highest dose group. The incidence in the high-dose group exceeded the range of historical control rates among mice in the same laboratory."

Therefore, based on the guidelines (USEPA 2005) for the use of benign tumors and their use in the assessment for 1,3-dichloropropene, USEPA may consider the colon tumors in female rats or the pancreatic tumors in male rats as suggestive of the carcinogenic potential of 1-bromopropane.

In conclusion, based on an independent assessment of the rat pathology tables from the NTP (2008a) study with 1-bromopropane, it is difficult to determine with any certainty how the USEPA would classify this compound for carcinogenic potential. For the endpoints with significant dose-related increases in incidence (skin tumors, pancreatic tumors and benign colon tumors), the results from the rat NTP (2008a) bioassay suggest weak, if any, carcinogenic potential of the compound. However, in the absence of the results of the mouse study, the conclusions reached by the NTP and further investigation into the potential modes of action for each endpoint, it cannot be concluded with certainty that 1-bromopropane would not be classified by the USEPA as potentially carcinogenic in humans. The available evidence may provide justification for the classification of *suggestive evidence of carcinogenicity* for 1-bromopropane under the new USEPA Cancer Guidelines (USEPA 2005), which does not necessarily require a quantitative assessment

Examples provided in the Guidelines (USEPA 2005) for compounds which may receive the classification *suggestive evidence of carcinogenicity* include:

- "a small, and possibly not statistically significant, increase in tumor incidence observed in a single animal or human study that does not reach the weight of evidence for the descriptor "Likely to Be Carcinogenic to Humans." The study generally would not be contradicted by other studies of equal quality in the same population group or experimental system."

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- "a statistically significant increase at one dose only, but no significant response at the other doses and no overall trend."

The results of the rat NTP (2008a) could be classified as consistent with these examples, depending upon the final determination of the NTP.

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Table 1

Incidences of Neoplastic Lesions with a Significant Pair-Wise or Positive Dose-Response Trend with 1-Bromopropane Inhalation Administration in Rats (NTP 2008)

Tumor Type	Incidence	Species
Pancreas: Islet Cell Adenoma	0/50, 5/50, 4/50, 5/50[a]	Male F344 rats
Pancreas: Islet Cell Adenoma or Carcinoma	3/50, 10/50, 9/50, 8/50[b]	Male F344 rats
Skin: Keratoacanthoma	0/50, 3/50, 6/50, 6/50	Male F344 rats
Skin: Squamous Cell Papilloma, Papilloma, Squamous Cell Carcinoma, Keratoacanthoma	1/50, 4/50, 6/50, 8/50	Male F344 rats
Skin: Basal or Squamous Cell Tumors[c]	1/50, 7/50, 9/50, 10/50	Male F344 rats
Intestine, Large: Colon/Rectum Adenoma	0/50, 1/50, 2/50, 5/50	Female F344 rats
Skin: Basal or Squamous Cell Tumors[a]	1/50, 1/50, 1/50, 4/50	Female F344 rats

[a] Significant by Poly 3 trend test and significant by pairwise comparison for all 3 treated groups

[b] Not significant by the Poly 3 trend test, significant pairwise comparison for the low- and mid-dose groups. A negative for carcinomas only (data not presented).

[c] Includes basal or squamous cell carcinoma, carcinoma, basosquamous tumors (malignant or benign), basal cell adenoma, adenoma, papilloma, squamous papilloma, keratoacanthoma, and trichoepithelioma

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Table 2
Individual Male Rats with Skin Tumors[a] and Chronic Inflammation of the Skin (NTP 2008)

Concentration	Animals with Skin Tumors	Animals with Chronic Inflammation of the Skin
Control	00028	00045
125 ppm	00204 00208 00210 00232 00241 00243 00250	00204 00213 00227 00239
250 ppm	00405 00420 00428 00430 00434 00439 00445 00446 00449	00409 00412 00435 00446 00450
500 ppm	00613 00614 00617 00619 00626 00636 00643 00646 00648 00649	00602 00603 00608 00609 00610 00618 00619 00624 00626 00631 00632 00638 00643 00650

[a]Includes basal or squamous cell carcinoma, carcinoma, basosquamous tumors (malignant or benign), basal cell adenoma, adenoma, papilloma, squamous papilloma, keratoacanthoma, and trichoepithelioma

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August 10, 2010

Thomas Huynh
Director
Air Management Services
Philadelphia Department of Public Health
321 University Avenue, 2nd Floor
Philadelphia, PA 19104

Re: Proposed Air Management Regulation XIV

Dear Mr. Huynh:

I write on behalf of the Halogenated Solvents Industry Alliance, Inc. (HSIA), an association of producers and users of the dry cleaning solvent perchloroethylene (perc), which is the primary subject of the proposed regulation. HSIA has participated, along with other industry stakeholders, in the rulemaking proceedings, and believes that, in general, the Department of Public Health has struck the right balance by establishing requirements for maximum concentrations of perc in adjacent commercial structures. This approach protects public health with a large margin of safety while allowing perc to continue to be used by dry cleaners who invest in and maintain state-of-the-art equipment with appropriate engineering controls.

We understand that some of the stakeholders may object to the proposed prohibition on n-propyl bromide (nPB) as a dry cleaning solvent. HSIA has generally not taken positions on the health and environmental merit (or lack thereof) of alternatives to perc and other chlorinated solvents, even though the suppliers of some of these alternatives have in the past engaged in predatory marketing practices. We would, however, commend the Department for having the foresight to realize that no purpose is served by imposing restrictions on a substance such as perc without giving consideration to the public health impact of the alternatives that may be used in its place.

In this regard, we would share an observation regarding what has come to be known as "regrettable substitution." The example concerns compounds that were used as replacements in automotive brake cleaners after perc was banned in that application by the California Air Resources Board:

> "Between 1995 and 2003, California auto repair workers were exposed to hexane, a well-known neurotoxic chemical found in automotive brake cleaners and many other commercial products. In 2000, several workers developed a neurological

disorder that caused decreased function of their arms and legs. Each year, millions of cans of hexane-based products were sold in California as an alternative to chlorinated solvents, which were also hazardous but were more heavily regulated in the state.

The use of hexane, which continues today, highlights problems that are universal to current chemical and product management:

• Uncontrolled use: Hexane was introduced without restrictions into the California market and used in higher volume and with fewer worker protections than anticipated by manufacturers.

• Disproportionate impact: The most highly exposed workers were those in entry-level jobs, held mainly by Latino and Asian immigrants.

• Lack of authority: Agencies lacked the authority to obtain sales data from manufacturers. As a result, they could neither assess the scope of the health threat nor identify specific workers at risk. Agencies also lacked the authority to phase-out the use of these products.

• Regrettable substitution: The phase-out of chlorinated solvents, though appropriate, occurred without an effective strategy for managing substitutes, resulting in the introduction of a new hazard, in the form of hexane.

• Barriers to safer alternatives: Safer, water-based cleaners were available but appeared more expensive than hexane-based products, whose true costs were externalized to the public. These costs included worker diseases, air pollution, and the disposal of 6 million aerosol cans of hazardous product waste each year into public landfills.

A comprehensive chemicals policy would simultaneously address this full set of problems by pairing the regulation of known hazards directly with the evaluation and adoption of safer alternatives."[1]

One of the authors of this report was quoted thereafter:

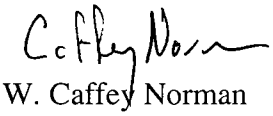
"One initiative goal is to prevent the unintended health consequences of chemical substitutions. UC Berkeley research scientist Michael Wilson studied auto

[1] UC Centers for Occupational and Environmental Health (COEH), Green Chemistry, Cornerstone to a Sustainable California (2008), p. 16; http://coeh.berkeley.edu/docs/news/green_chem_brief.pdf.

> mechanics disabled by a neurotoxic blend of hexane and acetone used as a brake cleaner. The product had been substituted for chlorinated solvents . . . . The next reformulation was no better: Hexane was swapped out for bromopropane [nPB], known to cause [present a risk of] sterility, Wilson said.
>
> "The current approach to managing chemicals is akin to an emergency response system, which is not enough. You also need to have a prevention system in place, Wilson said."[2]

We urge the Philadelphia Department of Public Health to consider fully the potential implications for public health of any alternative that would be used as a result of restrictions it imposes on the use of perc.

Very truly yours,



W. Caffey Norman

[2] http:/www.universityof california.edu/news/article/22772.

APPENDIX B –
PUBLIC HEARING SIGN-IN-SHEET

(2)

SIGN-IN SHEET

AIR POLLUTION CONTROL BOARD PUBLIC HEARING ON REGULATION XIV CONTROL OF PERCHLOROETHLENE FROM DRAY CLEANING FACILITIES

Thursday, AUGUST 12, 2010

	NAME	AFFILIATION	ADDRESS AND/OR E-MAIL
1	Hallie Weiss	City of Phila, AMS	hallie.weiss@phila.gov/321 University Ave Phila 19104
2	Myon Park	Phila	7569 Haverford Ave. Phila
3	Effie Baltle	APCB	MARSH
4	[illegible]		jiklee 06@gmail.com
5	Nak yul Kim		Nakyul Kim@Gmail.Com
6	Eunice Chin	PCA	Chineunice@Yahoo.Com
7	Susub Chin	PCA	" "
8	Anna Hwang		atua08240@temple.edu.
9	Andrew Zalewski	Envirco	Andrew@Greenleepartners.com
10	Kevin Andrews	Enviro Tech	Kevin@greenleepartners.com
11	Jason Kim	Korean D.C. Assoc.	
12	Patrick O'Neill	City Law Dept.	patrick.o'neill@phila.gov
13	Dennis Yuen	City Law	Dennis.Yuen@phila.gov
14	Ed Braun	AMS	edward.braun@phila.gov
15	THOMAS HUYNH	AMS	THOMAS.HUYNH@PHILA.GOV
16	Allen Finkel	Ulenn	afinkel@law.upenn.edu
17	Mia Nam		
18	Yong Kwak		1CYH1853@Yahoo.Com
19			
20	Rocio Vasquez		

3

SIGN-IN SHEET

AIR POLLUTION CONTROL BOARD PUBLIC HEARING ON REGULATION XIV CONTROL OF PERCHLOROETHLENE FROM DRAY CLEANING FACILITIES

Thursday, AUGUST 12, 2010

	NAME	AFFILIATION	ADDRESS AND/OR E-MAIL
1	Dae Tae Lee		wilee2@yahoo.com.
2	Lee.	Lee Cleaners 2554	Germantown Ave
3	Lee	Lee's Cleaners	2554 Germantown Ave
4	Chris Lee	Lee "	2554 Germantown Ave
5	Pedie Jmt	MIALA	9 PINDARPINDBAKER WAY, Princeton NJ
6	MARIA LEEE	KYL cleaners	2625 Germantown
7	SOU LEE	KYL Cleaners	" "
8	Dae Lee	Kye cleaner	2625 Germ. .
9	WAM Myong	New Hollywood cleaner	2246. N. 22 57
10	JeMin HAN	Betty Brite	ssamaihan@Gmail.com
11			
12			
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(4)

SIGN-IN SHEET

AIR POLLUTION CONTROL BOARD PUBLIC HEARING ON REGULATION XIV CONTROL OF PERCHLOROETHLENE FROM DRAY CLEANING FACILITIES

Thursday, AUGUST 12, 2010

	NAME	AFFILIATION	ADDRESS AND/OR E-MAIL
1	Barbara Rahke	Philaposh	3001 Walnut ST, 5th fl. Phila 19104
2	Mike Bassett	SBDC Wharton	Philadelphia PA
3	[illegible]		
4	JIN HUAN		Philai PA.
5	Phillip R	Concordville Cleaners	~~Bat~~ Bat Phillip.R@gmail.com
6	Mike R	"	" "
7	IL HYON NAM	New Hollywood cleaners	2846 N 22nd st. phila. PA. 19132
8	JAKE KANG	RIM'S CLEANERS	2203 South st. Jakewkang@AOL.COM
9	Sang Jeon	J-Brite cleaners	617 S 5th st Philadelphia PA 19147
10	IN GUN	Felix "	33rd Spring Garden PA 19123
11	Hoon Ju		413 N 63rd St phila 19151
12	Isaac An	Broad st cleaners	1541 S. Broad st 19147.
13	Soo H Lee	KYL Cleaners	2625 Germantown
14	Marija Borjan	NYC Dept. of Health	~~253 [illegible]~~ 253 Broadway, NY, NY
15	Eun T. Lee	Korean Daily News paper	1330 Willow Ave. Elkins Park 19027
16	Alyssa Tombler	Alyssa Tombler	1515 Walnut st.
17	JUNG HEE KANG		1620 COTTMAN AV Phila PA 19111
18	B/C SAVE Cleaners,		
19			
20			

(1)

SIGN-IN SHEET

AIR POLLUTION CONTROL BOARD PUBLIC HEARING ON REGULATION XIV CONTROL OF PERCHLOROETHLENE FROM DRAY CLEANING FACILITIES

Thursday, AUGUST 12, 2010

	NAME	AFFILIATION	ADDRESS AND/OR E-MAIL
1	DALE KAPLAN	PA DRY CLEANERS	KAPLANS1@aol.com
2	RICHARD MORFORD	EnviroTech Int.	RMORFORD@ENVIROTECHINT.COM
3	RAY ROCCON	"	rroccon@envirotechint.com
4	Jon Meijer	DLI	meijerj@dli.org
5	SCOTT Mondi	Poly Systems	mond.@fabrisolv.com
6	Dov Shellef	Poly Systems	shellef@fabrisolv.com
7	Carol Memberg	PDCA	cmemberg@aol.com
8	Jane Zellers	PDCA	JCzellers@verizon.net
9	JOSEPH IANNARULLI	ENVIROTECH INT	JIANNARULLI@ENVIROTECHINT.COM
10	Mark Stelljes	SLR Int'l. Corp	mstelljes@slrcorp.com
11	Hal Horning	National Clothesline	clothesline@mac.com
12	Mark Dann	Rutgers	dannmark2000@yahoo.com
13	Sue Minor	APCB	
14	SOVINN CHOU	LSD Translator	
15	Yong S. Kim	Flash cleaner	
16	[illegible]	HOST	1231 . 20TH yongkim3@msn.com
17	Bill Dunagan	PA SBDC EMAP	wdunagan@wharton-upenn.edu
18	Miriam Fallon	Greenpeace	mfallon@greenpeace.org
19	Cornell Brown	Germantown Jeweler Business	GLBMA 19133@gmail.com
20	Cliff McCallum	White Seal Cleaner	4904 Baltimore Ave

Testimony only – sign in sheet
Public hearing
Thursday August 12, 2010

(1)

	NAME	AFFILIATION	KOREAN INTERPERTER NEEDED - yes or no
1	RAY ROCCON	ENVIRO TECH INT. INC.	
	DALE KAPLAN	PA Dry Cleaners	
3th	RICH MORFORD	ENVIRO TECH INT, INC.	
	JON MULIJER	DLI	
5th	DOV SHELLEF	POLY SYSTEMS.	
	Carol Mentberg	PA-DE Cleaners Assn.	
2	JOSEPH IANNANNI	ENVIROTECH INT	
4	Mark Stelljes	SLR International Corp.	
	Mark Dann	Rutgers	
	Myriam Fallon	Greenpeace	
	CORNELL BROWN	Germantown Lehigh Business Association	
	Nuk Youl Kim	Happy Cleaners.	
	JASON KIM	Korean D.C. ASSOC.	
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Testimony only – sign in sheet
Public hearing
Thursday August 12, 2010

	NAME	AFFILIATION	KOREAN INTERPERTER NEEDED - yes or no
1	Mia Nam	Lee's Cleaners	
2	Sang Byung Gi	411 S 60th ST phila PA 19143	
3	Juan Manuel Irejo		
4	CORNELL BROWN	GERMANTOWN Lehigh Business Associat	
5	[redacted]	[redacted]	
6	Barbara RAHKE	PHILAPOSH -	
7	SOO LEE	KYL DRY CLEANERS.	NO
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Testimony only – sign in sheet
Public hearing
Thursday August 12, 2010

	NAME	AFFILIATION	KOREAN INTERPERTER NEEDED - yes or no
1	IL Hyon. AM	New Hollywood cleaners.	
2	Isaac An	Broad st cleaners.	N
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Testimony only – sign in sheet
Public hearing
Thursday August 12, 2010

	NAME	AFFILIATION	KOREAN INTERPERTER NEEDED - yes or no
1	Alyssa Tombler	Citizens for Pennsylvania's Future (PennFuture)	
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APPENDIX C –
PUBLIC HEARING TRANSCRIPT

0001

CITY OF PHILADELPHIA
AIR POLLUTION HEARING

- - -

IN RE: AIR MANAGEMENT REGULATION XIV

- - -

AUGUST 12, 2010

- - -

Public Hearing for the City of Philadelphia Department of Public Health Air Pollution Control Board held in the Spellman Building, 321 University Avenue, Philadelphia, Pennsylvania, in the above-referenced matter before Lori Marculini, Court Reporter-Notary Public at 6:15 p.m.

- - -

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- - -

0002

MR. BRAUN: We will now open the public hearing for the City of Philadelphia, Department of Public Health, Air Pollution Control Board, Air Management Regulation XIV, controlling of Perchloroethylene from dry cleaning facilities.

Good evening, my name is Ed Braun. I am Program Manager for the Air Management Services, AMS, a unit of the Philadelphia Department of Public Health.

With me today is Thomas Huynh, the Director of AMS. Eddie Battle, Chair of Air Pollution Control Board, the Board. Joe Minott, Member of the Board and the Divisional Deputy City Solicitor, Patrick O'Neil, of the City's Law Department.

AMS is responsible for the prevention, abatement and control of air pollution in the City and County of Philadelphia.

AMS's activities are conducted under authority provided by the Philadelphia Air Management Code, the Pennsylvania Air

23 Pollution Control Act, the Federal Clean Air
24 Act and the regulations promulgated
0003
1 thereunder.
2 On September 4th, 2007, the Board
3 directed AMS to draft a regulation to govern
4 the use of dry cleaning of Perchloroethylene
5 also known as PERC.
6 AMS presented an initial draft of the
7 proposed regulation at a Public Meeting of
8 the Board on August 5th, 2008.
9 On December 20th, 2008, the Board
10 appointed a committee to study, review and
11 revise the proposed regulation.
12 On February 16th, 2010, the Board
13 subsequently recommended that steps be taken
14 to prevent the use of other hazardous
15 substances, hazardous toxic substances as
16 dry cleaning solvents.
17 The Committee completed its review and
18 presented the current draft of the Air
19 Management Regulation XIV, control of
20 Perchloroethylene from dry cleaning
21 facilities to the Board on June 24th, 2010.
22 The Board voted and approved the
23 proposed regulation on that date.
24 The proposed regulation aims to one,
0004
1 minimize the health risks certain dry clean
2 solvents pose to individuals who live or
3 work next door to dry cleaning
4 establishments; and two, to reduce the
5 amount of dry cleaning solvents entering the
6 environment.
7 Copies of the proposed regulation and
8 the summary of its provisions have been made
9 available for your review.
10 Pursuant to the July 6th, 2010, notice
11 published is this Philadelphia Inquirer, The
12 Daily News and The Legal Intelligencer, we
13 are here today on behalf of the Board and
14 the City of Philadelphia Department of
15 Public Health to accept testimony on the
16 proposed regulation.
17 These proceedings will be transcribed
18 and forwarded to the Board for their
19 consideration.
20 The purpose of this hearing is limited
21 to the taking of testimony on the proposed
22 regulation.
23 No one will respond to comments about
24 the proposed regulation today. The Board
0005
1 will respond to the comments at a future
2 date.
3 After the public notice, comments on
4 the proposed regulation or request for a

5 hearing were received from the following
6 individuals and organizations:
7 Nora Neilis on behalf of the National
8 Cleaners Association.
9 Jason Kim on behalf of the Korean Dry
10 Cleaners Association.
11 Quick Clean Cleaners. Westbury
12 Cleaners. John Myer on behalf of the Dry
13 Cleaning and Laundry Institute. Carol
14 Memberg on behalf of the Pennsylvania and
15 Delaware Cleaners Association. Enviro Tech
16 International, Incorporated. Poly Systems
17 USA. Sung Ho Lee on behalf of Lee's
18 Cleaners. Royal Cleaners and W. Caffe
19 Norman of Patent Bogs, LLP, on behalf of
20 the Halogenated Solvents Industry
21 Alliance.
22 Although not required, all comments
23 that were received even those that were
24 submitted outside of the official comment
0006
1 period will be considered by the City.
2 Additional written comments on the
3 proposed regulation will now be taken until
4 August 20th.
5 If you have not already done so, please
6 remember to sign in at the desk at the
7 entrance to the room before leaving.
8 The sign-in information is necessary to
9 allow us to keep you informed of the status
10 of the proposed regulation.
11 Everyone will have an opportunity to
12 speak at the hearing.
13 We will begin by calling names in order
14 from the testimony sign-up sheet.
15 If you have not signed up yet but would
16 like to give testimony, you will have the
17 opportunity to do so after everyone on the
18 list has spoken.
19 We should have a Korean interpreter
20 present if you would like to give testimony
21 in Korean, and hopefully, that person has
22 arrived.
23 When you are called to speak, please
24 state your name and the organization you
0007
1 represent.
2 Please limit your testimony to five
3 minutes. Anyone who has written comments to
4 submit should do so now before we begin
5 testimony.
6 Is there anyone who has written
7 comments to submit at this time? No? No
8 written comments.
9 We will now begin the testimony. I
10 call the first speaker, Ray Roccon.
11 MR. MORFORD: Well, if it pleases the

12 Board, Ray, myself and two other speakers
13 are here specifically regarding the issue of
14 n-PB solvents.
15 I think with the rest of the people
16 here who may or not may not be interested in
17 that one should be allowed to go first and
18 that way they can come and go, you know, as
19 they please.
20 They certainly can stay if they are
21 interested in the n-PB issue.
22 But since it's such a single issue, we
23 will be directing our comments directly at
24 that one issue and not the overall.
0008
1 MR. BRAUN: Can you please state your
2 name for the record?
3 MR. MORFORD: My name is Rich Morford.
4 I am General Counsel for Enviro Tech
5 International.
6 MR. BRAUN: Thank you. We will go ahead
7 and do that.
8 MR. MORFORD: Thank you.
9 MR. BRAUN: Next speaker, Dale Kaplan,
10 Pennsylvania Dry Cleaners.
11 DALE KAPLAN: Hello. I am Dale Kaplan
12 from Pennsylvania Dry Cleaners. I am a dry
13 cleaner in Harrisburg, Pennsylvania.
14 Carol Memberg will be submitting our
15 written comments, but I just wanted to try
16 to bring some sensibility to the issue of
17 the reporting.
18 As a dry cleaner, one of the things on
19 Section 7 Reporting and Number Four, gallons
20 of spilled oil. Really, it's just a name
21 change, but when you're inspecting dry
22 cleaners, you want to use the term still
23 residue waste, not still oil waste because
24 they are going to understand what you are
0009
1 asking for if you are saying still residue
2 rather than a still oil.
3 The other thing that I wanted to
4 address specifically in this area of
5 reporting is that some of the things just
6 don't make sense.
7 MR. MINOTT: Can you step up so the
8 stenographer can actually hear what you are
9 saying?
10 DALE KAPLAN: Sure. In number seven
11 Reporting, which is Section A then number
12 four, in your reporting information for the
13 proceeding year including pounds of clothes
14 cleaned, easy to do. Solvent type, easy to
15 do. Gallons and solvents purchased, easy to
16 do. Gallons of solvents at the PERC dry
17 cleaning facility at the beginning, easy to
18 do. Gallons at the end, right now I can't

find where I was.
Janie, remind me where that was.
JANIE: A-3 or A-4.
DALE KAPLAN: Exhaust fans and all that. I lost it.
JANIE: Section 4A-3 and A-4.

DALE KAPLAN: Oh, it's under Record Keeping. I'm sorry.
Number six, Record keeping. The number of loads, this is Section A, then number three. The number of loads processed between regenerations.
As a dry cleaner on a typical dry cleaning machine, that you can do because on my machine, it comes up, time to regenerate.
We know that within twenty-four hours, I need to shut down my machine and cook it, steam and so on and do that.
Cleaning and replacement of lint filters, it's just not there anymore. On all these type number four generation machines, it's not there.
You don't change lint filters. I clean my lint filters every single load eight, ten, twelve loads a day.
You are going to make this so that they are going to fail my point is.
If they are cleaning their machine, they need to clean their machine so they are able to clean clothes.

Carbon Absorber pre-filters, I've called a few manufacturers and none of them understand that terminology.
There is just, we don't have pre-filters on our carbon absorbers; and between repair or replacement of exhaust fans, I am not sure what the Board means.
If it's an external exhaust fan through the wall through the building, yes, obviously that can be done, but we don't have an exhaust fan on our forth generation dry cleaning machines.
With PERC, it does not exhaust to the atmosphere at all. It's a total closed loop system.
So, there is no such thing as an exhaust fan on that.
Number four on that, the amount of activated carbon in the carbon absorbers dry weight in pounds.
There is no way to do that. I mean to tear apart the carbon absorber and pull it out and weight it and it put it back, it's somewhat innocuous. It just doesn't need to

be done.
The machine gets filled up. It tells you that this is done. It's finished absorbing.
On a fourth generation machine, you just have to stop it and cook the machine down so that you can continue to absorb or else, it won't absorb anymore.
So, I just wanted to try to bring some sensibility; and if you want me afterwards at another time if you are considering rewriting, I would be happy to work with you on these issues.
Thank you.
MR. BRAUN: Thank you for your comments.
MR. MINOTT: Let me just say if I could, don't forget, the comment period is open until August 20th.
So, if you want to put some of that stuff in writing, that would be very helpful.
DALE KAPLAN: Send it to Mr. Huynh?
MR. MINOTT: Tom Huynh.

0013

MR. BATTLE: Tom Huynh.
DALE KAPLAN: Okay. Thank you.
MR. BRAUN: We do have a couple of empty seats up here, at least one, if anybody wants to have a seat.
MR. BATTLE: There is a seat here, too.
MR. BRAUN: The next speaker, Rich Morford.
MR. MORFORD: That would be me with Enviro Tech.
MR. BRAUN: Okay. John Myer. DLI.
JOHN MYER: John Myer from DLI. The 20th, we can do additional written comments to subsidize what we have here.
I'm here on behalf of the Dry Cleaning Laundry Institute. We represent retail dry cleaners across the country and internationally.
MR. MINOTT: Can you step up? It just makes it easier with the fan right here.
JOHN MYER: I'm sorry. John Myer from the Dry Cleaning Laundry Institute.
Most of what I'm going to cover is

0014

going to be covered by other people as well, but with regard to n-PB and the banning of n-PB in dry cleaning facilities, it should be pointed out that Regulation XIV, control of Perchloroethylene from dry cleaning facilities, is not and was never developed to control emissions from other alternative

8 processes.
9 This is a PERC dry cleaning regulation,
10 and it has never been described as anything
11 else.
12 If AMS wants to control emissions from
13 other alternative dry cleaning processes,
14 then, it should use the platform already at
15 its disposal in which allows for due process
16 to any and all interested parties.
17 Co-located facilities. Very briefly,
18 and this was not brought up in previous
19 meetings but something that has come to our
20 intention, there is a twenty-five foot
21 buffer requirement. It has been told to us
22 that many of the plants physically because
23 of their locations are going to be well in
24 the twenty-five foot buffer.
0015
1 However, it probably should not make a
2 difference simply because we are talking
3 about performance based.
4 If the dry cleaner is performing, the
5 buffer itself probably does not have any
6 meaning as long as the dry cleaner is in
7 actual compliance with the numbers that are
8 described in the regulation.
9 Operation of Maintenance. Specifically
10 regarding the twenty degree temperature
11 differential, the machine's ability to meet
12 a forty-five Fahrenheit cold temperature
13 echoes the NISHAT requirement, and industry
14 has absolutely no objection.
15 However, most third and fourth
16 generation dry-to-dry machines are not
17 equipped with temperature gages before and
18 after the condensing coil which makes it
19 impossible for cleaners to take a
20 differential reading.
21 If it's the intention of the AMS to
22 distinguish between fourth and fifth
23 generation equipment or fourth and fifth
24 generation machines from earlier generations
0016
1 that might use that on refrigeration, then,
2 AMS needs to make that clear.
3 In the regulation, it seems like they
4 took two parts of a regulation and kind of
5 lumped them together when they are really
6 supposed to be separate.
7 Record Keeping, Part VI A3 regarding
8 the number of loads processed between
9 generations, I do not know what it means.
10 We have no idea what it means or what
11 AMS's intention is regarding this section.
12 From what I can tell, this section
13 probably should just be removed because it
14 does not add anything to the type of data

that you are actually looking for.
General Record Keeping. Dry cleaners are already obligated to keep the vast majority of records AMS is requiring in the new regulations.
Unfortunately, the actual regulation does not always mirror what is contained in other well-established PERC rules that are out there right now.
This creates regulatory duplication,

0017

additional paperwork burdens and just havoc for the small dry cleaner.
Already the current PERC dry cleaning regulation brought forth by AMS includes elements from other regulations including RICKRA with regard to hazardous waste including manifesting, storage, spill containment and other record keeping requirements.
Additionally, dry cleaners are already required to report spills and releases to the environment based on current reportable quantity rules and follow strict NICHAT requirements.
Simply put, there is no need to add, change or modify record keeping requirements over and above what is already in existence. It's a tremendous burden to ask the dry cleaners to duplicate these efforts.
Most of what the regulation is asking for is already in existence, but there is some subtle changes in the regulations that don't add anything to what is out there

0018

except additional paperwork because it's already covered by RICKRA or NICHA or some other regulation.
So, we ask that AMS look at not to reduce the regulation itself per se, but to reduce it since it's already covered by a similar regulation in another area, but it's slightly different enough that requires additional paperwork for the dry cleaner.
Thank you.
MR. BRAUN: Thank you.
MR. BATTLE: John, are your remarks written?
JOHN MYER: Well, yes, but you know, slashed. What I'll do is retype it and send it to you by the 20th.
MR. BATTLE: Send it to Tom. Thank you.
JOHN MYER: Okay. Thanks.
MR. BATTLE: Thank you.
MR. BRAUN: The next speaker.
DOV SHELLEF: Dov Shellef. Poly

22 Systems.
23 DOV SHELLEF: Yes. I'm Dov Shellef. I'm
24 with the group of the n-PB, and I will be
0019
1 talking later.
2 MR. BRAUN: Carol Memberg.
3 CAROL MEMBERG: My name is Carol
4 Memberg.
5 I am the Executive Director of the
6 Pennsylvania and Delaware Cleaners
7 Association.
8 First of all, PDCA would like to thank
9 the Board for listening to our input and
10 making changes in the original document to
11 meet at least some of our concerns.
12 At this point, we are not going to
13 challenge any of the major factors in the
14 regulation.
15 However, there are some items we feel
16 still need to be addressed.
17 Under Standards. The minimum
18 twenty-five foot buffer may not be feasible
19 in all plants. Some areas only allow for
20 a foot or two less than that.
21 For a properly run and well-maintained
22 plant, there should be some allowance for
23 difficult urban settings.
24 Prohibitions.
0020
1 The banning of n-PB. The solvent has
2 been banned without a proper hearing. We
3 feel that this is unfair since there has not
4 been any due process allowed.
5 There should be further studies to
6 determine its acceptability.
7 Record Keeping, and this has been
8 addressed before, but I'm going to repeat it
9 anyhow.
10 Dry cleaners are already obligated to
11 keep all the records you are asking for.
12 The air quality reports must be
13 maintained on the Pennsylvania Department of
14 Environmental Protection calender on which
15 they must report their PERC usage and
16 maintenance for each machine, and this is
17 actually very clearly stated out and easy
18 for a dry cleaner to follow. It's a
19 step-by-step week-by-week process.
20 This calender should be sufficient and
21 meets all your requirements. Any
22 duplication is a waste of time and effort.
23 We suggest it be mandatory for the
24 calender to be used and to be available for
0021
1 inspection.
2 The dry cleaners must also record their
3 waste handling, and those records are filed

4 according to the rules of RICKRUM. It's a
5 tremendous burden to ask a small business
6 owner who does not have a staff or attorneys
7 to duplicate all that paperwork.
8 Section 6-A3 is incomprehensible.
9 Since regeneration is computerized
10 and automatic, how does the dry cleaner
11 count the loads processed? What kind of
12 exhaust fan has to be replaced? There are
13 fans in the machines that help with the
14 drying.
15 Those machines I have been told by an
16 equipment company may sometimes have to be
17 replaced once but most of them last the life
18 of the unit. This section should be
19 removed.
20 Section IV, Section 6A-4 is not
21 doable. Cleaners cannot empty their
22 cartridge, weigh the contents and then
23 refill it.
24 There are also no standards on how much
0022
1 carbon should be in it. So, what is the
2 goal of the measurement?
3 It would make much more sense to
4 require the replacement of the cartridges
5 after eighteen months or two years.
6 It would be a good idea also to require
7 cleaners to subscribe to or affiliate with
8 an association that would provide them with
9 information and the assistance they need for
10 compliance.
11 MR. BATTLE: Thank you.
12 MR. BRAUN: Thank you.
13 Next speaker Joseph Iannetti.
14 JOSEPH IANNETTI: I will defer until
15 later with the n-PB crowd.
16 MR. BRAUN: Okay. Mark Stelljes. Same.
17 Thank you. Mark Dann.
18 MARK DANN: Good evening. My name is
19 Mark Dann, and I'm a resident of
20 Philadelphia. I am also an MBA candidate at
21 Rutgers University, and I'd like to testify
22 in support of Air Management Regulation XIV
23 control of PERC as a solvent in dry cleaning
24 facilities.
0023
1 To quote Plato, "Necessity is the
2 mother of invention." Sometimes industry
3 and business stagnates to some degree.
4 In order to spur innovation, business
5 often needs a nudge in the right direction.
6 Take, for example, lead regulations from the
7 1970s.
8 When the EPA banned lead in gasoline,
9 oil companies strongly opposed the
10 regulations.

However, over time the public has greatly benefited from less lead in the environment and cars run just fine.

We may find ourselves in a similar situation with PERC. This chemical has hazardous health affects on people and is known to cause a variety of serious health conditions.

There are hidden costs associated with PERC. Customers and people in neighborhoods whose are exposed to these chemicals face increased health costs including things like hospital or doctors' visits and even time off work.

As an MBA candidate, I believe that corporate social responsibility is an important part of doing business.

Dry cleaners are not immune to these hidden costs either. Their workers are among the most exposed to these chemicals and are thus the mostly likely to face the consequences.

Dry cleaners may find their employees are more productive, taking fewer sick days and needing less time off and become happier and healthier if they switched to environmentally sound alternative chemicals and processes.

The proposed regulations surrounding PERC could spur business in Philadelphia to innovate greener alternatives to PERC.

I do believe if we are going to ask small businesses to do the right thing environmentally such as switching to a greener solvent or process, it is incumbent upon the City to help such businesses financially through low cost financing, through preferences and City purposes and/or through marketing opportunities.

These regulations will put greener dry cleaners in a more competitive position and will allow them to market themselves as cleaner and better for the environment and peoples' health.

They will result in a healthier, happier work force because people will no longer be exposed to these chemicals.

Thank you very much for your time.

MR. BRAUN: Thank you. Okay.

The next speaker is Myriam Fallon.

MYRIAM FALLON: Hi. My name is Myriam Fallon. I am a Greenpeace campaign organizer in Philadelphia as well as a resident of the City.

I appreciate this opportunity to

18 express Greenpeace's support for Air
19 Management Regulation XIV.
20 The proposed regulations are a good
21 step forward but do not fully protect public
22 health in the environment.
23 Greenpeace has a very well-established
24 campaign to reduce toxics in the
0026
1 environment.
2 Toxic chemicals in our environment
3 threaten our rivers and lakes, our air, land
4 and oceans and ultimately ourselves and our
5 future.
6 Chemicals such as PERC and n-PB are
7 dangerous to public health, the environment
8 and are not needed for dry cleaning.
9 Their production trade, use, and
10 release of many synthetic chemicals are now
11 widely recognized as a global threat to
12 human health in the environment.
13 Yet the world's chemical industries
14 continue to produce and release thousands of
15 chemical compounds every year in most cases
16 with none or very little testing and
17 understanding of their impact on people and
18 the environment.
19 The Philadelphia Department of Health
20 should be commended for addressing this now
21 and not simply waiting for others to do so.
22 Greenpeace strongly supports the
23 determination by the Philadelphia Department
24 of Health that PERC is a threat to the
0027
1 public health. It threatens the health of
2 workers, residents living near dry cleaners
3 and consumers taking the dry cleaning
4 clothes home.
5 If the Philadelphia Health Department
6 is not prepared to outright prohibit the use
7 of PERC as a dry cleaning solvent, then,
8 their proposed regulations are an adequate
9 substitute.
10 The regulations over time will lead to
11 substantial reductions in PERC emissions.
12 Because of the hazardous solvents
13 involved, it is certainly a no-brainer for
14 the Philadelphia Department of Public Health
15 to review operations before allowing a dry
16 cleaner to install equipment.
17 Likewise, PERC using dry cleaners
18 should be required to get an operating
19 permit from the Health Department and
20 implement best management practices that
21 include leak detection, good record keeping
22 and regular testing.
23 Greenpeace supports the proposed
24 regulation's requirements prohibiting new

0028
1 dry cleaners that are situated adjacent to
2 residential or medical facilities from using
3 PERC as a solvent and mandating the
4 phase-out of PERC by July first, 2013, for
5 dry cleaning establishments already
6 operating that are adjacent to residential,
7 medical facilities and commercial
8 establishments.
9 Thank you.
10 MR. BATTLE: Thank you.
11 MR. MINOTT: Thank you.
12 MR. BRAUN: Thank you. Next speaker is
13 Cornell Brown.
14 CORNELL BROWN: Cornell Brown. Good
15 evening, everyone.
16 On behalf of the Germantown and Lehigh
17 Business and Merchants Association, I
18 represent Lee Cleaners owned and operated by
19 Jo Lee, 2557 Germantown Avenue.
20 Germantown and Lehigh Business and
21 Merchants Associations represent the
22 business along the Germantown corridor, 2500
23 to the 2800 block of Germantown Avenue.
24 My name is Cornell Brown five years,
0029
1 and I've been the President of the
2 Association for five years.
3 The concerns of the Air Management
4 Services is not without merit.
5 However, the Lee Cleaners operate a
6 quality dry cleaning service to the
7 residents of the community and have the
8 state-of-the-art equipment for over five
9 years.
10 The recent purchase of a newly
11 estimated 40,000 Real Star Dry Cleaning
12 Machine number 340-91096-03-15 according to
13 Real Star manufacturers specifically is
14 built with environment friendly parts and
15 the state-of-the-art machine.
16 All are proven operated throughout
17 America as well as Europe. Each of these
18 features air clean units incorporated in the
19 machine, double water separators and
20 automatic still cleanout systems.
21 We believe that Lee Cleaners poses the
22 standard state-of-the-art equipment that is
23 mentioned in this regulation and experiences
24 and desires to the best practices in the
0030
1 area of dry cleaning utilizing
2 environmentally friendly-conscious
3 equipment.
4 As President of the Association, it is
5 my job to make sure the businesses stay in
6 business and that we are environmentally

green-friendly.

We want to walk the fine line to make sure the environment is safe, sound and businesses can still operate without going out-of-business.

They just made a purchase, and they are still paying on this purchase, and any regulations or exemptions, we would like to work with you so it would not be a hardship for any business.

We want the businesses to stay open in Pennsylvania and Philadelphia.

So, that's my testimony, and also, Stan The Man Cleaners I just also found out is on our corridor as well.

And that's my testimony, and I appreciate the opportunity to stand before the Board.

0031

MR. BATTLE: Thank you.

MR. BRAUN: The next speaker is Nuk Youl Kim.

CORNELL BROWN: Oh, and I have this letter I wanted to submit.

NUK YOUL KIM: Thank you. My name is Nuk Youl Kim. My address is 111 East Mount Airy. Happy Cleaner.

This is I see that this is we have business. I been there nineteen years. I try to run a nice business. Also I take it the people nicely.

Also, this is a major concern that is my concern because I stay there twelve hours a day six days a week. That business nobody is inside than me. This is why? Because I come to this United States. Better life. Better health. Better chance. This is America dream. A lot of people say that.

We have a business operation. The regulations that already we have in Pennsylvania. This is the United States. They have all the regulation over there.

We got everybody ready to do this

0032

regulation.

Then, 2020 everybody we cannot use the PERC anymore. We have long period of time we are going to pre-pay. Still I'm looking for this and some other cleaning residents.

Fifty percent or more I do wet cleaning. Why? Because I concerned with my health. Why? Because I have three kids. I have to take care of them, too.

This every people we have to consider this is green, too, but a lot of people said it's not possible.

We have to finish the goal, but now

technology is so slow. We need some time. This is especially this section page seven, replace the door gasket every two years.

Because of the gasket, there is almost an eight or ten gaskets every machinery. This costs more than a thousand dollars.

I don't know how much they are going to charge for this labor. Maybe two thousand dollars. Why? Because it's not a big thing. Why do we have to replace that gasket?

0033

This I can understand.

We have to check with the manufacturer. Especially they made it fifty thousand, sixty thousand. Why they made it? This is a cheap gasket. We have to check that point. Why? Because it's some gasket more than three hundred dollars. One gasket.

In this kind of economy, we can't handle that kind of metal. We have to concentrate on that things.

Also, if we make Philadelphia more greener, we have to do this some kind of businesses. How we can prevent this kind of problem together? This is win-win.

This is for the business people and the City and the people, we have to have this idea together.

Why? Because a lot of people, many cleaners, they start the wet cleaning. Certain items we cannot wet clean. Why? Because we have wet cleaning. We have to pay back so much money.

We charge maybe ten dollars for a suit.

0034

If we mess up the one suit, maybe it costs sometimes two hundred, sometimes three hundred dollars. This is scarey. We have to make money. We don't want to lose the money

If we mess the garment, people they are not going to come.

This is what we have to do, but we are trying now. Used to be this is the first time study I started this dry cleaning, I used it every year, but now I use the eighty gallon.

Think about it. This is how much we have to try to. This is not too much. Give me sometime to figure out which ways is the better way. This is helping me. We are going to have to help somebody to get it.

Thank you.

MR. BATTLE: Thank you.

MR. MINOTT: Thank you.

21 MR. BRAUN: Next speaker is Jason Kim.
22 JASON KIM: Jason Kim. My name is Jason
23 Kim. I am the President of Korean Dry
24 Cleaners Association.
0035
1 After this regulation was passed, I
2 have spoke with many of our members. I
3 think a lot of the people have attended here
4 today. They are concerned.
5 But most overall, the problem that
6 we have, I already have stated before the
7 whole initiation of this new regulation that
8 needed to be set in the City of
9 Philadelphia, we just don't understand why
10 because, you know, there is a federal
11 guideline and also there is a state
12 inspection and outside of the City of
13 Philadelphia, the rest of the area under
14 the Department of Environmental Protection
15 Agency, DEP, they get inspected yearly.
16 They inspect their record keeping.
17 They inspect facilities, and they make sure
18 they comply with federal guidelines.
19 However, the City of Philadelphia under
20 AMS would have never done that.
21 Therefore, they may have some
22 conditions of these dry cleaners. They have
23 been carelessly operated where recently
24 maybe AMS has detected some high level of
0036
1 PERC in the air in certain stores which we
2 have stated before we have no problem with
3 shutting down businesses that are not
4 complying with the rules and regulations.
5 But to set it, to pass another
6 regulation, another set of rules for us just
7 in the boundary of the City, it does affect
8 the business just within the City because
9 everybody else outside does not have this
10 restriction, and we really think that that
11 is unfair.
12 I'm not even sure if it's
13 constitutionally right, why the Board has
14 picked a small business.
15 If you look at the whole scope of the
16 whole City, a hundred dry cleaners, maybe
17 less than sixty stores that has PERC that
18 might be, you know, pertained by this
19 particular regulation that may need to
20 change to a different solvent or different
21 equipment.
22 Even if there was pollution, how much
23 does that really affect?
24 I mean there is many other industry
0037
1 that pollutes the City in a much far worse
2 degree.

Why a small group of dry cleaners?
I just don't understand why the City is paying so much focus, time and effort on the dry cleaning industry. I really don't know there.
But as I have said from the beginning, I do not understand, and I do not agree with the initiation of this whole process, and I did not like some of the process that took place.
And even the regulation, if it passes, I think that gentleman from MBA suggested, you know, without any financial assistance.
If you want to go green, fine.
Like the State of New Jersey right now, we all heard that they are passing it; and when they pass it, the dry cleaners that are being affected, there is four million dollars in a system money set up.
The City, you flat out already told us that there is no money for it.
So, without considering these business

0038

people and how to cope with this situation if the regulation changes, you know, without any assistance, I don't understand how you can just set a rule and throw it at them and say you have to live by this.
So, there is just so many factors that I think we should really consider this, and also another point that I was making before.
If this regulation passes, a lot of the dry cleaners will probably operate a dry cleaning facility, but they will probably turn it into a drop store and take the business outside of the city limit.
If you do that, the City will lose revenue, employment, and there is going to be, I don't know what they are, I'm sure there is some gain the City will probably gain from, but I think there is going to be a bigger loss, and we have stated this before.
So, I just want to be, you know, my mind has not changed, and that's how I feel and many of my members feel the same way,

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and I just want to put it on the record.
Thank you.
MR. MINOTT: Thank you.
MR. BATTLE: Thank you.
MR. BRAUN: Thank you.
Next speaker is Mia Nam.
MIA NAM: That's me. Do you want me to stand or can I just stay here?
MR. BATTLE: Can you hear her? You're

10 fine.
11 MIA NAM: Good evening. My name is Mia
12 Nam, and I'm here representing my parents,
13 Sung Lee and Yung Lee, and they are the
14 owners of Lee's Dry Cleaners on Germantown
15 Avenue.
16 We are tonight to express our concerns
17 in regards to the proposal of the new PERC
18 regulations.
19 We understand that there is about like
20 a hundred dry cleaners that are going to be
21 affected by this. However, one hundred is
22 not a smaller number.
23 These one hundred dry cleaners are
24 small, family-owned businesses that the City
0040
1 of Philadelphia will be destroying.
2 My parents who are hard-working Senior
3 Citizens have been paying taxes for over
4 thirty years. They are well liked in the
5 community, and they also give back to the
6 community with donations and their loyalty.
7 This proposal will literally destroy
8 them.
9 At this moment, listen to what I have
10 to say in their shoes.
11 Basically my parents are still making
12 payments on their machine that they recently
13 replaced. So, if this proposal passes, they
14 will be stuck with the payments that they
15 have to pay for this machine that they
16 cannot be using.
17 It's imaging that you are buying a car
18 that is like a forty or fifty thousand car
19 and the City of Philadelphia is saying that
20 because of pollution, you are not allowed to
21 drive it, then, you know, it's unfair.
22 It's like you are paying for a car that
23 you can't even be driving, and it's the same
24 thing for my parents. They have a machine
0041
1 that they cannot use, but they still have
2 the moneys that they are still making the
3 payments for.
4 Then, as far as like I have heard some
5 people with, you know, going green and
6 saying that you know PERC is harmful. It
7 causes pollution and so forth, but like to
8 be honest with you, how much pollution are
9 these hundred dry cleaners really going to
10 cause?
11 You know, as long as the PERC is being
12 properly disposed of, the affect is already
13 minimal.
14 It's not like they are just dumping it
15 out in the river or just, you know, throwing
16 it out in buckets, and we have to think of

other causes that cause pollution like the millions of people who smoke. You know, the millions of cars that are being driven. The buses and trains and factories. People who use hair spray. Pesticides being used in our agriculture. The million household cleaning products that are being used.

The resolution is not to go through

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with this proposal but to regulate proper disposal of PERC.

I would like to make a comment. I heard someone say earlier that PERC causes illnesses to employers and their employees and that employers would like to have employees that are not sick and not taking days off.

Well, firsthand would be the dry cleaner owners. They are there longer than anymore. Longer than customers.

You know, not only do they run their business, but they also do their own dry cleaning there. I have gotten my dry cleaning done from my parents, and I'm not sick. No one in my family is sick.

My parents have been doing this over thirty years, and they are both healthy. I would like to see a study if it is so-called harmful to the human body.

You know, they need to have a study of dry cleaning business owners who are sick because I can probably tell you that in the City of Philadelphia, everyone is well and

0043

healthy.

Also, the machines that my parents have now is considered to be fairly new. It is the Real Star Dry Cleaning System, and the Real Star Dry Cleaning System meets and exceeds all current federal, state and local regulations for the use of PERC, and it is a fourth generation equipped with air clean carbon unit.

The emission levels for Real Star Ultra-Diamond Systems are tested to be consistently lower than those required by the federal regulation.

All systems are totally closed with no atmospheric venting. Solvent and solvent vapors are recleaned and regenerated. It also has a filtration system consisting of the Real Star Echo Filter Plus.

Therefore, it meets the required regulation.

Basically my parents are literally being punished for having a business in Philadelphia. It's not fair just based on

24 location, you know, that they are being
0044
1 affected.
2 This is like discrimination. It's
3 like discrimination of location.
4 IF there is two dry cleaners with the
5 same situation, same machine, you know, both
6 of course paying taxes, but one is being
7 affected just because it is in Philadelphia
8 and the other may be in the suburbs, it's
9 not fair.
10 I also understand that this proposal
11 gives exceptions to commercial and single
12 dwelling locations.
13 Then, my parents should be at this
14 exception. Why? Because they are located
15 on a commercial street and in between them
16 is an empty lot and a vacant building that
17 was out of business for about twenty years
18 with no intent to re-open. There is no
19 buildings behind the cleaners as well.
20 I know it is difficult for someone to
21 go out to each location that is being
22 affected, but because this is a serious
23 part, the time to go out to these locations
24 is needed.
0045
1 Please consider each location not just
2 as an address but as its own individual
3 case.
4 If this proposal passes, my parents
5 will not be able to afford the machine, the
6 new machine especially with the business at
7 its lowest in today's declining economy.
8 Furthermore, my parents should not be
9 affected by the proposal like I stated
10 earlier because of their machine, their
11 current machine which is considered new and
12 they are still making the payments on which
13 is the fourth generation system equipped
14 with the air clean carbon unit.
15 Also, they should be an exception
16 because they are on a commercial street.
17 This is not a street full of houses and
18 they are on the corner. This is all just a
19 commercial location.
20 I would also like to say that I believe
21 that this proposal should not be passed.
22 However, if the City of Philadelphia
23 should pass this law, then, the City of
24 Philadelphia should be the ones paying for
0046
1 the new machines and not putting this burden
2 on the small business owners or it should
3 have been able to be written as a hundred
4 percent tax deductible or there should be a
5 fund for these dry cleaners.

There is so many programs to help the people of Philadelphia. For example, Welfare. Unemployment benefits. Health insurance. Medicaid. Child care programs. Disability benefits, and this should be a program as well.

We have been paying taxes to the City of Philadelphia. The taxes paid are used for the good of its people, and these dry cleaner owners are people, too. It's now time for the City of Philadelphia to help us as well.

That's all.

MR. BATTLE: Thank you.

MR. MINOTT: Thank you.

MR. BRAUN: Thank you. Next speaker is Sung Byung Gi. Sung Byang Gi. He is not here.

Okay.

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MR. MINOTT: If he comes back can, you can tell us so that we know.

MR. BRAUN: Next on the list is Juan Manuel Frejo. Juan Manuel.

MR. MINOTT: With the Germantown Lehigh Business Association.

MR. BRAUN: Cornell has already spoken.

MR. MINOTT: Sorry.

MR. BRAUN: Barbara Rahke.

BARBARA RAHKE: My name is Barbara Rahke, and I am the Executive Director of Philaposh, an organization that has been in the Philadelphia area since 1975.

Philaposh stands for the Philadelphia Area Project on Occupational Safety and Health.

We are a non-profit organization, and we have spent many years carrying out not only our primary mission of advocating for occupational safety and health through education, training and advocacy, but also advocating for public health in not only the Philadelphia area but also all of Southeastern Pennsylvania and parts of New

0048

Jersey.

We have for a long time been advocating for health and safety issues in all industries, whether its refineries. Whether its been manufacturing. Whether its residential construction which is most recently what we have been involved with. Municipal water treatment facilities or dry cleaning facilities.

Looking at not only the risks to the public, the risks to workers in adjoining facilities but secondarily not as a primary

13 purpose but also the risks that might also
14 be posed for the workers themselves in the
15 facilities.
16 Over the years, we have spoken at many
17 public hearings, and I mention this just by
18 way of history in terms of the City of
19 Philadelphia because I think it's a quite
20 remarkable history.
21 I know many years ago, we were part of
22 the hearings that passed the first community
23 Right-To-Know Act in the country.
24 The first city in the country, and that
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1 was an historic event and I think began to
2 set the tone for the City looking at the
3 issue of the communities Right-To-Know, the
4 chemicals that they were exposed to not
5 only, you know, through facilities that were
6 close by, et cetera.
7 For example, we have worked closely
8 with the Southwest Philadelphia community,
9 the Tracking Committee in terms of the
10 emissions from the Sunoco refinery, how it
11 was impacting the community that surrounded
12 the refinery and what efforts could be done
13 to reduce those emissions and to better
14 protect the health of the community.
15 We have worked on similar issues, and I
16 recently found out another cause that the
17 City should be proud of. That six years
18 ago, the City voluntarily got rid of
19 chlorine gas at all of the six City water
20 treatment facilities.
21 Now, that was post 911 the City took
22 the initiative to do that and is the only
23 city in the State of Pennsylvania to have
24 done that, and I take pride in that, and I
0050
1 feel safer as a citizen of Philadelphia that
2 you took that action.
3 So, there is a long history of the City
4 involving itself in issues in different
5 industries to try and protect the health and
6 safety of the community and the workers.
7 So, we are very pleased to be here
8 today to speak in support of this regulation
9 which we feel is another very important
10 initiative by the City to take seriously the
11 health risks of the community and
12 particularly of children in co-sensitive
13 facilities as well as the workers at the
14 facilities.
15 We feel that actually the federal phase
16 down on this was long overdue, and so, it
17 particularly pleases us.
18 I mean the federal government has
19 dragged its heals on this. So, that should

20 not be the standard. That should be
21 something that we are happy that the City
22 wants to go one step better on, and we
23 applaud that.
24 I've made a few extra notes, so bear
0051
1 with me here as I was listening to people
2 speak.
3 I'm not going to speak about the
4 technical aspects of this.
5 I think that people from the dry
6 cleaning industry, others who have testified
7 can raise concerns they have about it except
8 to say that we support the monitoring. We
9 support the requirements if PERC equipment
10 is going to be purchased, that that get
11 prior approval.
12 But we do want to speak passionately
13 about the seriousness of health risks.
14 One of the things we also do as an
15 organization, we work with hundreds and
16 hundreds of people every year who are
17 suffering debilitating illnesses and
18 diseases as a result of exposure to toxic
19 substances, and one thing that's different
20 when you are injured in a safety situation,
21 you see the immediate results of that, but
22 the health affects from being exposed to
23 toxics frequently takes many, many years
24 to reveal itself.
0052
1 And so, I think it's one of the
2 reasons why we have been so slow as a nation
3 to address some of these issues, and that's
4 certainly been true in the case of PERC, and
5 I think we cannot wait longer even though I
6 am very sympathetic to the moving testimony
7 of people that are here about the hardship
8 it will place on many of the business
9 owners, and it's a difficult thing to weigh
10 the one against the other, but I think we
11 have an obligation to be sure that the
12 residents of our City are protected in that
13 way.
14 We also think that AMS has shown
15 tremendous foresight of the writers of this
16 regulation by including the prohibition of
17 n-PB as a dry cleaning solvent on the
18 effective date of this regulation.
19 You know, there is ample scientific
20 evidence to show that it's a very harmful
21 toxic, more harmful than PERC, and it would
22 be tragic let alone ironic to think this
23 important regulation would be passed only to
24 be replaced by a substance that makes us
0053
1 even sicker, that makes us even more

2 debilitated.
3 And quite frankly, using the asbestos
4 fight that the City took on also, if we
5 listened to the industry reasons why we
6 should allow people to continue to get sick,
7 we would never pass anything.
8 I'm not persuaded.
9 I think there is ample evidence.
10 I did take the time before this hearing
11 to read some of the scientific testimony on
12 the impact, on the affects of n-PB, and I
13 think it speaks for itself, and I commend
14 the Board on this, and we are strongly in
15 support of that prohibition staying in the
16 regulation.
17 Thank you.
18 MR. MINOTT: Thank you.
19 MR. BRAUN: Thank you.
20 The next speaker is Soo Lee.
21 SOO LEE: Here. Where is the other
22 gentleman going? I'll wait until he comes
23 back.
24 MR. BATTLE: Okay. We will wait just a
0054
1 few minutes.
2 - - -
3 (Whereupon, a brief recess was taken at
4 this time.)
5 - - -
6 (Whereupon, the following occurred back
7 on the record.)
8 - - -
9 MR. BATTLE: Okay. We are going to
10 move forward.
11 SOO LEE: All right. I represent Kyl
12 Dry Cleaners which is also known as Stan The
13 Man Cleaners on Germantown Avenue.
14 A couple of points, actually five
15 points that I would like to drive home with
16 this department.
17 Number one, the EPA.
18 Defining some PERC testing on animals
19 after human studies have been inconclusive;
20 and in addition, for every study proven PERC
21 is a toxic substance, there is another study
22 that refutes it. The jury is still out on
23 the health risks.
24 I would also like to point out that a
0055
1 study by the American Council of Sciences
2 and Health if I could show you guys here.
3 It proves that seven hundred and seventy-one
4 people that died from active smoking versus
5 five point eight million Americans would
6 yield one death from PERC.
7 Number two, to the point that PERC is a
8 cancer causing chemical, the proof is in

this room.
We are all independently owned family business dry cleaners.
Not one of us have been diagnosed with so-called affects that you put forth in your findings.
We mostly spend six days a week, ten to twelve hours a day doing this business. All you have to show for your study is inconclusive findings.
Additionally, there is no consensus in the scientific and regulatory community voting the likelihood of PERC as a carcinogen in humans. Thank you. Sorry about that.
Number three, as for machines due to

0056

the prior regulations and concern for the environment, we have all converted to dry-to-dry machines.
This eliminates the PERC emissions that the Department is so concerned about, and in addition, regulations that govern disposal of PERC waste matter is strictly adhered to.
This is evident in the US National Library of Medicine Tax Map, National Priorities List where it proves that leaks in the PERC chemical is minimal in Philadelphia.
Number four, for the replacement of chemical alternatives according to the CDC.
Number one, wet cleaning. Instead of complete replacement for PERC cleaning, there would be fabric duration thus compromising the structure composition of fabric. Sensitive fibers are subject to shrinkage. Bleeding of dyes.
Large quantities of contaminated waste water which should be a high priority, petroleum based dry cleaning, highly

0057

flammable presenting a fire hazard. Fire codes will limit where some shops using the solvent can be located encourages bacteria to thrive because of solvent additives.
Higher insurance premiums due to the higher risk and liquid CO2 which we all know what that is. Safety hazards. High pressure system. Asphyxiation. More expensive replacement of PERC machines.
Effectiveness of use not proven as it is to the relatively new application, i.e. removal of proteins, grass, lipstick, any dirt you have on your clothes.
None of these alternatives have proven to be an appropriate substitute for PERC.

Number five, in the event that the Department will still proceed in implementing this regulation, we are demanding subsidies from the City and state in order to carry out the requirements.

The cost of replacing the machine alone including the cleaning system will run each business about one hundred thousand dollars.

0058

There is a cost of disposing of the prior machines, disposal of the PERC and the purchase of the replacement chemicals.

In light of these economic times, I think it's prudent that the City if they are going to impose this restriction, they should also help pay for the costs.

I also would like to read a statement from another dry cleaners.

It's from New Hollywood Cleaners.

Will there be a grant or low interest loan available for purchasing the new cleaning technology?

If the answer is yes, how much is a grant or low interest loan amount and how and where do we apply for it?

If the answer is no, then, this is considered in a funded mandate.

The State of PA and Philadelphia have complained about a funded mandates imposed by federal governments.

Yet the City is turning around imposing the same to a small business. Dry cleaning business is a very labor intensive razor

0059

thin margin.

In this very challenging and very difficult economy, all of us are struggling with very hard to keeping our heads above the water. We all work long hours just to make ends meet. There just is no extra savings to go around, especially for a major expenditure like this.

Does the City recognize how hard it is for us? We do not have luxuries the City employees take for granted such as paid holidays, vacation days, sick days and pension programs.

If we do not come to work for whatever reason, we do not make money to pay the rent or taxes.

We believe that the timetable set forth by the City is very aggressive.

The average cost of an alternative cleaning machine is about forty to sixty thousand dollars.

While we acknowledge that phasing out

23 PERC based dry cleaning machines is
24 necessary, we wonder if the City's intent is
0060
1 to drive most of us out of business with
2 aggressive timetable.
3 Thank you.
4 MR. BRAUN: Thank you. The next
5 speaker is Il Hyon Nam. Il Hyon Nam?
6 Next is Isaac An.
7 Isaac An?
8 ISAAC AN: Hi. My name is Isaac An from
9 Broad Street Cleaners in South
10 Philadelphia.
11 I'm not going to talk about the
12 economic. I'm not going to talk about the
13 dry cleaning machines.
14 What I wanted to ask the Board Members
15 is how long did you guys study the
16 alternative solvent?
17 I put my foot in this industry in 1995,
18 and I've been following hydrocarbons, CO2
19 wet cleaning, but hydrocarbon, they are very
20 flammable. They can be very explosive.
21 Last year in Chicago, I'm not going to
22 say the brand name of the hydrocarbon
23 machine, but the hydrocarbon machine
24 exploded because during the drying cycle
0061
1 because their safety system did not work.
2 So, he lost some kind of a hearing
3 problem, and he got several burns on his
4 face.
5 I also wanted to go for the Green
6 Philadelphia.
7 However, pushing to 2013 is very short
8 of time.
9 From I believe 1980 the Superfund, the
10 waste, since then, they set the date for
11 2020. So, industry has been studying for
12 alternative solvent. They came you up with
13 Carbon Dioxide. Hydrocarbon.
14 In there, you guys did not mention the
15 Rynex. Rynex came out and here n-PB you
16 guys abandoned.
17 There is so many alternative solvents,
18 we don't know which to choose. We do not
19 know which hydrocarbon we should choose.
20 There are one hydrocarbon solvent, but
21 there are four, five different kinds of
22 hydrocarbon machines. Some they don't
23 distill.
24 Some they do separate distillation.
0062
1 If you give us some time, the industry
2 will study more about hydrocarbons. They
3 will make better equipment for us, and we
4 can make a better City.

Here it says silicones and hydrocarbon alternative solvents are less toxic than PERC.

They did not say non-toxic. They said less toxic.

That means hydrocarbon also can cause what PERC is causing right now, but the possibilities are very minimal.

However, studies conducted by the manufacturer shows that the Green Earth silicone solvent caused cancer in a rat.

The USEPA is in the process of completing a list if those solvents should be classified as a hazard.

The solvent is on the market due to this inconclusive studies not for its conform non-toxic status.

The hydrocarbons are VOC, volatile organic compound. That can also contribute to air pollution. They can destroy the

0063

ozone layer.

I mean if we use hydrocarbon and if that's going to break the ozone layer, what is the purpose of going for green?

The only green right now we can go for is the wet cleaning, but that has a downside, too.

If we all use the wet cleaning, we are going to make a tremendous waste water.

Sooner or later, there will be a regulation on the wet cleaning.

So, I would like to go for the hydrocarbons but not now. We still have time till 2020. Let them study more and let us choose.

On the PERC machine, we use one solvent and one equipment. Everything runs the same. Hydrocarbons so complicated to choose.

Everybody is making a different kind of machine and industries are producing a different kind of solvent.

Like I said, n-PB, they showed maybe last year or two years ago, but I don't know

0064

how you guys study it, but you guys abandon it.

So, the hydrocarbons sooner or later it may be problem.

So please give us somemore time than 2013.

Thank you.

MR. BATTLE: Thank you. Its been a little over an hour. So, let's take a stretch for about a minute or so.

If you need to use the facilities, now

is a good time.
MR. BRAUN: We have one more and then we have the --
MR. BATTLE: There is one more? Great. Never mind.
MR. MINOTT: There may be others.
Is there anyone that has not signed up that would like to testify?
MR. BRAUN: Alyssa Tombler.
ALYSSA TOMBLER: Hello. My name is Alyssa Tombler and I'm here tonight on behalf of Citizens For Pennsylvania's Future. Penn Future.

0065

Penn Future works to create a just environment where nature, communities and economy thrive. We enforce environmental laws and advocate for the transformation of public policy, public opinion and the marketplace to restore and protect the environment and safeguard public health.
Penn Future is the lead organization behind The Next Great City Initiative which advocates for common sense, cost-effective policies that enhance environmental quality, strengthen neighborhoods and increase our economic competitiveness.
I would like to thank the Philadelphia Department of Public Health for this opportunity to express our support for the Air Management regulation, control of PERC from dry cleaning facilities.
Penn Future agrees that Perchlorethylene or PERC is a threat to public health and welfare and that Air Management Services must limit public exposure to this chemical.
Other jurisdictions are also protecting

0066

the public from exposure to PERC from dry cleaners. PERC is a man-made chemical used mostly in the dry cleaning industry. It is a non-flammable colorless liquid that easily evaporates into the air.
PERC is a hazardous chemical. The health impacts of PERC depend on the amount and duration of exposure, acute health reactions to elevated levels of PERC include dizziness, headaches, confusion, nausea, sleepiness and difficulties with speaking and walking.
Chronic reactions included damage to the nervous system, liver, kidneys, cancer and reproductive impacts.
The Philadelphia Department of Public Health must protect the public from exposure to these dangerous chemicals. The biggest

19 threat from PERC comes from older dry
20 cleaning machines.
21 The proposed regulations will over time
22 result in dry cleaners in Philadelphia
23 switching to less toxic solvent or
24 purchasing more modern equipment that will
0067
1 lower emissions of PERC.
2 The highest exposure occurred among
3 dry cleaning workers. These workers and
4 even their families will benefit from the
5 proposed regulation furthering the broader
6 goals of the Department of Public Health.
7 The proposed regulations will also
8 help protect people living adjacent to dry
9 cleaning establishments, workers at
10 establishments co-located with dry cleaners
11 and the public.
12 We agree that dry cleaners should
13 obtain a permit before installing a dry
14 cleaning machine that uses PERC and an
15 operating license to use a PERC dry cleaning
16 machine.
17 Requiring such permits will allow the
18 Health Department to better monitor the use
19 of PERC in Philadelphia.
20 We also support proposed requirements
21 for improving operating practices, leak
22 detection procedures and record keeping
23 requirements which should reduce emissions
24 in PERC.
0068
1 Penn Future is particularly supportive
2 of the provisions that prohibit new dry
3 cleaners that are adjacent to residential or
4 medical facilities from using PERC as a
5 solvent.
6 The phase out by 2013 for the use of
7 PERC in cleaning establishments that are
8 adjacent to and prohibit dry cleaners from
9 using n-PB as a solvent.
10 Thank you for the opportunity to
11 testify today.
12 MR. MINOTT: Thank you very much.
13 MR. BRAUN: Okay. I guess we will take
14 a ten minute break.
15 ISAAC AN: Isaac An from Broad Street
16 cleaners. I got a Fact Sheet from
17 California who was the first state to pass
18 this law.
19 I see a lot of people come here saying
20 we should ban PERC. I'm sure they are just
21 doing their job. I'm sure your clothes have
22 been cleaned by PERC.
23 I'm sure you are not sick, but other
24 alternative solvents can cause the same as
0069

PERC, and here it says the hydrocarbon which is the number one alternative solvent on the market right now.

They say ozone which is linked to many ill health affects including respiratory irritation, asthma and premature death.

You have to understand, every solvent is a chemical that is going to affect you. Then we should go back to Genesis I. We should just cover our private parts.

MEMBER OF THE AUDIENCE: Don't wear clothes.

ISAAC AN: No. I'm serious.

MR. BATTLE: Thank you.

ISAAC AN: Every solvent is chemical.

So, we have to wait until the industry build best dry cleaning machine for us.

MR. MINOTT: Thank you.

MR. BATTLE: Thank you.

MR. BRAUN: Thank you.

MR. BATTLE: Let's take a break, and then, we will pick up again. Let's not make it ten. Five. Take a break. Be back here in five minutes, please.

0070

- - -

(Whereupon, a brief recess was taken at this time.)

- - -

(Whereupon, the following occurred back on the record.)

- - -

MR. BATTLE: Thank you all for reconvening.

MR. BRAUN: We have the representatives from Enviro Tech, Ray Roccon.

RAY ROCCON: Yes. Good evening. My name is Ray Roccon. I am with Enviro Tech International. I am a resident of Pennsylvania.

I just want to briefly highlight a consequence of this regulation both banning n-Propyl Bromide Dry-Solv and the regulations on PERC.

That is the energy consumption that you are going to be mandating on these cleaners. The alternative choices that they have being Petroleum, Green Earth, CO2 or wet cleaning, three out of those four alternatives have

0071

much higher energy consumption costs.

The 2009 study of utilities in Southern California Edison comparison of electricity and natural gas use of five garment care technologies, they rate Silicone at 54.2 kilowatts per hour, Petroleum at 35.5, CO2 at 30.9.

PERC as it stands right now is 26.6.
Dry-Solv which was not in this study but we know through our testing of it and development of it over the last five years would be around twenty kilowatts per hour.
It's about twenty percent less than PERC.
With those numbers in mind, both the through-put with hydrocarbon and Green Earth and CO2 is reduced as far as it takes longer to clean clothes. So, you'll be running at higher electrical impact for a longer amount of time during the day.
All right. So, you are using quite a bit more energy, and as I'm sure you are all aware and I'm aware as a resident of Pennsylvania, the cap comes off of the

0072

electric cap this year.
And so, rates are expected to go up conservatively ten to twenty percent.
So, aside from all the other economic impact, this is one consequence I don't think the Board has taken into consideration.
Appreciate the time. Thank you.
MR. BRAUN: Thank you. The next speaker, Rich Morford.
MR. MORFORD: I am going to let Joe Iannarelli speak.
JOE IANNARELLI: My name is Joseph Iannarelli. I am a former dry cleaner. I am Past President of the Pennsylvania and Delaware Cleaners Association, and I'm a consultant for the industry.
I just wanted to speak briefly about the economic impact on the dry cleaners.
Most of the small cleaners do between a hundred and fifty and two hundred thousand dollars per year. At a ten percent profit, that comes out that they make twenty thousand dollars a year. That's after

0073

working sixty hours a week.
The cost of the hydrocarbon machine is basically fifty thousand dollars. The cost of CO2 is over a hundred thousand dollars.
Fifty thousand dollars over a five year payment plan is about nine hundred dollars a months. That's interest free.
If the City does not want to come up with any money to help these people out, those are not viable alternatives to most cleaners. You have to be an extremely large cleaner to be able to afford that.
Plus with hydrocarbon, it's just takes twice as long to do.

15 n-PB is a different solvent. You can
16 convert a solvent safely with our
17 recommendations for about five thousand
18 dollars, a one time fee, and that's it.
19 So, economically speaking, those are
20 not good choices where n-PB is a good choice
21 economically and a safe choice
22 environmentally for the dry cleaners.
23 Thank you.
24 MR. BRAUN: Thank you.
0074
1 MR. BATTLE: Thank you. Rich Morford.
2 MR. MORFORD: Hi. I am Rich Morford. I
3 am General Counsel for Enviro Tech
4 International.
5 We have the manufacturers of Dry-Solv
6 dry cleaning solvent.
7 If anybody who does not know what
8 General Counsel means, I am the company's
9 lawyer. You can tell by the legal pad.
10 Now, we have heard a lot from these dry
11 cleaners today, and we have a lot of the
12 same arguments for using our Dry-Solv and
13 n-PB solvents as a replacement for PERC.
14 We are not going to talk too much about
15 the PERC rule. You have heard it.
16 What we are going to talk about is the
17 complete ban on n-PB solvents.
18 Again, lawyers do what lawyers do. I'm
19 not going to get into a whole bunch of legal
20 points here, but I will say something.
21 The way I understand it today, you have
22 been working on PERC since 2007. It's 2010,
23 and you are coming up with a proposed final
24 rule.
0075
1 And yet, you based a complete ban on a
2 solvent from February 2010 to June, July
3 2010.
4 On its face, I can tell you that that
5 is not adequate time to fully digest the
6 information that is available on n-PB.
7 On the toxicology, the health and
8 safety issues, and that's what Doctor
9 Stelljes will talk about next.
10 You have heard about a lot of
11 unintended consequences, a ban on n-PB as
12 dry cleaning as a replacement of PERC. It
13 causes people to must use something else.
14 We have talked about what they have
15 been calling Green Earth.
16 It's a Siloxin. Basically D5.
17 This chemical is on the road to being
18 banned in Canada because it bio-accumulates
19 in the environment.
20 It also has its own cancer and
21 reproductive issues.

22 Going to it, I don't think it actually
23 meets the Board's goal of making it, of
24 making health and environment safer for
0076
1 either workers or anybody outside of there.
2 Hydrocarbons as you can tell, we have
3 already heard, they can blow-up. They are
4 combustible. They are very flammable. They
5 are petroleum based.
6 We are from the Chicago area. So was
7 our guy whose machine blew up. Two
8 employees in the business were injured in
9 the blast and resulting fire. One of them
10 came out with his clothes on fire and had to
11 be put out by the people at the restaurant
12 next door.
13 I'm wondering what your Fire Marshall
14 and firemen are going to think about a
15 hundred stores moving to highly flammable,
16 highly combustible machinery.
17 All of those machines, yes, can be
18 operated safely. All of those machines,
19 yes, can malfunction, and you no longer have
20 just a vapor issue. An inhalation issue.
21 You have explosion and fire issues.
22 Happened in 2009 with new machinery and
23 new solvents.
24 C02 no better really. It operates at
0077
1 between four hundred to six hundred PSI.
2 Have never been able to, maybe some of
3 our industry people can tell us, have not
4 been able to verify it, but there are rumors
5 all through the industry, I'm sure everybody
6 here has heard them, of that pressure
7 blowing off the submarine door that is
8 installed on those to keep the pressure in
9 and blowing it through a brick wall.
10 I don't believe any of the health and
11 safety people in Philadelphia would like
12 that in a co-residential or co-sensitive
13 building.
14 These are risks that they are going to
15 be taking. We talked about wet cleaning. I
16 doubt that your Water Department is going to
17 be happy with a hundred new cleaners using
18 water and then emitting into the waste
19 treatment system non-bio-degradeable
20 surfactants and other chemicals that are
21 going to cause, could cause havoc for their
22 waste treatment facilities.
23 So, by banning n-PB solvents, by
24 banning Dry-Solv, you have taken out the
0078
1 only replacement solvent that can be used in
2 the existing machinery and have forced these
3 dry cleaners to take on capital expenditures

4 of fifty thousand dollars or more.
5 We heard a hundred thousand dollars;
6 and frankly you know it, I know it, they
7 really know it that no bank or lending
8 institution in this economy in this day is
9 going to give a one hundred thousand dollar
10 loan to a business that does two hundred
11 thousand dollars gross in a year. It just
12 won't happen. We all know that.
13 So, it makes it pretty impossible for
14 some of these people to stay in business on
15 that alone, and from what I heard today, the
16 Board has already said it, you have no money
17 for them.
18 There is very few options. A fourth or
19 fifth generation machine, PERC machine
20 running now can be modified to use Dry-Solv
21 for five thousand dollars or less.
22 Certainly if you need to ban PERC, Dry
23 Solv, n-PB solvents are really the only
24 economic replacement where most of these dry
0079
1 cleaners, these small businessmen can go.
2 And I just have one other point.
3 From what I've read on what you put on
4 your website prior to this week, one of the
5 problems that was pushed into the report
6 right there on page one and two was that
7 Dry Solv, n-PB that we, that I, okay,
8 marketed is non-regulated, and that is
9 absolutely true.
10 Why? It's not that we have been non-
11 regulated. It's that the USEPA had taken
12 thirteen years to do the most exhaustive
13 toxicology, health and safety investigation
14 into n-PB.
15 Thirteen years in order to approve it
16 under it's SNAP Program.
17 And during those thirteen years, a
18 number of things came up.
19 In 2003, USEPA proposed a rule for
20 reporting for a contaminant in n-PB called
21 IPB.
22 At that time, it was point one percent
23 there by weight and more. IPB was known to
24 be much, much more toxic than n-PB.
0080
1 By 2007 when final approval by the US
2 EPA was made, they had said we will no
3 longer propose that regulation reporting
4 because the industry by themselves
5 unregulated has brought down IPB
6 contamination by over five hundred percent
7 to point zero one percent by weight and
8 sometimes under the ability to even know
9 it's there.
10 That's where we are today, and that is

11 the product that is used in n-PB solvents
12 today, whether they be dry cleaning or vapor
13 degreasing.
14 Again in 2003, UPS proposed a
15 twenty-five part per million workplace
16 exposure level meaning you can't go over
17 twenty-five part per million.
18 In 2007, the USEPA said that they were
19 not going to propose any workplace exposure
20 level.
21 Why? Because the industry users have
22 shown that they were far under twenty-five
23 part per million in normal operations with
24 regular good work practices. In the case of
0081
1 vapor degreasing, it's NISHAP.
2 In the case of PERC for dry cleaning,
3 it would be NISHAP also.
4 We have shown, we have the data that
5 operating enclosed loop dry cleaning
6 machines, the exposures to n-PB from
7 Dry-Solv are well under ten part per
8 million.
9 Generally in the four part per million
10 range for the actual operator of the machine
11 and either one part per million or below for
12 those other people who happen to be in the
13 dry clean establishment itself.
14 But in sum, the EPA on the federal
15 level did a thirteen year investigation on
16 the health and safety issues regarding n-PB;
17 and afterwards, they did not put in one
18 regulation toward n-PB use. Not one after
19 thirteen years of looking at it.
20 Over a hundred and sixty-five pier
21 reviewed published articles in scientific
22 journals. They looked at them all.
23 I really don't think again to the Board
24 that the Board has had even the time to find
0082
1 them all because they did not call me.
2 I've got them and certainly if they
3 can't find them all, okay, they have not
4 considered them all.
5 So, I'm going to stop by just saying
6 whether it's the energy uses, more coal,
7 more air pollution from coal burning
8 furnaces and power plants, more global
9 warming, economic deficits that I doubt most
10 of the dry cleaners in Philadelphia can
11 meet, okay, and as Doctor Stelljes is going
12 to tell you, n-PB as a safe and useful
13 solvent, the entire one sentence which bans
14 the use of n-PB solvents should be dropped.
15 I would also like to give the Board
16 today a brand new evaluation from the CDC
17 from NIOSH which is an evaluation of one

18 Bromylproprane use in four New Jersey
19 commercial dry cleaning facilities.
20 What it says in sum is that they found
21 no human health hazard in the four cleaners
22 and that when you use good work practices
23 and have your machine professionally altered
24 to run Dry-Solv, your exposure levels to
0083
1 yourself in the workplace are going to be
2 well under the very conservative of ACGIHTLV
3 of ten part per million, and that your
4 exposure outdoors to the public is going to
5 be well under the proposed reference
6 concentration of one part per million that
7 the EPA has proposed.
8 Dry-Solv is a safe and workable
9 solution if you indeed feel the need to ban
10 PERC.
11 I'd like now to introduce Doctor Mark
12 Stelljes. Doctor Stelljes has a, well,
13 where is he? He has got his PhD from UC
14 Davis in Environmental Toxicology. He also
15 has a PhD in Pharmacology. He is a
16 published writer in peer review scientific
17 journals and probably the most noted expert
18 on n-PB toxicology in the States but
19 probably in the world.
20 DOCTOR STELLJES: Thanks. For the
21 record, I am Doctor Mark Stelljes. I am
22 Director of Risk Assessment and Toxicology
23 with SLR International.
24 MR. MINOTT: You said you had a report
0084
1 that you were going to give us.
2 MR. MORFORD: I do. I was going to give
3 it after the meeting, but here it is.
4 MR. MINOTT: Thank you.
5 DR. STELLJES: I'm here to talk about
6 health affects and hopefully high level
7 where I am not going to bog people down with
8 chemicals and acronyms, but we have heard
9 things here that talks about a lot of
10 toxicity studies available on n-Propyl
11 Bromide, and the consensus of the people
12 that said anything on n-Propyl Bromide here
13 is that it's a very bad chemical.
14 What that tells me is that those people
15 are not familiar with the literature and/or
16 they have preconceived ideas about how they
17 think n-PB should behave considering its
18 structure activity relationships to other
19 chemicals.
20 Well, in the next five minutes, I'm
21 hoping that I can go through enough of those
22 points to make it clear to the Committee
23 that I don't believe that there has been
24 adequate review of the key documents that

0085
1 substantiate the things that I am about to
2 say and do not come across in the Finkle
3 article that I believe was the primary basis
4 for your decision from a toxicity
5 standpoint.
6 I am also on the Health Affects
7 Advisory Committee with Cal O.S.H.A., and my
8 job there as a volunteer is to update
9 permissible exposure limits for occupational
10 settings for chemicals that are undergoing
11 revision through USEPA.
12 So, I am intimately familiar with the
13 industrial hygiene aspect as well as the
14 toxicology aspect.
15 I have been working on n-PB since
16 1990.
17 I was the first person to publish an
18 occupational exposure limit in the pier
19 review journal articles for n-PB. That was
20 in 2001.
21 That was followed in 2002 by an article
22 by Rozman & Dule, two of the most noted
23 names in toxicology from the University of
24 Kansas who found a range of sixty to ninety
0086
1 parts per million as a safe concentration
2 for human volunteers from some of these
3 cushion companies that were evaluated in the
4 HADA documents by NIOSH.
5 And then, there was also another
6 article that was published by Doctor
7 Rodricks of eighty-eight parts per million.
8 The value that we provided was anywhere
9 from 109 to 156 parts per million.
10 So, you see that there is a range in
11 the published literature from three
12 different authors ranging from sixty to a
13 hundred and fifty parts per million.
14 From the regulatory standpoint, we have
15 a lot of, we have the twenty-five parts per
16 million from EPA.
17 We have the one part per million from
18 Cal EPA.
19 We have the ten parts per million TLB
20 that was actually calculated incorrectly
21 according to the authors of the article that
22 the conclusions by Issu Jays were based on.
23 The actual reason why the ten parts per
24 million became an issue even though it was
0087
1 not repeated in a longer term study by the
2 same laboratory was that they changed the
3 methodology of how they weighed their little
4 neonatal one day old pups.
5 Instead of weighing them at the
6 beginning of the day, they weighed them at

7 the end of the day.
8 They gain about point two grams a day
9 at that age, and the difference in the body
10 weights between the two exposed and
11 non-exposed was point two grams.
12 You take that away, there is no
13 difference. The ten is not a scientifically
14 defensible number.
15 USEPA came to that same conclusion in
16 their lack of determining that there was a
17 need to set an occupational exposure limit
18 for n-PB in the victor degreasing industry.
19 In terms of toxicity information, there
20 are over a hundred studies looking at acute
21 long-term what happens to the chemical once
22 it gets inside the body. What kind of
23 metabolic pathways does it have, very
24 similar to the kinds of studies that have
0088
1 been done on PERC.
2 Based on the animal data, the
3 reproductive end points are the most
4 sensitive.
5 Both all three of the groups that have
6 developed their own occupational exposure
7 limits, myself, TERA, Toxicological
8 Excellence for Risk Assessment, and EPA all
9 have come to that same conclusion.
10 Not neurological. That does not occur
11 at the lowest levels. Reproductive affects
12 do.
13 Two more things I would like to
14 mention. One is on the cancer data.
15 There has been a two-year cancer study
16 done on n-Propyl Bromide. The draft data
17 have been reviewed by Master Toxicology
18 Program, but they have not yet come up with
19 a determination of whether there is
20 carcinogenic potency that can be
21 quantified.
22 If it were regulated today, n-Propyl
23 Bromide would be regulated as a
24 non-carcinogen as opposed to PERC which is
0089
1 regulated as a carcinogen.
2 If you look on the Prop-65 List For
3 California, PERC is on there as a
4 carcinogen.
5 So, you know you have got a carcinogen
6 that you are dealing with right now.
7 The question is is the alternative
8 n-Propyl Bromide just as bad or is it
9 safer?
10 Given the data on the human studies
11 which I'll be providing you more
12 documentation with in written comments, the
13 concentrations that were reported in the

14 articles were actually concentrations that
15 were measured after modifications were made
16 to lower the concentrations to numbers that
17 were then reported in the literature.
18 I have actually seen videos of one of
19 these sites in Utah where this has all been
20 done as adhesive spraying, not in dry
21 cleaning.
22 So, it's uncontrolled. No fans. No
23 ventilation. No respirators. No gloves.
24 No shirts. You have those kind of
0090
1 situations, and you have upwards of two
2 hundred and fifty to three hundred parts per
3 million which should cause problems.
4 It would cause problems whether it's
5 PERC or whether it's n-PB or whether it TPH.
6 Petroleum. It's not going to matter.
7 Lastly, there has been some comments
8 about how this chemical is a lot like other
9 compounds that are chlorinated or brominated
10 like Diabromo Chloropropane which is known
11 to cause male sterility or Isopropyl Bromide
12 or Two Bromapropane which only differs in
13 where the chlorine atoms sits on the
14 compound.
15 Those little differences make a huge
16 difference in the metabolism and toxicity of
17 the compound.
18 If I could take thirty seconds to do a
19 little school work here. If I can find a
20 pen that works good. Is there a pen that
21 goes with this?
22 Well, if I can't use that, then what I
23 will do is I will just borrow this pen.
24 So, I'm just going to draw two c's
0091
1 here. Carbon. Carbon. And I'm going to
2 put another one here. That is Propane.
3 All these other things around there attached
4 to the Carbon are Hydrogen.
5 So, you put a couple of Chlorines on
6 here. You put a Bromine on here. You have
7 Diobromidechloropropane.
8 What happens when it gets inside the
9 body, this goes away, this goes away, and
10 you form a nice a little triangle here with
11 Oxygen in the middle.
12 This little ring is what causes the
13 cancer.
14 When you look at the metabolism of one
15 Propopropane and compare it to two
16 Bromopropane and compare it to DBCP, that
17 does not form in one Bromopropane.
18 There is a 2008 article by Doctor
19 Garner from RTI which was a study sponsored
20 by the National Toxicology Program whether

21 they did an exhaustive disposition study
22 that figured out what are the metabolic end
23 points in the metabolites that you get from
24 exposure to this compound.
0092
1 What's called this Epoxide is not
2 something that is in the metabolic scheme.
3 Therefore, the results of the cancer
4 study that have shown that there are some
5 relatively unique tumors that have been
6 found in these rats and mice are under
7 evaluation and review by the NTP because
8 number one, the metabolic processes of the
9 chemical are not consistent with finding
10 these tumors; and secondly, the point of
11 action of the chemical from a non-cancer
12 standpoint is completely removed from every
13 place where tumors have been found in any
14 kind of elevated fashion with dose, and
15 those points alone is one of the bases for
16 me saying that right now, n-PB would be
17 regulated as a non-carcinogen.
18 I will close with a comparison of this
19 reference concentration of one part per
20 million that EPA was recommending as a draft
21 compared to what the reference concentration
22 is for PERC.
23 MR. MORFORD: Mark, what's a reference
24 concentration?
0093
1 DR. STELLJES: Thank you.
2 A reference concentration is a
3 concentration to which somebody can be
4 exposed on a daily basis over the course of
5 their lifetime without any adverse affects.
6 So, in essence, it's a safe
7 concentration. Okay?
8 So, the value for and this is available
9 through EPA. I do risk assessments where I
10 evaluate hazardous waste sites. I look at
11 Perchloroethylene in probably fifty of the
12 sites that I've done over the last twenty
13 years, and the value for PERC is 0.0003
14 parts per million. n-PB is one.
15 I think the decision as to which one is
16 safer has just been answered.
17 Thank you.
18 MR. BRAUN: Thank you.
19 Dov Shellef.
20 DOV SHELLEF: Hi. My name is Dov
21 Shellef, and I'm the President of Poly
22 Systems, USA.
23 We are the manufacturers of Fabrisolv.
24 Fabrisolv is an n-PB based material.
0094
1 The difference between Fabrisolv and
2 Dry-Solv is just the way that its been

3 stabilized, but other than that, both of
4 them are n-PB based material.
5 I have thirty years, more than thirty
6 years experience in Bromide. I am a
7 Chemical Engineer. Chemist. I'm not an
8 attorney. I'm not a Toxicologist. I'm a
9 Chemical Engineer with more than thirty
10 years experience in Bromide chemistry.
11 We started with the n-PB back fourteen
12 years ago, thirteen years ago, and we
13 formulated the n-PB for cleaning of
14 electronics and metals for aerosols and even
15 for adhesives, and we developed several
16 patterns along this line.
17 In the last thirteen years, we have
18 learned n-PB inside and out, and there is
19 nobody else in the world that knows n-PB
20 like we do, and I want to tell you that the
21 application, I'm not going to throw you
22 numbers, but I'm going to tell you stories
23 and so you can understand qualitatively and
24 not quantitatively the meaning of n-PB.
0095
1 Within these thirteen years that we
2 have been developing n-PB for usage as a
3 cleaner, also it was that it can do a good
4 job as a dry cleaning.
5 However, we hold back on it for many,
6 many years because we wanted to make sure
7 that when we come out to the market with
8 n-PB solvent for dry cleaning, it's going to
9 be a responsible solvent, and it's going to
10 be as possible, fool proof as possible that
11 people will not make mistakes with using
12 n-PB.
13 So, about five years ago, we bought a
14 dry cleaning machine, and we put it in our
15 laboratories in Bayonne, New Jersey. We
16 operate out of Bayonne, New Jersey. You are
17 welcome to visit us.
18 And we put a dry cleaning machine about
19 four years ago, almost five years ago in our
20 laboratory, and for two years, a year-and-a-
21 half to two years, we worked on this dry
22 cleaning machine.
23 We put this dry cleaning machine, we
24 attached it into a computer, and we
0096
1 collected data. Any possible place in the
2 dry cleaning machine we collected data.
3 From the cooling water to the pressure
4 of the gas, the Freon and the distillation,
5 the cooking, and we developed a manual,
6 developed an operation and developed a
7 product that can be used safely by people.
8 Now, during this operation, we learned
9 what is the consumption of solvent during

every cycle and how much solvent is emitted to the environment and how we can reduce these numbers.

We found out that under certain and good condition, practically every cycle dry cleaner would lose about two ounce of solvent into the air.

And if you make this calculation, and we made this calculation and we monitored the air around, we never got into a situation where the concentration was too high. Meaning too high for us too high is about twenty ppm.

And then, we started, three years ago, we supplied several dry cleaners, we choose

0097

two or three dry cleaners, and we ran a program with them for a full year to see how they operate in a regular course of business to see if the dry cleaners know how to use it. If they understand the way with what we tell them to do and how to operate the machine.

And after a year which we collected data practically on a daily basis from these dry cleaners, we got to the decision that it's now safe and practical to start selling Fabrisolv into the dry cleaning industry as long as the dry cleaner knows what he is doing.

So, besides this learning curve and cleaning how to make the Fabrisolv safe for a dry cleaner to use, we started to learn the impact on the environment and the impact on the people, not just health wise but also economically wise, and we found out that although Fabrisolv costs about three to four times as much as PERC, practically the cost for the dry cleaner in the machine, to use Fabrisolv in the machine will be the cost

0098

like they are using PERC.

Why? Because as you heard before, the consumption of the energy is much less with Fabrisolv.

And by the time that the PERC machine brings out fifty pounds of dry cleaning, the Fabrisolv when it runs in the machine brings twice as much poundage because the cycle is half the time of the PERC.

And if you run the cooking or the distillation according to the instruction that we give people and you're using the temperature controllers on the distillation as-needed to be, they are very, very minimal emission into the atmosphere.

And actually, while I was working on

17 that, I found out practically that dry
18 cleaners are using more detergent per cycle
19 than solvent per cycle which brought us to
20 totally different ballgame.
21 What are the other alternatives for
22 PERC that we all have? CO2, Green Earth,
23 hydrocarbons and maybe Rinex. All of them
24 are not cleaning solvents.
0099
1 They are just media in which you bring
2 the clothing, you tumble around and then you
3 put the detergent in.
4 Actually the detergent for the CO2, the
5 Green Earth needs to contain water, solvent
6 and surfactant that ties the water and the
7 solvent together.
8 So now, all of a sudden, we don't know,
9 but we buy detergents which is poison if you
10 do not use PERC.
11 If you use hydrocarbon or CO2 or Green
12 Earth, all your detergents contain a certain
13 solvent that will do the job because Green
14 Earth does not dry green. It's the
15 detergent inside the dry clean.
16 Okay?
17 So, there is no greener proposition
18 than Fabrisolv right now; and for all the
19 people here that come here from the
20 Greenpeace, I'm a green person. I can tell
21 you one thing.
22 Regarding the environment, you have no
23 issue with Fabrisolv or n-PB because in
24 eleven days whatever you release from your
0100
1 dry cleaning or any operation, the
2 Fabrisolv, the n-PB will break in the air
3 and disappear in eleven days. Gone.
4 And if somebody decides one day that it
5 is wrong to use n-PB and everybody shuts off
6 the n-PB, in two weeks there is no n-PB in
7 the air in the world.
8 It's not like the CFC and the other
9 stuff which is five thousand years in the
10 atmosphere.
11 In eleven days, it's gone.
12 Now, if you have some n-PB, some
13 Fabrisolv and around six hundred ppm goes
14 into the water in the water separator and
15 it's going to the waste stream in between
16 sixty to a hundred and twenty days, it's
17 gone. Disappeared.
18 Any n-PB, any Fabrisolv that is
19 dissolved in water and goes to the drain,
20 it's disappearing from the face of the earth
21 in sixty to a hundred and twenty days.
22 So, Fabrisolv --
23 MR. MINOTT: Excuse me, sir. Can you

24 wrap up now, please?

0101

1 DOV SHELLEF: Yes. Fabrisolv has no
2 footprint in the environment.
3 In regard to personal safety, if you
4 work, if we all work with this chemical the
5 way it should be, you should not see any
6 personal health problem.
7 Thank you very much.
8 MR. BRAUN: Thank you.
9 MR. MINOTT: Thank you.
10 MR. BRAUN: Is there anyone else that
11 would like to give testimony?
12 MR. MORFORD: One minute. Okay. One
13 minute. Rich Morford. Enviro Tech
14 International.
15 I just thought it would be instructive
16 to tell you some of the people who are using
17 n-PB based solvents in the United States
18 today.
19 Boeing Aircraft Company. We have the
20 only n-PB based solvent that is approved by
21 Boeing to be used on aircraft.
22 The Department of Defense. A number of
23 Air Force bases use it. Aniston Army Depot
24 uses it. Corpus Cristi Army Depot uses it

0102

1 for M1 tanks.
2 You name the company. Lockheed Martin.
3 Martin Marietta. Honeywell. Goodrich.
4 MacDonald Douglas. They are all using n-PB
5 safely. Have been using it from my company,
6 Dov's company and others for the past
7 fifteen years with one reported inhalation
8 problem from a person, from a user on a
9 vapor degreaser who not using it properly.
10 Fifteen years is a pretty good record.
11 Fifteen years.
12 In the literature where you will find
13 problems with n-PB is in the adhesives
14 coatings and inks where they use it to melt
15 glue and then they spray it all over the
16 place coming up with doses up to three
17 hundred, four hundred parts per million
18 which is a criminal dose in my book.
19 That does not happen in vapor
20 degreasers. That will not happen in closed
21 roof dry cleaning machines.
22 It's used safely by a number of
23 well-known companies all around the world
24 safely for fifteen years.

0103

1 MR. BATTLE: Thank you.
2 MR. BRAUN: Thank you. Anyone else want
3 to give testimony?
4 Since we have no more speakers, the
5 hearing is now closed.

MR. BATTLE: Thank you all.
MR. MINOTT: Thank you very much.
- - -
(Whereupon, the hearing was concluded at 8:15 p.m.)
- - -

0104

C E R T I F I C A T E

I hereby certify that the proceedings and evidence noted are contained fully and accurately in the notes taken by me of the foregoing matter, and that this is a correct transcript of the same.

LORI MARCULINI

(The foregoing certification of this transcript does not apply to any reproduction of the same by any means unless under the direct control and/or supervision of the certifying reporter.)

APPENDIX D –
PUBLIC HEARING SUBMISSIONS

PDCA

Pennsylvania & Delaware Cleaners Association

PDCA thanks the board for listening to our input and making changes in the original document to meet at least some of our concerns. At this point, we are not going to challenge any of the major factors in the regulation. However, there are some items that we feel still need to be addressed.

Standards

The minimum 25 ft. buffer may not be feasible in all plants. Some areas may only allow for a foot or two less. For a properly run and well maintained plant, there should be some allowance for difficult urban settings.

Prohibitions:

Banning of nPB: The solvent has been banned without a proper hearing. We feel that this is unfair, since there has not been due process allowed. There should be further studies to determine its acceptability.

Record keeping

Drycleaners are already obligated to keep all the records you are asking for. The air quality reports must be maintained on their Pennsylvania Department of Environmental Protection calendar, on which they must record their perc usage and maintenance for each machine. This calendar should be sufficient and meets your requirements. Any duplication is a waste of time and effort. We suggest that it be mandatory for the calendar be used and be available for inspection.

Drycleaners also must record their waste handling, and those records are filed according to the rules of RCRA. It is a tremendous burden to ask a small business owners, who do not have a staff or attorneys, to duplicate all that paperwork.

Section IV (a) (3) is incomprehensible. Since regeneration is computerized and automatic, how does the cleaner count the loads processed? What kind of exhaust fans need to be replaced? The fans in the machines may possibly be replaced once, but most can last for the life of the unit. This section should be removed.

Section IV (a) (4) is not doable. Cleaners cannot empty the cartridge, weigh the contents and then refill it. Since there are no standards, what is the goal of the measurement? It would make more sense to require their replacement after 18 months or two years.

It would be a good idea to require cleaners to subscribe to or affiliate with a association that would provide them with the information and assistance they need for compliance.

Carol Menberg

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Phone: 800-822-7352 • (215) 830-8495 • Fax: (215) 830-8490

Germantown-Lehigh Business & Merchants' Association

P.O. Box 60960
Philadelphia, PA 19133
Mr. Cornell Brown, President

www.glbma.blogspot.com
glbma19133@gmail.com
267 385 1939

August 12, 2010

City of Philadelphia
Department of Public Health, Air Management Services
321 University Avenue, 2nd Floor
Philadelphia, PA 19104

Dear Sir/Madam;

On behalf of the Germantown Lehigh Business & Merchants' Association, I am representing Lee's Cleaners, owned and operated by **Saung Jo Lee of 2554 Germantown Avenue**. Germantown Lehigh Business & Merchants' Association is represented by businesses on the Germantown Avenue Business Corridor from 2500 to 2800 on Germantown Avenue. My name Cornell Brown and serve as association president for five years under as a Pennsylvania State Corporation.

The concerns of Air Management Services isn't without merit, however Lee's Cleaners provides quality dry cleaning services to the residents of the community and uses state-of-the-art equipment for nearly five years.

The recent purchase and installation of their new $40,000.00 RealStar Dry Cleaning Machine; No.340 91096-0315 according to **REALSTAR Manufacturer** specifications has been built with the environmentally friendly parts and are current state of the art machines for use with perchloroethylene solvent. All are approved for operation throughout America as well as Europe. Each features an Air Clean unit incorporated into the machine, double water separator, and automatic still clean out system.

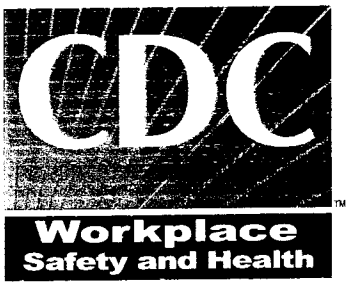
We believe that Lee's Cleaners possess the standard, state-of-the-art equipment that is mentioned in this regulation due to their experience and desire to provide the best practices in the area of dry cleaning utilizing environmentally friendly, energy conscious equipment.

Thank you so much for your time and attention on this matter.

Sincerely,

Mr. Cornell Brown, President,
Germantown-Lehigh Business & Merchants' Association
cc: Lee's Cleaners, File

This Health Hazard Evaluation (HHE) report and any recommendations made herein are for the specific facility evaluated and may not be universally applicable. Any recommendations made are not to be considered as final statements of NIOSH policy or of any agency or individual involved. Additional HHE reports are available at http://www.cdc.gov/niosh/hhe/



Evaluation of 1-Bromopropane Use in Four New Jersey Commercial Dry Cleaning Facilities

Judith Eisenberg, MD, MS
Jessica Ramsey, MS

Health Hazard Evaluation Report
HETA 2008-0175-3111
New Jersey Department of Health and Senior Services
July 2010

Submitted by Rich Medford of Enviro Tech at 8/12/10 public hearing on Reg XIV EB

Department of Health and Human Services
Centers for Disease Control and Prevention

NIOSH *National Institute for Occupational Safety and Health*

The employer shall post a copy of this report for a period of 30 calendar days at or near the workplace(s) of affected employees. The employer shall take steps to insure that the posted determinations are not altered, defaced, or covered by other material during such period. [37 FR 23640, November 7, 1972, as amended at 45 FR 2653, January 14, 1980].

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ABBREVIATIONS

1-BP	1-bromopropane
ACGIH®	American Conference of Governmental Industrial Hygienists
cc/min	Cubic centimeters per minute
CDC	Centers for Disease Control and Prevention
cfm	Cubic feet per minute
CFR	Code of Federal Regulations
CT	Computed tomography
ED	Emergency department
ft^2	square feet
IARC	International Agency for Research on Cancer
LEV	Local exhaust ventilation
LOD	Limit of detection
LOQ	Limit of quantification
mcg/mL	Micrograms per milliliter
meq/L	Milliequivalents per liter
mg/L	Milligrams per liter
µg/sample	Micrograms per sample
MMWR	Morbidity and Mortality Weekly Report
NAICS	North American Industry Classification System
NIOSH	National Institute for Occupational Safety and Health
NJ DEP	New Jersey Department of Environmental Protection
NJ DHSS	New Jersey Department of Health and Senior Services
OEL	Occupational exposure limit
OSHA	Occupational Safety and Health Administration
PBZ	Personal breathing zone
PEL	Permissible exposure limit
perc	Perchloroethylene
PPE	Personal protective equipment
ppm	Parts per million
REL	Recommended exposure limit
STEL	Short term exposure limit
TLV®	Threshold limit value
TWA	Time-weighted average
U.S. EPA	United States Environmental Protection Agency
WEEL	Workplace environmental exposure limit

Highlights of the NIOSH Health Hazard Evaluation

The National Institute for Occupational Safety and Health (NIOSH) received a technical assistance request from the New Jersey Department of Health and Senior Services. The request concerned a report of health effects in an operator using 1-bromopropane (1-BP) at a dry cleaning facility.

What NIOSH Did

- In August 2008, we visited four dry cleaning facilities that had converted their systems from perchloroethylene (perc) to 1-BP.
- We interviewed owners, operators, and an employee about their work and any symptoms they thought were work related. We later reviewed medical records.
- We collected air samples for 1-BP at the same facilities in November 2008.

What NIOSH Found

- An operator reported lightheadedness when cooking 1-BP. This is a symptom that can occur with general solvent use.
- No cases of peripheral neuropathy were found among owners, operators, or employees.
- Work practices, how conversions were done, and the amount of 1-BP used varied widely.
- Operators who converted machines on their own or who cooked 1-BP were exposed to high concentrations of 1-BP in the air.
- Respirators, gloves, and eye protection were not being used. Respirators were not equipped with the correct cartridges for 1-BP.

What Owners Can Do

- Use a qualified technician to convert the machines from perc to 1-BP.
- Follow the manufacturer's guidelines for safe product use. This includes the use of ventilation, specific temperatures, and appropriate system settings.
- Use general building ventilation to reduce 1-BP concentrations in the air.
- Use local exhaust ventilation or open the doors to outside when loading or unloading machines, pouring solvent, and maintaining equipment.

What Operators Can Do

- Do not cook 1-BP or cut the drying periods short as this may increase 1-BP exposures to operators.

- Wear eye protection, gloves, and a respirator when handling 1-BP.
- If personal air monitoring indicates the above steps are not effective at reducing exposures below applicable occupational exposure limits, then respiratory protection should be used. Employees should be fit tested and trained how to use and store respirators properly.

What Owners, Operators, and Employees Can Do

- If you become lightheaded, short of breath, or nauseated, or develop a headache when handling 1-BP, stop immediately and go outside. If symptoms do not resolve within minutes or if you develop muscle weakness or sensory problems, seek care at the nearest emergency department. Tell the healthcare provider about your workplace exposure to 1-BP.

SUMMARY

On May 2, 2008, NIOSH received a technical assistance request from the NJ DHSS regarding potential health effects of 1-BP in drycleaners. This solvent can be used in the same machine as perc after a conversion process. One New Jersey dry cleaner owner required medical evaluation after becoming symptomatic while doing the 1-BP conversion himself. Initial reports indicated the possibility of peripheral neuropathy. Because 1-BP has been documented in the medical literature to cause peripheral neuropathy, NIOSH was asked to evaluate possible exposures and health effects among dry cleaner operators who used 1-BP.

We found no cases of peripheral neuropathy among dry cleaners who had switched from perc to 1-BP. 1-BP levels that exceeded the ACGIH TLV-TWA of 10 ppm were found. We recommend that dry cleaning facilities using 1-BP as a perc alternative use a qualified technician to convert the machines.

In August 2008, we visited four of eight facilities in New Jersey that had been approved to use 1-BP in dry cleaning operations. We interviewed owners, operators, and an employee about the conversion process, work practices, and adverse health effects they associated with 1-BP use. PBZ and area air sampling was performed during normal operation of the 1-BP system during our second site visit in November 2008.

Six interviews were conducted with owners, operators, and employees. One person reported transient lightheadedness, which is consistent with general solvent exposure. The owner who sought prior medical care for symptoms that occurred while handling 1-BP had no residual neurological deficits at the time of our visit. Review of this individual's medical records did not reveal neurological abnormalities at an ED visit when symptoms first developed, and serum bromide levels obtained during that ED visit were well under levels associated with adverse health effects.

Full-shift sampling for 1-BP conducted at one of the facilities resulted in PBZ air concentrations of 40 ppm for the operator and 17 ppm for the cashier. PBZ concentrations ranging from 1.5 to 160 ppm were found in partial shift samples taken at the other three facilities. These results confirmed the release of 1-BP into the environment at all four locations, indicating a potential hazard to employees.

We recommend that dry cleaner operators using 1-BP as a perc alternative use a qualified technician to convert the machines. Operators should not cook the solvent nor cut drying periods short, as doing so may increase exposure to 1-BP. Until 1-BP exposures can be consistently documented to be below the OEL, respirators are recommended. Use of respirators should occur within the setting of a comprehensive respiratory protection

program. General ventilation should always be used to dilute 1-BP concentrations in the air.

Symptoms such as lightheadedness, headache, and nausea are consistent with solvent exposure. If employees notice these symptoms they should leave the area. Employees should not resume work until the source of the exposure has been indentified and corrected. If symptoms do not resolve shortly after leaving the work area, employees should seek immediate medical attention and inform their healthcare provider of their potential exposure to 1-BP.

Keywords: NAICS 812320 (Dry Cleaning and Laundry Services (except Coin-Operated)), dry cleaning, 1-bromopropane, n-propyl bromide, solvent, neurotoxicity

INTRODUCTION

On May 2, 2008, NIOSH received a request for technical assistance from the NJ DHSS regarding potential health effects from exposure to 1-BP (1-bromopropane), also known as n-propyl bromide, and marketed under the trade names of Dry-Solv™ and Fabri-Solv™. The request was prompted by a suspected case of peripheral neuropathy in an owner of a dry cleaning establishment who had handled a large amount of 1-BP while converting a machine to 1-BP operations. The dry cleaning businesses we visited are small establishments. The owner is the individual responsible for making business decisions. Operators are those personnel who refill the machines with 1-BP and who load and unload clothes from the machine. Often the owner is also an operator. Employees, such as cashiers and press machine operators work in the facility but do not work with the dry-cleaning machine containing 1-BP.

Background

Perc has been the solvent of choice in commercial dry cleaning for more than 50 years. In December 2007, the administrator of New Jersey's Bureau of Air Compliance and Enforcement in the NJ DEP estimated that 1500 of the 1700 dry cleaning facilities in the state utilized perc systems [McAneny 2007].

Although the IARC recognizes perc as a probable human carcinogen, its use has only recently been restricted in the United States because of its ozone depletion properties and environmental pollution contributions. Perc was noted to be one of the top ten air contaminants in New Jersey and has also been identified as a source of soil and water pollution [NJ DEP 2010a]. The U.S. EPA will ban the use of perc in coresidential dry cleaning facilities as of December 20, 2020 [40 CFR 63.323(5) (i)]. In 2007, California became the first state to ban perc use in dry cleaning ahead of the federal ban, and other states, such as North Carolina, New York, and Massachusetts, are contemplating similar actions. More recently, the NJ DEP has encouraged owners to replace their perc machines with hydrocarbon dry cleaning systems or professional wet cleaning systems [NJ DEP 2010b].

Several perc alternatives are available to dry cleaning owners, including 1-BP, aliphatic hydrocarbons (DF-2000), silicone-based cleaner (GreenEarth®), carbon dioxide, and wet cleaning methods. However, 1-BP is the only perc alternative that can be used in the original perc machines with alterations. The cost of converting an existing perc machine to use 1-BP is approximately $4,000, compared to approximately $50,000 to buy a new machine that uses aliphatic hydrocarbon or silicone-based cleaners. A 2007 nationwide industry survey revealed that of those owners who were considering replacing their perc systems, 24% would choose to convert to 1-BP [American Drycleaner 2007]. The NJ DEP has instituted a reimbursement program offering grants to owners to help offset the costs of switching to nonperc systems [NJ DEP 2010b].

Introduction (continued)

Anticipated increased use of 1-BP as a perc alternative suggests the need for a better understanding of the exposures of dry cleaner operators and potential adverse health effects. High 1-BP exposures in electronics degreasing and foam cushion manufacturing have resulted in cases of peripheral neuropathy in employees [NIOSH 2001; NIOSH 2002; NIOSH 2003]. In some cases, these neurologic deficits were permanent. In February 2008, the NJ DHSS was made aware of one dry cleaning owner believed to have developed symptoms consistent with peripheral neuropathy during an exposure to 1-BP, which prompted its request to NIOSH for technical assistance. At the time of the request, eight dry cleaning facilities in the state were licensed to use 1-BP; four of these facilities consented to participate in the NIOSH evaluation.

Assessment

On August 26–28, 2008, we made initial site visits to the four dry cleaning facilities, and interviewed the owners, operators, and an employee about the conversion process from perc to 1-BP, work practices involving 1-BP, and health effects related to 1-BP. Medical records release forms were completed by the owner who was evaluated for possible 1-BP related symptoms, and these records were reviewed.

On November 18–20, 2008, we returned to the facilities to collect PBZ and area air samples for 1-BP. We collected PBZ air samples on the operators who ran the machines and the cashiers at the front of the store who received and distributed items. The employees wore sampling devices with the sample media placed in their breathing zones. Area samples were collected in various places around the shops, including behind the machines to quantify exposures from any leaks. Air samples were only collected during times when the dry cleaning equipment was operating because the owners requested we stop monitoring when they stopped using the 1-BP machines. We collected air samples using NIOSH Method 1025 for 1-BP [NIOSH 2009]. In this method, air is drawn through a standard charcoal tube (SKC Anasorb® CSC Lot 4936) using a calibrated personal sampling pump at a nominal flow rate of 50 cc/min. After sampling, the charcoal tubes were capped and shipped refrigerated to the analytical laboratory. Samples were analyzed for 1-BP using gas chromatography with flame ionization detection. The 1-BP LOD was 1 µg/sample, and the LOQ was 4 µg/sample. The OELs and potential health effects for 1-BP are discussed in Appendix A.

Results

Health Concerns

A published report of the owner exposed to 1-BP stated that he experienced symptoms of headaches, fatigue, visual disturbances, tremors, and "muscle twitching" [CDC 2008]. During our interview

with this owner regarding the incident, he recalled a slightly different set of symptoms including headache, shortness of breath, fatigue, and chest tightness while converting his machine to 1-BP from perc. He contacted the local poison control center and was advised to report to the nearest ED for evaluation. Review of his ED medical records showed that the physical examination, chest x-ray, and head CT were normal. The only abnormality on the standard blood tests was an elevated serum chloride level of 110 meq/L (reference range: 96–106 meq/L). A serum bromide level was ordered during his ED visit, but the laboratory that analyzed the sample did not have this result available until 4 days after the visit. As per the reporting laboratory, bromide toxicity is expected with serum levels greater than or equal to 1250 mcg/mL, which is much higher than the 144 mcg/mL level reported for this owner [Quest Diagnostics Incorporated, Chantilly, Virginia]. This owner reported no persistent neurological deficits and developed no signs or symptoms that would indicate a need for an evaluation by a neurologist.

Another owner reported often feeling lightheaded and "buzzed" while handling 1-BP particularly when "cooking" the solvent (boiling the solvent to remove impunties). These symptoms resolved minutes after he went outside. None of those interviewed reported persistent weakness, sensation deficits, or balance disturbances.

Environmental Sampling

PBZ air sampling results for 1-BP are included in Table 1.

Table 1. Personal breathing zone air concentrations of 1-BP at four dry cleaning facilities

Job Title	# of Loads	Cooking	Sampling Time (minutes)	Concentration (ppm)	Full Shift TWA (ppm)
Operator – Facility 1			07:43 – 11:43 (241)	56	40
			11:45 – 15:44 (240)	23	
	10	Yes			
Cashier – Facility 1			07:44 – 11:47 (243)	24	17
			11:47 – 15:52 (245)	10	
Operator – Facility 2			08:35 – 12:04 (209)	7.2	N/A*
	3	No			
Cashier – Facility 2			08:37 – 12:09 (212)	1.5	N/A
Operator – Facility 3	1	No	07:10 – 09:52 (163)	11	N/A
Operator – Facility 4			11:43 – 15:43 (241)	160	N/A
	1	Yes			
Cashier – Facility 4			11:41 – 15:45 (246)	2.4	N/A

*N/A = not applicable

RESULTS (CONTINUED)

Facility 1 was using a Multimatic 35-pound machine (Multimatic, Northvale, New Jersey). The machine had been converted from perc to 1-BP by the owner. During sampling, 10 loads of dry cleaning were run. No solvent was added to the machine during the sampling period. Although most modern machines can run multiple loads through an automated software program, the operator at this facility manually ran each load and cooked after every load. Full-shift TWA exposures were calculated for the owner/operator (40 ppm) and cashier (17 ppm). Other employees were using press machines next to the dry cleaning machine while the cashier moved around the shop retrieving finished items and handling customer transactions. Area air samples were collected behind (103 ppm in the morning and 48 ppm in the afternoon) and in front (66 ppm in the morning and 36 ppm in the afternoon) of the dry cleaning machine for approximately 8 hours. In the morning, at the beginning of the sampling period, the building's ventilation system was off, the doors were closed, and the front windows were open. In the afternoon, the back door was open, and the ventilation system was on to improve dilution and air mixing.

Facility 2 was using a VIC 35-pound machine (Dalex, Concord, Ontario). The machine had been converted by Enviro Tech International, the company that provided this dry cleaner with the 1-BP material. During sampling, three loads of dry cleaning were run. No solvent was added to the machine during the sampling period, and no cooking was performed. An oscillating fan next to the door of the dry cleaning machine was on during the sampling period. The fan blew air towards the operator as he loaded and unloaded the machine. Other employees were using press machines next to the dry cleaning machine; after the operator had loaded and started the machine, he also used a press machine. The cashier in this facility mainly stayed in the front of the building taking clothing from customers, writing receipts, and handling payment transactions. Area air samples were collected behind (1.5 ppm) and in front (6.4 ppm) of the dry cleaning machine for the 3.5-hour sampling period while PBZ air sampling was performed.

Facility 3 used a Frimair 20–25-pound machine (Frimair, Turnersville, New Jersey). The machine had been converted to 1-BP use by Enviro Tech International. On the day of sampling, only one load of dry cleaning was run, and the operator had just started the load before we began sampling. The operator was the only employee on the premises, and he did the dry cleaning while also handling front counter duties, which included clothing intake, writing receipts for customers, and payment transactions. We collected an area air sample at the front counter that measured 8.6 ppm, similar to the operator's PBZ air concentration of 11 ppm. After the single run was completed, the operator explained that he would only perform counter duties for the remainder of the work day. Because he planned to do no more runs that day, the operator asked that we discontinue sampling at the end of the cycle. No solvent was added to the machine, and no cooking was performed during the sampling period.

RESULTS (CONTINUED)

Facility 4 was using a Frimair 30–35-pound machine (Frimair, Turnersville, New Jersey). The owner of the facility had converted the machine. During sampling, most of the operator's time was spent behind the machine, monitoring it while cooking the solvent. One load of dry cleaning was run at the end of the sampling period. Another employee performed the cashier duties in this facility; he also used a press machine next to the dry cleaning machine. Area air samples were collected behind (170 ppm) and in front (33 ppm) of the dry cleaning machine for the approximate 4-hour period that PBZ air sampling was performed. The front door of the facility was open, and a large building exhaust fan was on during the sampling period. The operator explained that he always ran the exhaust fan while he was cooking. Although he did cook solvent, none was added to the machine during the sampling period.

General Observations

None of the operators at the four locations used gloves or eye protection when handling or pouring the solvent. Two of the four operators had elastomeric half mask respirators; however, they did not have the correct organic vapor cartridges.

DISCUSSION

At the time of the request, eight dry cleaning facilities in the state of New Jersey were licensed by the NJ DEP to use 1-BP. We collected PBZ and area air samples at four of the eight locations that elected to participate in our evaluation. No two locations were performing the same amount or type of work, and work practices varied greatly, making comparisons difficult. The work volume at the facilities ranged from one to ten loads of dry cleaning over a workday, and some operators cooked the solvent, while others did not.

Because of initial reports that one owner had developed symptoms while using 1-BP, including some that were consistent with peripheral neuropathy, we were asked to focus on this health effect in our evaluation. Previous investigations have linked peripheral neuropathy to high-level 1-BP exposure in electronics degreasing [NIOSH 2001] and foam cushion manufacturing [NIOSH 2002; NIOSH 2003]. Case reports in the medical literature describe debilitating, sometime permanent, motor weakness and chronic neuropathic pain in young workers exposed to 1-BP as part of the spray adhesive used in foam cushion manufacturing. In one series of case reports of peripheral neuropathy associated with high level 1-BP use, affected employees had a 7-hour TWA exposure to 1-BP of 108 ppm [Majersik et al. 2007]. In a study of employees working in a 1-BP production facility, investigators found decreased vibration sense, decreased conduction velocity in sensory nerves, difficulty in digit recall, and decreased visual tracking ability [Ichihara et al. 2004]. This study found no motor deficits. Inhalational exposure studies on rats exposed to 200–

800 ppm 1-BP over several weeks revealed both motor and sensory neuropathies [Ichihara et al. 2000]. 1-BP has also been associated with adverse effects on the reproductive system [NIH 2003].

Human exposure to 1-BP can be assessed using a serum bromide level. This test is not usually available as a routine laboratory test. The results of a serum bromide level may not be available for several days, so this test is used to confirm an exposure, rather than to help establish an initial diagnosis. As per Goldfrank's Toxicological Emergencies, "Normal serum bromide concentrations are less than 500 mg/L" (this converts to 500 mcg/mL). Background levels of bromide result from intake of trace bromide in water due to absorption from surrounding rocks/soil containing bromide, produce treated with bromide-containing fumigants (methyl bromide and ethylene dibromide) and not washed thoroughly before eating, taking over-the-counter medications that contain bromide (e.g., dextromethorphan bromide used as a cough suppressant in cold medicine, brompheniramine maleate used as an antihistamine, bromo-seltzer, etc.), or after general anesthesia with halothane [Flomenbaum et al. 2006]. Toxicity from bromide had been reported with acute exposure to methyl bromide fumigant, overdose of medications containing bromide, or ingestion of bromide-containing neutralizers used in permanent wave hair products [Perez and McKay 2007]. Because the owner involved in the initial exposure incident did not have a serum bromide level done prior to this incident, we have no baseline for comparison to determine if the serum bromide level increased as a result of his exposure. However, the serum bromide level of 144 mcg/mL at the time of the exposure is well under the 1250 mcg/mL level associated with adverse health effects.

A laboratory finding of immediate use in determining exposure to 1-BP and other bromides is the chloride level on a routine standard metabolic assay. Depending on the equipment used to run the test, the chloride level may be elevated because of the bromide ion being counted as a chloride ion [Burkhart 2006]. Bromide can also be measured in the urine. This test was developed and evaluated against inhalational 1-BP exposure in workers exposed via use of spray adhesives; however, this test is not widely available [Hanley et al. 2006].

Full-shift sampling for 1-BP conducted at Facility 1 resulted in PBZ air concentrations of 40 ppm for the operator and 17 ppm for the cashier. This operator's exposure to 1-BP was well in excess of the current ACGIH TLV of 10 ppm. This operator ran a high number of loads on the day of sampling and cooked the solvent after each load, a practice that is not recommended by the manufacturer. Even the cashier, who did not operate the machine, had a PBZ air concentration that exceeded the recommended level, indicating that 1-BP poses a potential hazard to other employees in this facility (e.g., press operators who work next to the machines). Area air samples confirmed the release of high concentrations of 1-BP into

Discussion (continued)

the environment surrounding the machine. At this facility, air concentrations of 1-BP were higher in the morning, possibly because the general ventilation system was turned off during that time.

Partial shift sampling was conducted at the other three facilities because the owners requested that we remove the sampling equipment once they had finished running the dry cleaning machines. However, employees can have continued exposure to 1-BP after the last load is finished because of existing contamination in the environment. This exposure can be significant for facilities that do not have good general dilution ventilation or whose ventilation systems are not always in operation. PBZ concentrations ranging from 1.5 to 160 ppm were found in these 3.5- to 4-hour PBZ air samples collected at facilities 2, 3, and 4. The highest concentration (160 ppm) was measured at Facility 4. Although only one load was run by this operator, most of his time was spent cooking the solvent. Even if the operator had no further exposure to 1-BP during this work day, his full-shift PBZ concentration would be well in excess of the ACGIH TLV. An area air sample collected behind the machine at this facility confirmed the release of a high concentration of 1-BP into the work environment (170 ppm), again indicating a potential hazard to others in this work area. Machine leaks may have contributed to the high exposures; the owner had converted the machine himself and indicated that he had difficulty finding the correct materials for the conversion. Opening the front door of this facility and using an exhaust fan near the dry cleaning machine may have helped to keep this cashier's exposure low (2.4 ppm) on the day of sampling. This improvement was evident from the marked decrease in solvent odor after the fan was turned on and the front door was opened.

Conclusions

The NIOSH evaluation revealed that exposures to 1-BP can exceed the ACGIH TLV for 1-BP even for employees who do not operate the machines. It is expected that 1-BP exposures on a given day can be higher or lower at a given facility depending on work volume and work practices. Although we cannot make definitive conclusions based on our limited sampling, the highest concentrations of 1-BP were found at the two facilities that had converted the machines themselves and were cooking the solvent, a practice that had been performed widely for perc but is no longer recommended by the manufacturers for 1-BP operation. Further evaluation is needed to understand the relative contributions to the overall 1-BP exposures from possible machine leaks and practices such as cooking the solvent. This evaluation has shown that operators often rely on natural ventilation (opening doors and windows) for controlling exposures to 1-BP. This is not a good practice because weather conditions may preclude it. Although one owner reported transient symptoms consistent with general solvent exposure, we found no evidence of symptoms suggesting peripheral neuropathy in dry cleaners using 1-BP.

RECOMMENDATIONS

Based on our findings, we have several recommendations to create more healthful work places. We encourage owners of dry cleaning establishments to use these recommendations to develop an action plan based, if possible, on the hierarchy of controls approach (Appendix A: Occupational Exposure Limits and Health Effects). This approach groups actions by their likely effectiveness in reducing or removing hazards. In most cases, the preferred approach is to eliminate hazardous materials or processes and install engineering controls to reduce exposure or shield employees. Until such controls are in place, or if they are not effective or feasible, administrative measures and/or personal protective equipment may be needed.
If operators or employees develop symptoms consistent with 1-BP exposure (such as lightheadedness, headache, or nausea), they should leave the area until the source of the exposure has been indentified and remediated. If symptoms do not resolve shortly after leaving the work area, or if the individuals develop extremity muscle weakness or sensory problems, they should seek immediate medical attention and notify their healthcare provider of the potential exposure to 1-BP.

Elimination and Substitution

Elimination or substitution of a toxic/hazardous process material is a highly effective means for reducing hazards. Incorporating this strategy into the design or development phase of a project, commonly referred to as "prevention through design," is most effective because it reduces the need for additional controls in the future.

1. Consider switching to wet cleaning methods. A wide variety of garments that are currently dry cleaned can be wet cleaned satisfactorily while controlling fabric deterioration and shrinkage [Gottlieb et al. 1997]. Wet cleaning has fewer health and safety concerns, as well as a reduced burden of environmental regulations [NIOSH 1997a]. Other alternatives include selecting a dry cleaning machine that uses petroleum-based solvents; these solvents are generally considered less toxic, although they are flammable and present a fire hazard [NIOSH 1997a].

Engineering Controls

Engineering controls reduce employee exposures by removing the hazard from the process or placing a barrier between the hazard and the employee. Engineering controls are very effective at protecting employees without placing primary responsibility of implementation on the employee.

1. Isolate machines from other work areas to reduce the exposure of employees who do not run the machine, such as press operators and cashiers.

2. Use LEV at or near the machine door to reduce worker exposure during machine loading and unloading and while performing maintenance. Airflow capacity through a retrofit hood should not be less than 100 times the door opening area in square feet (i.e., a 4 ft^2 door opening would need a flow rate of at least 400 cfm). The exhaust hood should be isolated from crossdrafts caused by general ventilation, floor or other shop fans, and high personnel traffic areas [NIOSH 1997b].
3. Use general ventilation to dilute background 1-BP concentrations. Generally accepted guidelines recommend 12 air changes per hour with a minimum of 30 cfm of outside air per person for dry cleaning establishments. The direction of airflow should move from a clean area (customer counters) to one that is less clean (dry cleaning machine area). A qualified ventilation system contractor should be contacted for assistance [NIOSH 1997b].

Administrative Controls

Administrative controls are management-dictated work practices and policies to reduce or prevent exposures to workplace hazards. The effectiveness of administrative changes in work practices for controlling workplace hazards is dependent on management commitment and employee acceptance. Regular monitoring and reinforcement are necessary to ensure that control policies and procedures are not circumvented in the name of convenience or production.

1. Use a qualified technician to convert the machines from perc to 1-BP to ensure the use of proper materials for replacement parts (e.g., gaskets), correct machine settings, and proper safety measures during the process.
2. Follow manufacturer guidelines on the use of ventilation, temperature, and system settings when using 1-BP.
3. Conduct air sampling periodically for 1-BP and whenever changes in work practices, procedures, or ventilation may affect employee exposures.
4. Do not cook the solvent. The manufacturer of Dry-Solv states that, unlike perc, the solvent does not require cooking.
5. Keep the machine door closed except when loading and unloading.
6. Advise the operator to keep his or her head out of the machine and stay as far away as possible from the door when loading and unloading. A tool with a long handle could be used to retrieve clothes from the back of the drum.

7. Use the full drying period, as cutting drying periods short may cause solvent to remain on the items and increase operator exposure.
8. Consider limiting the number of loads per day to reduce exposures below the OELs.

Personal Protective Equipment

PPE is the least effective means for controlling employee exposures. Proper use of PPE requires a comprehensive program, and calls for a high level of employee involvement and commitment to be effective. The use of PPE requires the choice of the appropriate equipment to reduce the hazard and the development of supporting programs such as training, change-out schedules, and medical assessment if needed. PPE should not be relied upon as the sole method for limiting employee exposures. Rather, PPE should be used until engineering and administrative controls can be demonstrated to be effective in limiting exposures to acceptable levels.

1. Wear safety glasses/goggles and gloves appropriate for 1-BP when handling the solvent as the Dry-Solv Material Safety Data Sheet suggests. Viton® or SilverShield® gloves offer the best protection.
2. Ensure that employees whose exposures can exceed the ACGIH TLV wear respirators until ventilation and administrative controls can be demonstrated to reduce employee exposures below applicable guidelines.
3. Instruct employees at Facility 1 to wear a minimum of an elastomeric half-mask air-purifying respirator with organic vapor cartridges, because air sample results indicate that the operator and cashier were exposed to 1-BP above the ACGIH TLV of 10 ppm. This respirator has an assigned protection factor of 10, meaning that exposures would be expected to be reduced by a factor of 10 if the respirator is properly fitted and worn in full accordance with the OSHA respirator standard. At Facility 4, the operator's exposure was much higher, indicating the need for a respirator with a higher assigned protection factor if cooking solvent is continued. This would include a minimum of a full facepiece air-purifying respirator or a powered air purifying respirator equipped with organic vapor cartridges. Although full-shift air sampling was not conducted at Facilities 2 or 3, it is possible that operators' full-shift exposures could exceed the 10 ppm guideline depending on the workload and other factors. We recommend conducting additional full-shift sampling at these facilities over multiple days to determine if respiratory protection is needed as an interim measure until additional ventilation and administrative controls are implemented.

RECOMMENDATIONS (CONTINUED)

4. Ensure that all applicable requirements of the OSHA Respiratory Protection Standard (29 CFR 1910.134) are met where respirators are used. This includes medical screening, annual fit testing, training on the proper use and limitations of the respirator, and instruction on how to properly clean and store the respirator. A Small Entity Compliance Guide for the OSHA Respiratory Protection Standard is available at http://www.osha.gov/Publications/SECG_RPS/secg_rps.html. Additional information regarding respirator cartridge changeout is also available online at http://www.osha.gov/SLTC/etools/respiratory/change_schedule.html.

Other Recommendations

OSHA has a consultation service that is free to businesses that may prove helpful in conducting air sampling and establishing a respirator program. This service is separate from the OSHA compliance office, and use of its services cannot result in citations. Please see the OSHA website for further information at http://www.osha.gov/dcsp/smallbusiness/consult.html.

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Appendix A: Occupational Exposure Limits and Health Effects

In evaluating the hazards posed by workplace exposures, NIOSH investigators use both mandatory (legally enforceable) and recommended OELs for chemical, physical, and biological agents as a guide for making recommendations. OELs have been developed by Federal agencies and safety and health organizations to prevent the occurrence of adverse health effects from workplace exposures. Generally, OELs suggest levels of exposure that most employees may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. However, not all employees will be protected from adverse health effects even if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a preexisting medical condition, and/or hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the employee to produce health effects even if the occupational exposures are controlled at the level set by the exposure limit. Also, some substances can be absorbed by direct contact with the skin and mucous membranes in addition to being inhaled, which contributes to the individual's overall exposure.

Most OELs are expressed as a TWA exposure. A TWA refers to the average exposure during a normal 8- to 10-hour workday. Some chemical substances and physical agents have recommended STEL or ceiling values where health effects are caused by exposures over a short period. Unless otherwise noted, the STEL is a 15-minute TWA exposure that should not be exceeded at any time during a workday, and the ceiling limit is an exposure that should not be exceeded at any time.

In the United States, OELs have been established by federal agencies, professional organizations, state and local governments, and other entities. Some OELs are legally enforceable limits, while others are recommendations. The U.S. Department of Labor OSHA PELs (29 CFR 1910 [general industry]; 29 CFR 1926 [construction industry]; and 29 CFR 1917 [maritime industry]) are legal limits enforceable in workplaces covered under the Occupational Safety and Health Act. NIOSH RELs are recommendations based on a critical review of the scientific and technical information available on a given hazard and the adequacy of methods to identify and control the hazard. NIOSH RELs can be found in the *NIOSH Pocket Guide to Chemical Hazards* [NIOSH 2005]. NIOSH also recommends different types of risk management practices (e.g., engineering controls, safe work practices, employee education/training, personal protective equipment, and exposure and medical monitoring) to minimize the risk of exposure and adverse health effects from these hazards. Other OELs that are commonly used and cited in the United States include the TLVs recommended by ACGIH, a professional organization, and the WEELs recommended by the American Industrial Hygiene Association, another professional organization. The TLVs and WEELs are developed by committee members of these associations from a review of the published, peer-reviewed literature. They are not consensus standards. ACGIH TLVs are considered voluntary exposure guidelines for use by industrial hygienists and others trained in this discipline "to assist in the control of health hazards" [ACGIH 2009]. WEELs have been established for some chemicals "when no other legal or authoritative limits exist" [AIHA 2009].

Outside the United States, OELs have been established by various agencies and organizations and include both legal and recommended limits. Since 2006, the Berufsgenossenschaftliches Institut für Arbeitsschutz (German Institute for Occupational Safety and Health) has maintained a database of international OELs from European Union member states, Canada (Québec), Japan, Switzerland, and the United States available at http://www.dguv.de/bgia/en/gestis/limit_values/index.jsp. The database contains international limits for over 1250 hazardous substances and is updated annually.

Employers should understand that not all hazardous chemicals have specific OSHA PELs, and for some agents the legally enforceable and recommended limits may not reflect current health-based information.

However, an employer is still required by OSHA to protect its employees from hazards even in the absence of a specific OSHA PEL. OSHA requires an employer to furnish employees a place of employment free from recognized hazards that cause or are likely to cause death or serious physical harm [Occupational Safety and Health Act of 1970 (Public Law 91-596, sec. 5(a)(1))]. Thus, NIOSH investigators encourage employers to make use of other OELs when making risk assessment and risk management decisions to best protect the health of their employees. NIOSH investigators also encourage the use of the traditional hierarchy of controls approach to eliminate or minimize identified workplace hazards. This includes, in order of preference, the use of: (1) substitution or elimination of the hazardous agent, (2) engineering controls (e.g., local exhaust ventilation, process enclosure, dilution ventilation), (3) administrative controls (e.g., limiting time of exposure, employee training, work practice changes, medical surveillance), and (4) personal protective equipment (e.g., respiratory protection, gloves, eye protection, hearing protection). Control banding, a qualitative risk assessment and risk management tool, is a complementary approach to protecting employee health that focuses resources on exposure controls by describing how a risk needs to be managed. Information on control banding is available at http://www.cdc.gov/niosh/topics/ctrlbanding/. This approach can be applied in situations where OELs have not been established or can be used to supplement the OELs, when available.

1-Bromopropane

As with other solvents, occupational exposure to 1-BP may occur via both inhalation and skin absorption. Health effects related to overexposure to 1-BP (and many other solvents) may include irritation of the eyes, mucous membranes, upper respiratory tract, and skin. At higher levels of exposure, central nervous system depression (characterized by headache and dizziness, and possibly loss of consciousness) may occur.

Neither NIOSH nor OSHA has OELs for 1-BP. However, NIOSH is developing an REL. The ACGIH has set a TLV of 10 ppm for 1-BP as an 8-hour TWA exposure [ACGIH 2009]. The primary basis for the TLV is liver damage, embryo/fetal damage, and neurotoxicity.

The U.S. EPA determined that 1-BP is acceptable for use as a substitute for ozone-depleting substances in metal cleaning, electronics cleaning, and precision cleaning applications. This determination was based upon the conclusion that 1-BP exposures in the range of 17-30 ppm in such applications would not likely cause adverse human reproductive effects. However, the U.S. EPA also proposed that the use of 1-BP in aerosol or adhesive applications is not acceptable based on higher than anticipated workplace exposures. U.S. EPA does not regulate the use of solvents in dry cleaning under the Significant New Alternatives Policy Program [72 Fed. Reg. 30142(2007)].

Previous investigations have linked peripheral neuropathy to high level 1-BP exposure in electronics degreasing [NIOSH 2001] and foam cushion manufacturing [NIOSH 2002; NIOSH 2003]. Case reports in the medical literature describe debilitating, sometimes permanent, motor weakness and chronic neuropathic pain in young workers exposed to 1-BP as part of the spray adhesive used in foam cushion manufacturing. In one series of case reports of peripheral neuropathy associated with high level 1-BP use, affected employees had 7-hour TWA exposure to 1-BP of 108 ppm [Majersik et al. 2007]. In a study of employees working in a 1-BP production facility, investigators found decreased vibration sense, decreased conduction velocity in sensory nerves, difficulty in digit recall, and decreased visual tracking ability [Ichihara et al. 2004]. This study found no motor deficits. Inhalational exposure studies done on rats exposed to 200-800 ppm 1-BP over several weeks revealed both motor and sensory neuropathies [Ichihara et al. 2000].

Human exposure to 1-BP can be assessed using a serum bromide level. This test is not usually available as a routine laboratory test. The results of a serum bromide level may not be available for several days, so this test is used to confirm an exposure, rather than to help establish an initial diagnosis. However, a laboratory finding of immediate use in determining exposure to 1-BP and other bromides is the chloride level on a routine standard metabolic assay. Depending on the equipment used to run the test, the chloride level may be elevated because of the bromide ion being counted as a chloride ion [Burkhart 2006]. Bromide can also be measured in the urine. This test was developed and evaluated against inhalational 1-BP exposure in workers exposed via use of spray adhesives; however, this test is not widely available [Hanley et al. 2006].

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Acknowledgments and Availability of Report

The Hazard Evaluations and Technical Assistance Branch (HETAB) of the National Institute for Occupational Safety and Health (NIOSH) conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employers or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found. HETAB also provides, upon request, technical and consultative assistance to federal, state, and local agencies; labor; industry; and other groups or individuals to control occupational health hazards and to prevent related trauma and disease.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of NIOSH. Mention of any company or product does not constitute endorsement by NIOSH. In addition, citations to websites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these websites. All Web addresses referenced in this document were accessible as of the publication date.

This report was prepared by Judith Eisenberg and Jessica Ramsey of HETAB, Division of Surveillance, Hazard Evaluations and Field Studies. Health communication assistance was provided by Stefanie Evans. Editorial assistance was provided by Ellen Galloway. Desktop publishing was performed by Robin Smith.

Copies of this report have been sent to the New Jersey Department of Health and Senior Services and the Occupational Safety and Health Administration Regional Office. This report is not copyrighted and may be freely reproduced. The report may be viewed and printed at www.cdc.gov/niosh/hhe. Copies may be purchased from the National Technical Information Service at 5825 Port Royal Road, Springfield, Virginia 22161.

Below is a recommended citation for this report:
NIOSH [2010]. Health hazard evaluation report: evaluation of 1-bromopropane use in four NJ commercial dry cleaning facilities, various locations, NJ. By Eisenberg J, Ramsey J. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA No. 2008-0175-3111.

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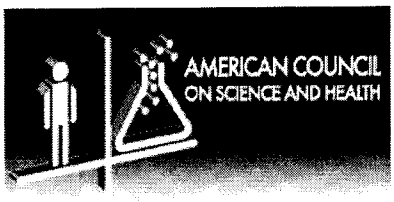


- Home Page
- Riskometer
- Risk Rings
- Data

RISKOMETER.ORG

Risk Rings: Exposures

Exposures to behaviors and our environment offer all sorts of risks. Here we present a full spectrum of exposures that caused American deaths - the size of each ring is proportional to the number of deaths from the specified cause.

Use your mouse and click the rings. See the "odds of dying" from any of the exposures presented. The 'odds of dying' is reported here as the number of people expected to produce one death from a particular cause. This number is calculated by dividing the United States population, approximately 300 million people, by the number of deaths from each cause during 2002. Using this method, 771 people would be expected to yield one death from active smoking . In contrast, 5,882,353 Americans would yield one death from exposure to the dry cleaning chemical, perchloroethylene.

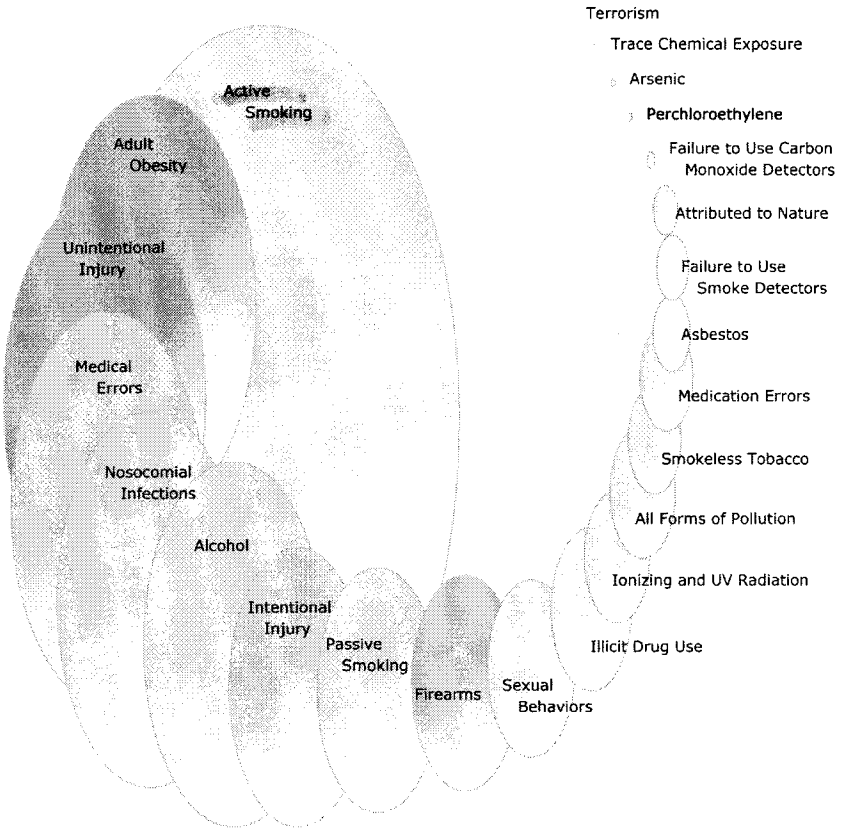
Active Smoking was the leading cause of exposure death. In contrast, exposure to the dry-cleaning fluid, Perchloroethylene and to numerous environmental chemicals-resulted in virtually no deaths at all.

Explore the other Risk Ring page, "Leading Causes of Death", by pressing the menu button at top. Or visit the Riskometer, and the Data pages.

If you have questions, contact us.

American Council on Science and Health
New York

Year 2002 statistics were the most recent complete statistics available. Total USA deaths in 2002 were 2,443,387.



8-12-10
KYL DRY CLEANERS
Ed Battle

APPENDIX E –
COMMENTS AFTER PUBLIC HEARING
THRU 8/20/10

Memorandum City of Philadelelphia

Date: 8/30/10

To: Dr. Donald Schwarz, Commissioner Department of Public Health

From: Jeanne Reedy, Administrative Services Director, Records Dept.

Subject: The Department of Public Health Proposed Filing of Air Management Regulation XIV – Control of Perchloroethylene from Dry Cleaning Facilities

---

The enclosed letter from Scott Mondi, on behalf of Poly Systems USA Inc of 39 Avenue C, Bayonne, NJ 07002, has comments on the above Regulation.

Please notify interested parties of the date and time of the scheduled hearing.

Cc: Thomas Huynh, AMS Director

August 19, 2010

Philadelphia Department of Records
City Hall, Room 158
Philadelphia, PA 19102

The proposed air management regulation XIV "Control of Perchloroethylene From Dry Cleaning Facilities" also contains a ban on dry cleaning fluids that contain nPB. It is the position of Poly Systems USA that the ban on nPB is unfair because there has not been adequate time for evaluation of this dry cleaning fluid. Poly Systems USA requests reasonable due process concerning the evaluation of nPB as a dry cleaning fluid. Thank you.

Scott Mondi
Poly Systems USA
39 Avenue C
Bayonne, NJ 07002

336689

DEPARTMENT OF RECORDS
2010 AUG 30 AM 9:40

From: "Meijer, Jon" [jmeijer@ifi.org]

Sent: 08/19/2010 01:45 PM AST

To: Thomas Huynh

Subject: Public Hearing Comments - DLI

Hi Thomas,

I only sent you the information that is most critical to DLI. DLI is not asking AMS to make any changes to the regulation that would affect (everyone's) desire to protect human health and the environment. The recommended changes simply seek to minimize regulatory duplication, additional paperwork burdens, and just general havoc for the drycleaner.

Thank you for your time and effort. If you need any assistance, please do not hesitate to call.

Regards,

Jon Meijer

Philadelphia Comments

Hello, my name is Jon Meijer, and I am here on behalf of the Drycleaning and Laundry Institute (DLI) which is a national and international trade associations representing retail dry cleaners, launderers, and wet cleaners in the United States. Thank you for your time.

- **Co-located Facilities – 25 ft. Buffer –** It has come to our attention that the 25 ft. minimum distance between with regard to ventilation. The distance maybe difficult if not impossible to achieve. However, you have already established performance criteria that all cleaners have to achieve. We believe that should be sufficient to meet the needs of AMS.

- **Operation and Maintenance – 20 degree temperature Differential –** A machine's ability to meet a 45°F cold air temperature echoes the NESHAP requirement, and industry has no objection. However, most third or fourth generation dry-to-dry machines are not equipped with temperature gages before and after the condensing coil, which makes it impossible for cleaners to take differential readings. If it is the intention of AMS to distinguish fourth and fifth generation machines from earlier generations that might use ad on refrigeration technology, then AMS should make this section more clear.

- **Record Keeping VI (a) (3) – "the number of loads processed between generations"??**
  Quite frankly, we have no idea what neither this means nor what AMS's intension is with this section. Simply put, this section makes no sense and should be removed.

- **Record Keeping VI (a) (4) – "recording the amount of activated carbon in the carbon adsorber" ?** My question why? For what purpose? And to tell AMS that this is not doable!

- **General Record Keeping –** Drycleaners are already obligated to keep the vast majority of the records AMS is requiring in the new regulations. Unfortunately, the actual regulation does not always mirror what is contained in other well establish rules for perc drycleaners. This creates regulatory duplication, an additional paperwork burden, and just general havoc for the drycleaner. Already, the current perc drycleaning regulation brought forth by AMS also includes elements from other regulations, including RCRA with regard to hazardous waste, including manifesting, storage, spill containment, and other record keeping requirements, Additionally, drycleaners are already required to report spills and releases to the environment based on current "reportable quantity" rules, and follow strict NESHAP requirements. Simply put, there is absolutely no need to add, change or modify record keeping requirements over and above what is already in existence. It is a tremendous burden to ask a small business owner, who does not have a staff or attorneys to duplicate all that paperwork.

"Mark Stelljes"
<mstelljes@slrcorp.com>

08/20/2010 02:20 PM

To <DPHAMS_Service_Requests@phila.gov>
cc
Subject Comments on Proposed Regulation XIV Control of Perchloroethylene from Dry Cleaning Facilities

This email is intended for Tom Huynh:

Attached please find my written comments on the above-referenced Regulation. This is a follow-up to my oral presentation at the public meeting last week.

Please contact me if you have any questions.

Thank you.

Mark Stelljes, Ph.D.
Director of Risk Assessment and Toxicology
SLR International Corp
925-229-1411 (v)
925-595-4951 (c)
http://www.slrcorp.com

WHITE PAPER ON THE TOXICITY OF 1-BROMOPROPANE

In Response to the Proposed Air Management Regulation XIV Control of Perchloroethylene from Dry Cleaning Facilities

Prepared by Dr. Mark Stelljes
SLR International Corp

August 20, 2010

Introduction

This white paper is prepared in response to the statement in the Proposed Air Regulation XIV, Control of Percholoroethylene from Dry Cleaning Facilities, dated June 24, 2010, that "no person shall use n-propyl bromide as a dry cleaning solvent". n-Propylbromide, also called 1-bromopropane or nPB, is an approved solvent under USEPA SNAP, and a 2007 decision by USEPA (Federal Register, May 30) indicated that no occupational exposure limit was necessary since the industry was adequately self-regulating its use as a vapor degreaser. As stated by USEPA "we believe that proper use of nPB in solvent cleaning would not pose measurable risks to the general population". Therefore, it is puzzling that the City of Philadelphia would propose a ban on this chemical, while merely restricting the use of perchloroethylene (PCE) in dry cleaning.

It is apparent that the statement to ban nPB in dry cleaning comes from a single report prepared for the Department of Public Health/Air Management Services of the City of Philadelphia by Adam Finkel in June of 2010 entitled "Increased Toxicity and Carcinogenicity of n-Propyl Bromide (1-Bromopropane) Relative to Perchloroethylene". Reading only the title of this document is clearly misleading, and there are numerous factual errors and key omissions in this paper that preclude adequate comparison of the toxicity of the two chemicals.

Rather than being more toxic than PCE, nPB is much more likely to be a safe chemical not associated with toxicity at typical workplace exposure levels, assuming both chemicals are handled appropriately. The following text is divided into two subsections that focus on (1) factual errors and omissions associated with the above-referenced report, and (2) an overview of the broad spectrum of nPB toxicological literature that support my conclusion that nPB is less toxic than what is reported by FInkel (2010).

Based on this information, I urge the City to eliminate the sentence banning the use of nPB in dry cleaning from the Proposed Regulation. At a minimum, passage of the regulation should be deferred until adequate review of the toxicity of nPB is conducted by the City.

Factual Errors and Omissions in Finkel (2010)

1. The inhalation LC50 values (concentrations causing death in 50 percent of exposed organisms) reported on page 6 could not be confirmed through review of available literature. Rather than the LC50 for nPB being lower than that for PCE, the following information is factual:
    a. LC50 for nPB: 50,600 parts per million (ppm) (Elf Atochem, 1997).
    b. LC50 for PCE: 1,750 to 5,200 ppm across four studies (ATSDR, 1997).
    c. Using the same argument presented by Finkel (2010), the acute toxicity of PCE is approximately tenfold greater than nPB. This is opposite to the conclusion reached by Finkel (2010).
    d. This argument assumes that both PCE and nPB have identical dose-response relationships, which is also incorrect (see item 6 below).

2. The summary of Ichihara et al. (2004a) on page 6 is incomplete and misleading.
    a. There is no such thing as an “nPB production factory”. According to industry information, the subject facility is a chemical factory that makes brominated compounds, only one of which was nPB. Prior to 1996, this facility used 2-bromopropane and some of the same employees were historically exposed to that solvent as well. The most common symptom reported by the workers was sore throat (i.e., irritation of mucus membranes), which was common to exposures to both solvents. Symptoms and results cannot be directly ascribed to nPB since workers were exposed to a variety of brominated compounds during their tenure.
    b. This study included only 24 female and 13 male workers. The worker exposure durations ranged from 1 month to ten years, their ages at the time of the study ranged between 25 and 60, and time weighted average nPB concentrations ranged from 0.6 to 170 ppm. The four workers with the longest exposure durations (six years or more) were estimated to be exposed to time weighted average concentrations between 25 and 107 ppm.
    c. Workers at a beer factory were used as the control population; both the sample size and design impedes making causal statements about toxicity.
    d. Dizziness, light-headedness, headache, and feeling intoxicated were the most common neurological symptoms reported. As stated by the authors in a follow-up article (Ichihara et al, 2004b), “the present neurological or mucous-irritating symptoms may not be specific to 1-bromopropane exposure but could be also caused by 2-bromopropane. This argument is based on the fact that the frequencies of almost all symptoms did not differ from those of the 1996 investigation, when 2-bromopropane was the main product, although the frequency of headache rather decreased significantly.”
    e. The authors conclude by saying “there were no severe chronic symptoms suggestive of neurological damage in workers exposed to less than 170 ppm.” This is far different than the inflammatory statement in Finkel (2010) that 1.1 ppm exposure to nPB resulted in complete loss of sensitivity in fingers and toes.
3. The summary of the Majersik et al. (2007) case study on page 6 is somewhat inaccurate.
    a. Neurological symptoms were reported following at least 3 months of exposure, but air concentrations during exposure were not measured, making interpretations of causality difficult.
    b. After three affected workers presented to the doctors, air concentrations were estimated using personal monitors, which do not afford much precision.

c. Finkel (2010) states that these workers used nPB to glue together foam pieces, but it was left unsaid that all of these workers were using nPB as a spray adhesive in unventilated buildings. Therefore the chemical was available for exposure in both liquid and vapor form. Based on discussions with Dr. Majersik and evaluation of the workplace video, workers did not wear any protective equipment, such as goggles or gloves, and often did not even wear shirts, thus violating the company's standard operating procedures. Therefore, skin exposure was also high for these workers.
d. Concentrations estimated in the Utah study four days later, after air exchange was implemented by installing large fans, averaged about 130 ppm, with some concentrations as high as 176 ppm. Therefore, it is likely that actual exposure concentrations during the time the affected workers were engaged in their activities were substantially higher than these estimates.
e. These are unreasonably high concentrations relative to those associated with working in either a dry cleaning facility or any other legally operating entity. The false assumption implicit in Finkel (2010) is that the same symptoms and toxicity would occur from much lower concentrations.

4. The summary of the Raymond and Ford (2007) case study is incomplete.
    a. The range of concentrations was 18-254 ppm; it is not known to what concentrations those employees with symptoms experienced.
    b. As reported by Raymond and Ford (2007) and NIOSH (2003), high levels of urinary arsenic (average of 242 micrograms per liter; ug/L) were present in the affected workers in the absence of any known source of arsenic. According to the authors, the drinking water, diet, and soil were tested and not shown to contain elevated levels of arsenic, and hobbies were similarly ruled out as potential sources. NIOSH (2003) identifies arsenic as a "confounding factor" in the assessment.
    c. This is a key statement because arsenic toxicity can cause some of the same symptoms as reported by the workers exposed to nPB. A typical noncancer syndrome associated with arsenic includes neurotoxicity of both the peripheral and central nervous systems. It typically begins with sensory changes, numbness, and tenderness followed by muscle weakness. Peripheral neuropathy can progress, leading to demyelination and motor dysfunction, which is similar to that seen in the case studies discussed during the symposium.
    d. Typical arsenic levels in urine are below 10 ug/L, while levels above 100 ug/L are referred to as "excessive exposure" in *Casarett & Doull's Toxicology* (Klaassen,1996). These elevated urinary arsenic levels were measured between two and three weeks after the workers presented with their illnesses. Since the biological half-life of arsenic in the body is about

3 days, approximately 6 half-lives elapsed between the time the workers stopped working and their urinary arsenic levels were measured. Since urinary levels of arsenic are the best indicator of recent exposure, this implies that the urinary levels were much higher while the workers were still on the job, and could be completely responsible for the reported effects.

   e. NIOSH (2003) concludes, “We did not find evidence that 1-BP exposure caused nerve or reproductive problems, or problems with blood counts”.

5. The summary of the CDC (2008) case study is incomplete and misleading.
   a. The New Jersey case study described on Page 7 is incomplete. The affected person did not follow the distributor’s instructions for modifying the machine from PCE to nPB. This lack of standard of care likely resulted in high nPB concentrations relative to those operating the machine consistent with instructions.
   b. Additional cases should occur only if operators do not follow recommendations for safe operation, which is likely for any chemical improperly handled.
6. The summary discussion on page 7 lacks basic understanding of dose-response relationships, which are the underpinning of the entire discipline of toxicology.
   a. Finkel (2010) states “the clear danger of nPB at higher exposures makes controlling nPB levels an important addition…”. The implicit assumption behind this statement is that nPB is toxic at all concentrations even those typically associated with properly operated workplace settings. Such a statement ignores the dose-response relationship of a chemical.
   b. For a chemical regulated as a carcinogen, such as PCE, there is no safe exposure level because exposure to any amount of a carcinogen is associated with some level of risk. This is because the assumed dose-response relationship is linear down to zero.
   c. For a chemical regulated as a noncarcinogen, such as nPB, all concentrations below the threshold for toxic effects are without risk because the body can safely handle such concentrations. For these types of chemicals, the dose-response line is not linear down to zero. Instead, the response (i.e., toxicity) is zero up until a certain concentration, and above that a relationship exists.
   d. Therefore, it is neither appropriate nor accurate to imply that neurological problems occurring at very high exposure concentrations (above 100 ppm in all of these cases) will occur at typical concentrations in properly conducted dry cleaning facilities.
7. The summary of reproductive toxicity on page 8, including discussion of 2-bromopropane is outdated and inaccurate.

a. While it is correct that nPB is listed by California as a developmental toxicant, it is also true (but unstated by Finkel [2010]) that PCE is listed by California as a carcinogen.
b. 2-Bromopropane is no longer present at the levels presented by Finkel (2010) in nPB formulations. It is now near or below detection limits, rendering the argument irrelevant.
c. The "sterility" at the "factory" in Korea ascribed to 2-bromopropane has no relationship to the reproductive toxicity of nPB. Several authors have identified that the metabolism, mechanism and site of action of 2-bromopropane is different than for nPB (Ichihara, , indicating that structure-activity relationships are not appropriate for extrapolating the toxicity of one to the other.
    i. For example, Ichihara (2000) first implied that the toxic action of nPB was inhibition of spermiation, while the toxic action of iPB is impairment of spermatogonia. The authors state "the histopathological changes in the testis induced by nPB are much different from those by 2-bromopropane…1-bromopropane does not have the severe toxicity toward spermatogonia which 2-bromopropane has."
    ii. In a more recent study, Yamada et al. (2003) state "1-bromopropane is less toxic to spermatogonia when compared with 2-bromopropane…the underlying mechanism of the toxic effects of 1-bromopropane on the reproductive system is different from those of 2-bromopropane in rats." Focusing on female rat reproductive toxicity, these authors go on to say "in contrast to the…findings on 2-bromopropane, 1-bromopropane seems to mainly alter the maturation of follicles and is less toxic to follicles at early stages." Finally, they provide the following summary:
        i. "The above differences between the toxic effects of 1-bromopropane and 2-bromopropane on female reproductive organs seem to parallel the differences in the actions of the two isomers on the male reproductive system. Previous studies showed that long-term exposure to 2-bromopropane resulted in reductions in the numbers of all types of spermatogenic cells and that acute or subacute exposure impaired spermatogenesis, followed by apoptosis of spermatocytes. On the other hand, 1-bromopropane had little effect on spermatogonia, spermatocytes, and round spermatid, and only a mild effect on weight gain of seminal vesicles and a failure of spermiation in seminiferous tubules in male rats. Considered together, these results indicate

that 1-bromopropane has adverse effects on both male and female reproductive organs, although the mechanisms of these effects are different from those of 2-bromopropane."

d. It is also correct that the NTP monograph cited by Finkel (2010) incorporates exposure concentrations in their conclusion. Importantly, this was not the finding of the expert CERHR panel, which concluded, "the Expert Panel expressed serious concern at the upper end of the exposure range, as in the example of the poorly controlled spry adhesive applications" (CERHR, 2002). These poorly controlled situations led to case studies described above. A concentration of 18 ppm is not at the high end of the occupational exposure range, and none of the studies summarized above included symptoms at such concentrations. The "high end" of human occupational exposure, based on the above information, is in excess of 100 ppm. As discussed in point 7 above, impacts at typical workplace concentrations (less than 10 ppm based on indoor air measurements at active dry cleaners) are well below any level of concern.

8. The summary of the carcinogenic potency of nPB on pages 8-9 is premature and speculative, since the authoritative body (USEPA) has not yet completed its interpretation of the results.
    a. The NTP internal draft report on the carcinogenesis of nPB (scheduled Peer Review Date: November 19, 2009) is currently in internal peer review within the regulatory agencies. As stated on the cover page to the report, "It has not been formally disseminated by the NTP. It does not represent and should not be construed to represent NTP determination or policy."
    b. This information notwithstanding, four conclusions were provided in the report:
        i. In female mice and rats, "clear evidence of carcinogenic activity" was found based on tumors of the large intestine.
        ii. In male rats, "some evidence of carcinogenic activity" was found.
        iii. In male mice, there was "no evidence of carcinogenic activity".
    c. According to the report, "some evidence" of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
    d. Therefore, clear evidence was found for females, but not for males. This indicates that additional interpretation is necessary before overall conclusions about the carcinogenic potential of nPB in humans are reached.

9. The paragraph above the conclusions on page 11 is inaccurate.
    a. While I agree that dry cleaners deserve the regulatory agency's best current judgment about which substance(s) should not be used as substitutes, USEPA's own ruling (2007) demonstrates that nPB is a safe alternative to 1,1,1-TCA in precision cleaning. Current information indicates that nPB would be equally safe in dry cleaning when used according to the manufacturer's directions.
    b. The weight of evidence does not support the conclusion that nPB is more toxic than PCE.
10. The conclusions on page 11 are unsupportable based on the weight of the scientific literature on nPB and PCE.
    a. It is incorrect to state that nPB is currently "unregulated". As previously discussed, after several years of review USEPA determined that no regulation was required since the industry was adequately self-regulating use and exposures of nPB in precision degreasing, and no reports of toxicity have occurred from that use. There is no reason to anticipate that nPB will suddenly become toxic when used at these same concentrations by dry cleaners.
    b. One way to evaluate the overall toxicological literature is to compare reference concentrations (RfCs) developed by USEPA. RfCs are concentrations to which people can be exposed daily throughout their lifetime without adverse effects. For PCE, the current RfC listed by USEPA (2010) is 0.41 ug/m^3 (0.0000604 ppm), while the draft RfC for nPB is 1 ppm. This implies that, based on the overall toxicological database for these two compounds, PCE is regulated at concentrations 1,000 times lower than nPB. This is consistent with the assumption that PCE is far more dangerous a chemical to be exposed to than nPB.

Overview of the Toxicological Database for 1-Bromopropane

nPB has been the subject of over 150 toxicological articles over the past 15 years. One of these has included a two-species disposition study sponsored through the National Toxicology Program, which elucidated the metabolic pathways for nPB in rats and mice (Garner et al., 2006) and provides demonstrative proof that:

- The epoxide formation that occurs in 2-bromopropane, PCE, and dibromochloropropane does not form in nPB metabolism. This reduces the likelihood that nPB is a direct acting carcinogen.
- Metabolism is different in rats and mice, similar to that seen for TCE. Neither species appears to form the epoxide intermediate identified above.
- nPB has a short biological half-life; long-term exposure to elevated levels likely leads to elevated bromine in the blood. This can be addressed medically through salt therapy.

Additionally, four independent bodies (other than ACGIH) have developed recommended Occupational Exposure Levels for nPB, none of which were mentioned by Finkel (2010). These documents, along with the recommended OELs, are listed below.

- Rozman and Doull (2002) used human volunteers from the NIOSH case studies and identified a range between 60 and 90 ppm that was protective of headache. No other symptoms were reported.
- USEPA (2003) in their proposed regulation recommended an OEL between 18 and 25 ppm using benchmark dose software and incorporating most of the key toxicological studies.
- Stelljes and Wood (2004), using the same software and studies, developed an OEL of 110 to 158 ppm. The only difference between this range and that recommended by USEPA (2003) was in the use of uncertainty factors.
- TERA (2004) re-evaluated the three studies listed above and identified an OEL of 20 ppm.

Given the information provided above and indoor air data from 8-hour workshifts in dry cleaning establishments using nPB, exposure concentrations should be below all of these concentrations when used in accordance with the manufacturer's recommendations.

All chemicals are inherently toxic at some concentration, and nPB is a typical solvent in that it primarily causes narcotic effects (e.g., sleepiness) at lower concentrations (i.e., between 20 and 100 ppm). At high concentrations (e.g., over 150 ppm), nPB can cause neurological impacts. However, there is no need to ban the use of nPB in dry cleaning since this chemical is safe when used as directed, and appears to be safer than PCE given the carcinogenicity of the latter chemical.

If it would assist the City of Philadelphia in making a decision about the use of nPB in dry cleaning, I would be available to meet with your staff to further discuss this White Paper or any aspect of the toxicology of nPB.

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APPENDIX F –
AIR POLLUTION CONTROL BOARD AD HOC MEETING WITH N-PB INDUSTRY SIGN-IN-SHEET

SIGN-IN SHEET
AIR POLLUTION CONTROL BOARD - Ad Hoc Meeting with nPB Industry
Thursday, October 7, 2010

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16			
17			
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APPENDIX G –
AIR POLLUTION CONTROL BOARD AD HOC MEETING WITH N-PB INDUSTRY MINUTES

Ad Hoc Meeting Minutes
Thursday, October 7, 2010
First floor Conference Room
321 University Avenue

The meeting of the Air Pollution Control Board Ad Hoc Committee and the n-Propyl Bromide (nPB) Industry was held Thursday, October 7, 2010, at The Spelman Building, 321 University Avenue, 1st floor Conference Room

Eddie R. Battle, Chairman, presided

ATTENDING: Eddie Battle, Chair, APCB
Tom Edwards, Member, APCB
Nan Feyler, Health Commissioner's Chief of Staff

STAFF: Thomas Huynh, Director, Air Management Services (AMS)
Edward Braun, Program Manager, AMS
Henry Kim, Chief, Program Services, AMS
Hallie Weiss, Program Services, AMS
Edward Wiener, Chief, Source Registration, AMS
Patrick O'Neill, Council for the City of Philadelphia
Dennis Yuen, Council for the City of Philadelphia

GUESTS: Scott Mondi, Poly Systems USA
Kevin Andrews, Enviro Tech Intl, Inc (ETI)
Andrew Zalenski, ETI
Dov Shellef, Poly Systems USA
Joseph Iannarelli, ETI
Ray Roccon, ETI
Richard Morford, ETI
Mark Stelljes, SLR Intl
Chris Creelman, City Council

1. **WELCOME**
   Eddie Battle welcomed everyone and told everyone that this would be a two part meeting
   a. Presentation from Industry
   b. A Closed Session of the Ad Hoc Committee
      Mr. Battle asked all the attendees to introduce themselves

2. **DISCUSSION AND/OR QUESTION/ANSWER PERIOD**
   Speakers:

   Dr. Mark Stelljes, SLR International Corp
   Presented - Carcinogenic Potential of 1-Bromopropane (nPB) (see attached)

Richard Morford: If operated correctly you will be below the testing levels that are required.

Dov Shellef: We have been helping Perc customers to convert machines from Perc to nPB but sometimes we have found that the machines are too old or too broken to work - cannot control the emission coming out of the machines - in that case we tell the people they cannot use nPB in their machines - recently the dry cleaning machine makers (most are in Italy) have resisted getting into making nPB machines because they can make the more expensive Perc or C02 machines - they have now started to making nPB machines - the 1st machine came into the US about 1 ½ months ago into Indiana and we started running it with fabric solvent - one of the first things we found was that the exposure limit of the emission - 2/5th of the loading door was 1.3 ppm - this was using badges - (Richard Morford stated that their study was done using sinacasters - comparable but different) - 10 feet away at the pressing area it was 0.47 ppm - this was a brand new machine produced just for use of nPB - we, ourselves went there to help tune up this machine check - we made sure everything was okay and you could not even smell any solvent.

Some background on nPB - I have worked with bromine for about 35 years - there was a problem with iPB - it was the largest manufacturer in Israel (actually in the world at that time) - people were using it carelessly - all of a sudden there was a problem with infertility - there was a lawsuit and people began to use it in a more responsible way - the largest manufacturers are now in China - Dr. Finkel sent a report about China and I answered his questions - most of these plants are now out of business - the way they run these plants in China very poorly - but to use these correlations in plants here is irresponsible - the body of evidence shows that this is a good chemical when used responsibly - from environmental and personal point of view these are very useful chemicals.

Eddie Battle - Asked that copies of the reports be given to Tom Huynh - he stated that he would like to start the discussion at about 10:45 and so who else would like to speak.

Dr. Mark Stelljes: I would like to continue on and kind of summarize - our worse case 9 ppm and our best case on a new dedicated machine 1.6 ppm are both as safe as they can possibly be - under the ACGHTLB which is the most conservative - if you look at the US EPA under the 2007 SNAP- they are concerned with 18 to 30 ppm - we are far below that by about ½

Pat O'Neill: We should be careful as SNAP is only concerned with ozone and depleted chemicals.

Dr. Mark Stelljes: That is incorrect - we have the Federal Register which we can give you a copy of - and out of the 37 pages - probably 35 of them are on toxicity

and work place exposure levels - not on SNAP - the 13 years that it took to get SNAP was because of toxicity testing which they asked the Industry to do and the Industry did - SNAP does have to do with Ozone depletion.

Tom Huynh: Soes PERC also have monitoring on SNAP as well?

Dr. Mark Stelljes: Yes PERC was approved in about 15 words.

Tom Huynh: In the SNAP are PERC and NPB treated the same?

Dr. Mark Stelljes: Well they weren't treated the same - but they both have SNAP approval - but since the EPA did such an extensive look at the toxicity under the SNAP program they came out 18 to 30 ppm - we are far, far less than that.

Dennis Yuen: It was irrelevant to the actual use of the n-Propyl bromide - if you look at the register they are looking at the exposure of the chemical not at the use of the chemical.

Dr. Mark Stelljes: And the EPA under the SNAP program has developed acceptable exposures for the work place for most the chemicals it looked at that did not have OSHA PEL's.

Tom Huynh: That is true but it was done at an industrial Facility not at a co-located dry cleaner.

Dr. Mark Stelljes: They came up with an acceptable exposure level and then compared their findings to the exposure levels in the precision cleaning sector which includes the vapor degreasers - and they saw that maybe 81% of vapor degreasing machines were well under 10 parts per million - this is one of the reasons they approved it in precision cleaning - the AEL which the EPA came up with in those 37 pages is for chemical itself regardless of its use - the EPA at the same point has proposed that nPB be disapproved, basically banned in the adhesive coating and ink sector - that sector is where you find all - 100% - of the literature where there has been effects on humans - if you read thru the NIOSH HEADING - you will find out that nPB which was used to solidify glue which was then sprayed on foam cushions to make airline seats in factories with no ventilation - exposures were up to 398 ppm - and there was also a detrimental component because these people in NC were not wearing shirts, just shorts and getting it all over them - every one of the reported case was in this adhesives and coating and ink where you're getting exposures well over 200 - 400 ppm and NIOSH has come out with that information.

The reason we point to the SNAP approval in precision cleaning is that vapor degrease is a vapor control machine the same as a dry cleaning machine. As we go through the newer generation of dry cleaning machines there is less and less emission of whatever solvent you are using - and the data that Dov has just

produced proves that the 6th generation made for nPB have got the exposures down to 1.6 ppm - the only way it can be at higher levels is if you just don't give a damn about work practices.

Nan Feyler: Thank you very much - as the Chief of Staff on behalf of the Commissioner - I just want to say that our mission is to protect the public health so this is really about risk analysis and through a precautionary principal this is where we end up - I appreciate your efforts to translate this for us - What I just wanted to question is that you both mention the machine - what I don't understand is can a Dry Cleaner that has an older machine for PERC use this nPB - is there any kind of concern we should have for exposure - so that we don't want people to use this in older/bad machines

Joseph Iannarelli: I can probably answer that better than anyone - in an older machine you do not want to run it unless the machine is completely sealed - which is very easy - we will not put it in anything older than a 4th generation machine - all it takes is replacing the existing gaskets - Which should be done every 4 to 5 years - not matter what they are running - Adjust the temperature controls and the computer controls and it will run fine - 4th generation are all computer controlled and this limits the exposure.

Nan Feyler: A lot of the local dry cleaners are interested in learning and getting guidance around safety issues - they don't want to do anything to put them at risk.

Joseph Iannarelli: We at Enviro Tech have put through a comprehensive job of putting together a stewardship package - to go thru the conversion process and evaluation process on machines - we have spent a lot of money going and evaluating machines before we convert them - I am on my way to Canada to do just that - you will see it on the CDC article where they mention our company - the industry tends to please itself in that solvent is very much more expensive than PERC - on a dollar to dollar basis - to the point of about 3 to 4 times per gallon - so you will go thru it much faster than PERC - so it will not be cost effective - There have been alternatives to PERC in the last 30 years but PERC is 70% to 80% of the market because it works - nPB is the only cost effective alternative.

Nan Feyler: Are there other manufactures that don't do that?

Richard Morford: We are the only manufactures there are - you have the industry right here at this table.

Joseph Iannarelli: We have a least 50% Koreans involved in this industry and we are translating our website into Korean for just this reason.

Dov Shellef: If I may permitted to say a few things - before we brought this into the dry cleaning market we actually went out and purchased machines and for two years we monitored and learned how to operate a dry cleaning machine on nPB the right way- and we connected the machine to a computer which monitored every 10th of a second on every place in the machine that might leak - so we learned it for the last 10 years - I actually went to dry cleaner school to learn it - we then made a manual which we gave away to competitors to see exactly how to run a dry cleaning machine - every dry cleaner must sign that they have read the manual and understand it - and we go there and we check to see if they understand it - and not only do we have it in English but we have written it in Korean - so we have the tech data sheet/ manual and people who talk with Dry Cleansers.

Joseph Iannarelli: Our plant ran for 4 years - when we started we converted one plant and the workers came and asked us to convert the other plants.

Eddie Battle: How often did you have to maintain the machines

Ray Roccon: You have to do maintenance just as you have to maintain your car or any other machine - there is a list of maintenance on our web site - there is daily, weekly, monthly and yearly maintenance that must be done.

Nan Feyler: Do you have to do more or less than PERC for nPB?

Ray Roccon: Actually less because nPB runs without a filtration system just a distillation system so it is simpler.

Patrick O'Neill: But you did say it shouldn't be used on anything older than a 4th generation machine right?

Ray Roccon: Yes, that is my belief personally.

Everyone speaking together

Nan Feyler: If the dry cleaner does not do the maintenance - is there a greater risk of this kind of solvent being an issue?

Ray Roccon: This kind of a solvent does not stay there - these people can tell you better than me - as far as this solvent it cuts it in ½ the solvent you are using.

Unknown speaker: I would say absolutely not because there are certain things that you must do for the machine to work - if you don't do them the machine will not work - you lower the temperature and put less stress on the machine.

Unknown Speaker: Using less solvent is costing less - you are reducing machine to its most simple use or form.

Eddie Battle: It is 11:00 and we want to wind down.

Unknown Speaker: It is not a good conversion on older machines because its function of internal components and exposure.

Dov Shellef: We have a flag if a person who has one machine that is a 35 to 50 lb machine and he is using more than 15 gallons a month we call this guy and to check what is going on with the machine.

Patrick O'Neill: Dr. Finkel has determined that nPB is more toxic than PERC - do you disagree with that?

Dr. Mark Stelljes: What I can tell you is that below 150 ppm there has been no evidence that in humans or animals of any neuro effects - regards of what he has written there.

Patrick O'Neill: Okay there are a couple of reports for Dr Lee and a couple of other people and there is something from NIOSH that indicate the contrary.

Dr. Mark Stelljes: There has never been anything published by NIOSH that says there has been anything directly ascribable to nPB toxicity in the plants we have looked about.

Unknown Speaker: Those reports that we indicated were with the glue mixture - so we fully expect and in fact request the ban on nPB within the adhesive sector.

Patrick O'Neill: He has a similar conclusion about the carcinogenic effect of PERC verses nPB and he thinks that nPB would be more potent than PERC.

Dr. Mark Stelljes: Totally disagree - when you develop a cancer potency from a chemical you don't take the single end point that causes the effect and say that we are going to base the regulation on that - typically what is done is you look at your weight of evidence and base it on that.

Patrick O'Neill: Did your evidence did cause cancer in the mice in the reproductive organs?

Nan Feyler: Yes, if we should revisit the possibilities in the reproductive.

Dr. Mark Stelljes: There have been no carcinogenetic tumors in the reproductive organs.

Nan Feyler: I guess in the Female Rats.

Dr. Mark Stelljes: You mean the rats that have the colonic tumors in the large intestines?

Nan Feyler: What does that say to you?

Dr. Mark Stelljes: I guess it says it is an unknown ideology.

Patrick O'Neill: I guess we take that precautionary approach in the past that were done only on men even if no studies were done on females.

Dr. Mark Stelljes: All studies have had both sexes tested and only females have shown any response to the chemical and you are getting different organs.

Dov Shellef: And they were different organs.

Nan Feyler: So your conclusion is that it is not something to worry about/

Dr. Mark Stelljes: The entire weight of evidence is one positive and all the others are negative - the assumption that Dr Finkel made is the same at the high concentration and the lowest concentration - but this is not correct So the major questions are IS THAT ACURATE? And based on all the studies the question is not do we regulate it as a carcinogen but at what level do we regulate it.

Patrick O'Neill: It looks like all the tests have been financed by the industry.

Richard Morford: This is not true - none of the carcinogenic studies have been paid for by the industry.

Patrick O'Neill: The Health concerns are the risk here.

Richard Morford: I don't believe we are on the EPA cancer risk list.

Dr. Mark Stelljes: No we are not.

Richard Morford: But of the 150 tests that were done only two were financed by the industry.

Tom Huynh: Can someone explain to me why the TLB for PERC is 25 when for nPB is only 10?

Dr. Mark Stelljes: Because EPA has not looked at it - AICGH has not looked at PERC - the PCL for PERC is 100.

Patrick O'Neill: If we made the nPB regulation the same as the PERC would that be reasonable?

Richard Morford: Well, others may not be the same as my answer but yes I think that would be reasonable.

Kevin Andrews: The worst case scenario is that it will evaporate a short time - but not at the rate where it will get anywhere.

Kevin Andrews: There is more information on our website that may be helpful.

Eddie Battle: Thank you so much it was very helpful.

APPENDIX H –
AIR POLLUTION CONTROL BOARD AD HOC MEETING WITH N-PB INDUSTRY SUBMISSIONS

Carcinogenic Potential of 1-Bromopropane (nPB)

Presented by Dr. Mark Stelljes, SLR International Corp

Presented to the Department of Public Health/Air Management Services
City of Philadelphia

October 7, 2010

Scope of Cancer Studies on nPB

- Genotoxicity tests
- Bioassays using *in vitro* methods
- Two-year inhalation rat and mouse cancer study

Genotoxicity Tests

- Ames Assay (mutagenicity)
  - Salmonella: negative
  - Salmonella (TA 100): negative
- Micronucleus test (B6C3F1 mice)
  - Chromosomal damage test, bone marrow
  - Negative (both male and female tested)
- http://ntp.niehs.nih.gov/go/GT for more information

Bioassays Using *in vitro* Methods

- Human hepatocyte cell lines
- Four tests conducted on multiple solvents
  - nPB, iPB, PCE
- DNA breakage (GenoMed I) and DNA repair (GenoMed II) bioassays relevant to cancer potential
- Paper published in Toxicology and Industrial Health 2006 (Adeli, Hasspieler, and Stelljes)

In vitro Bioassays: Results

	CytoMed (cell toxicity)	GenoMed I (DNA breakage)	GenoMed II (DNA Repair)
PCE	Positive (all doses)	Positive (all doses)	Negative
iPB	Positive (at and above 150 ppm)	Positive (at and above 150 ppm)	Positive (at and above 150 ppm)
nPB	Positive (500 ppm only)	Negative	Negative
EnSolv	Positive (500 ppm only)	Negative	Negative

Two-Year Cancer Study

- Rats and Mice
- Inhalation Exposure
  - Whole-body exposure
  - Fur/Skin exposure likely
- Doses
  - Rats: 0, 125, 250, 500 ppm
  - Mice: 0, 62.5, 125, 250 ppm

Two-Year Cancer Study: Results

- Skin tumors in both species
  - May be due to skin absorption; unlikely linked to inhalation exposure
- Lung/Bronchiolar tumors in female mice
- Pancreatic Islet Cell adenomas in male rats
  - Unclear etiology
- Colonic tumors in female rats

Two-Year Cancer Study: Relevant Noncancer Information

- Irritant to skin and upper respiratory tract
- nPB metabolized through MFO in liver and conjugation with glutathione
  - No liver tumors reported
- Reproductive toxicity site of action:
  - Sperm cells (spermiation) and follicle maturation
- Mechanism of action:
  - Glutathione depletion → decline in neuroproteins (enolase/kinase) → toxicity

NTP Draft Conclusions from Study

- "No evidence" of carcinogenic potential
  - Male mice
- "Some evidence" of carcinogenic potential
  - Male rats (skin tumors)
- "Clear evidence" of carcinogenicity
  - Female rats (colon tumors)
  - Female mice (lung/bronchiole tumors)

Weight of Evidence Summary

- Negative in genotoxicity tests
- Negative in mutagenicity tests
- Negative in *in vitro* bioassays (DNA damage)
- No evidence of tumors associated with sites of action of nPB
  - No reproducible tumors across sex or species
- Not on any EPA list of potential carcinogens

Conclusions

- No definitive dose-response relationships to quantify carcinogenic potential of nPB
- Regulate and classify nPB as a non-carcinogen
  - Noncancer effects discussed in memorandum submitted to the Department of Public Health/Air Management Services
- nPB is less toxic than PCE based on review of cancer and noncancer information

ATTACHMENT D

GENERAL POPULATION EXPOSURE ASSESSMENT FOR N-PROPYL BROMIDE (NPB)

1. INTRODUCTION

N-propyl bromide (NPB) is used in various solvent, aerosol, and adhesive formulations as an alternative to ozone-depleting substances (ODS) such as methyl chloroform. However, in animal studies, NPB has been shown to exhibit toxicity to the liver and reproductive system following inhalation exposure. To date, the potential for significant exposure of the general populations living near facilities that use n-propyl bromide has not been adequately assessed. This document attempts to provide a brief assessment of these exposures.

This assessment focuses on the long-term general population exposure as a result of routine adhesive application. This end use was chosen because adhesive use is more emissive than either the solvents cleaning or the aerosol solvent end uses[1]. Thus, EPA expects that the greatest NPB exposure to the general population will result from adhesive operations.

2. APPROACH

A risk screening exposure assessment has been conducted with the objective of determining a reasonable foreseeable worst-case scenario for general population exposure associated with the use of n-propyl bromide. The exposure assessment uses a hypothetical adhesive application facility based on data collected from actual facilities (EPA 2001). The collected data have been used in this analysis to characterize the typical high-use adhesive application facility and an average-use adhesive application in an urban locale, assuming a row-house-type warehouse setting.

Two emission release scenarios were considered in the analysis:

1. Emissions released from the average-size adhesive application facility for the bonding of furniture and mattresses (S5); and

2. Emissions released from the urban row-house-type warehouse setting in which application of n-propyl bromide is used to bond furniture and mattresses (S6).

Please refer to the document entitled, "Occupational Exposure Assessment for NPB" for a description of the potential exposure setting in adhesives operations.

[1] In cleaning applications, use of vapor degreasers generally reduces emissions of NPB to very low levels in the ambient air. Although NPB used in aerosol solvents is an emissive use, aerosol solvents are typically used intermittently and in relatively small amounts. This is in contrast to adhesive applications where NPB is aerosolized to the ambient air in large amounts throughout a typical workday.

Average Size Adhesive Application Facility (S5)

The general characteristics used in the modeling of the average adhesive-application facility for the bonding of furniture and mattresses are:

- Average size facility: 65.7 meters x 65.7 meters;
- Average height of the facility: 7 meters;
- Typical lot size of 100 x 100 meters (~ 2.5 acres);
- Urban setting;
- Average high use adhesive emission rate of 12.3 g/s;
- Facility operates 2000 hours per year (40 hr/week, 50 weeks/year);
- Average breathing height of 1.8 meters; and
- For the vented scenario the facility operates a ventilation system at the ASHRAE recommended flow rate of 0.50 cubic feet per minute/ft^2 of floor space. (i.e., 1.3 air exchanges per hour) (ASHRAE 1999). The stack was located on the roof, a short 0.3-m stack with an inside diameter of 0.8-m was assumed. Estimates of concentration included the effects of building downwash within cavity region, for both the near- and far-wake regions.

Within S5, three types of releases were considered:

1. Emissions released as a fugitive (non-vented) area source released upwards through the roof of the facility;

2. Emissions released as a single point source (vented) upwards on the roof of the facility; and

3. Emissions released as a fugitive (non-vented) source horizontally through cracks, leaks, window ventilation and shaft ventilation (natural ventilation).

Urban Row-house-type Warehouse Adhesive Application Operation (S6)

The general characteristics used in the modeling of the urban row-house-type warehouse adhesive application operation are:

- Three-story (30 feet) house, with a footprint of 25 feet x 40 feet;
- Urban setting;
- Average high use adhesive emission rate of 1.23 g/s;
- Facility operates 50 weeks per year, 8 hours per day, 5 days per week;
- Average breathing height of 1.8 meters;
- Nearest resident is adjacent to the house at a distance of 3-m; and
- For the vented scenario the facility operates a ventilation system at the ASHRAE recommended flow rate of 0.50 cubic feet per minute/ft^2 of floor space (i.e., 1.3 air exchange per hour) (ASHRAE 1999). The stack was located on the roof with a short 0.3-m stack with an inside diameter of 0.8-m. Estimates of concentration included the affects of building downwash within cavity region, for both the near- and far-wake regions.

Within S6, four types of releases were considered:

1. Emissions released as a fugitive (non-vented) area source upwards through the roof of the warehouse;

2. Emissions released as a single point source (vented) upwards on the roof of the warehouse;

3. Emissions released as a fugitive (non-vented) source horizontally through cracks, leaks, window ventilation and shaft ventilation (natural ventilation); and

4. Emissions released as a fugitive source horizontally using commercially available fans capable of accomplishing at least 1.3 air exchanges per hour.

3. MODELING SYSTEM

EPA's SCREEN3 (EPA 1995) air dispersion model was used to assess dispersion of emissions using the full range of meteorological conditions (all stability classes and wind speeds) to estimate the highest 1-hour concentration. The SCREEN3 model is a "screening" model used to assess the likely maximum-potential concentration from a single source. The technique used here is typically used to evaluate air quality impacts of sources pursuant to the requirements of the Clean Air Act, such as prevention of significant deterioration (PSD), new source review, and existing sources of air pollutants, including air toxics. The approach applied here is the initial-phase approach used to determine if either (1) the source clearly poses no air quality problem or (2) the potential for an air quality problem exists. If a potential problem exists then a more refined analysis is necessary following approaches discussed in the Guideline on Air Quality Models (Revised) (40 CFR Parts 51 and 52). For a site-specific analysis using site-specific meteorological data the use of the long-term dispersion model, Industrial Source Complex Long Term (ISCLT) is preferred, but unfortunately this approach cannot be used in this analysis because the site-specific meteorological data are not available.

EPA's screening procedures (EPA 1992) for annual average concentration require that estimates be developed by multiplying the maximum 1-hour concentration determined by SCREEN3 by a factor of 0.10. The multiplying factors are based upon general experience with relationships between maximum short-term concentrations and annual average concentrations based on observations. The factors account for the fact that the meteorological conditions that produce the highest 1-hour concentrations do not occur throughout the year (i.e., variations in wind speed, direction, atmospheric stability). The factors are intended as a way to estimate the maximum annual concentrations from short-term averages, and a degree of conservatism is incorporated in the factors to provide reasonable assurance that maximum annual values will not be underestimated. The range of factors that may be used with this model is (0.06 to 0.10). Using a factor of 0.10 in this risk screen incorporates an additional degree of conservatism since this number represents a worst-case maximum annual average concentration assuming that aerodynamic downwash and/or low stack height is a problem for most adhesive application facilities.

The SCREEN3 model can provide estimated concentrations for distances less than 100 meters (down to one meter as in other regulatory models). However EPA/OAQPS recommends caution when using results at distances of less than 100 meters, as concentrations may be suspect. A recent model validation study (EPA 1998) for similar conditions (flat terrain, non-buoyant, near-surface release, measurements at arcs positioned 50 m to 800 m downwind) using the short-term Prairie Grass tracer study have shown that the

ISC3 model[2] predicts well within a factor of 2 for all downwind distances. According to the Prairie Grass study, Industrial Source Complex (ISC3) shows an overall tendency to over predict by an average of 50% for all downwind distances further supporting that the results from this screen results are conservatively based and fair estimates of the near source concentration of NPB.

The accuracy of the ISC3 and SCREEN3 type model estimates have been evaluated by comparison with observed concentrations in two studies (EPA 1982; EPRI 1983). The studies found that: (1) these types of models are more reliable for estimating longer time-averaged concentrations than for short-term concentrations; and (2) the models are reasonably reliable in estimating the magnitude of the highest concentrations occurring sometime, somewhere within an area. Errors in the highest estimated concentrations of 10 to 40 percent were found to be typical, and well within the factor of 2 accuracy recognized for these models noted in the Guideline on Air Quality Models (Revised) (40 CFR Parts 51 and 52).

4. RESULTS

Results from the two scenarios are presented in Table 1 and 2 with a comparison to the reference concentration (RfC) for NPB (See Attachment B)[3]. For the average sized high adhesive use facility (S5) the vented emission concentrations are lower than the non-vented emissions and are well below the RfC. These values include building downwash. The additional momentum from the ventilation system appears to be of sufficient magnitude to lower the concentrations over the non-vented scenario. None of the ventilation scenarios for S5 showed concentrations exceeding the RfC.
For urban row-house-type warehouse (S6), again none of the scenarios show an exceedance of the RfC, although it is worth noting that the non-vented horizontal release with fans case shows relatively high values compared to other S6 cases. The two vertical release scenarios show maximum concentrations occurring at a distance of 30 meters from the house due to the height and upward momentum associated with the release.

[2] The basic dispersion algorithms contained within the SCREEN3 are identical to ISC3 – the ISC3 model allows the user more flexibility in inputting meteorological data, multiple sources, and source locations.
[3] An RfC is an estimate of a continuous inhalation exposure to the general public (including sensitive subgroups) that is likely to be without an appreciable risk of adverse health effects during a lifetime.

TABLE 1. SCENARIO 5: MAXIMUM ANNUAL AVERAGE AIR CONCENTRATIONS IN THE VICINITY OF AN AVERAGE SIZED HIGH ADHESIVE APPLICATION FACILITY USING N-PROPYL BROMIDE (S5)

Distance	Non-Vented Vertical Release Scenario	Vented Vertical Release Scenario	Non-Vented Horizontal Release Scenario	Reference Concentration Level
(m)	(ppm)	(ppm)	(ppm)	(ppm)
100	0.06	0.01	0.08	1
200	0.04	0.01	0.04	1
300	0.03	0.01	0.03	1
400	0.01	0.01	0.01	1
500	0.01	0.01	0.01	1
600	0.01	0.01	0.00	1
700	0.00	0.00	0.00	1
800	0.00	0.00	0.00	1
900	0.00	0.00	0.00	1

TABLE 2. SCENARIO 6: MAXIMUM ANNUAL AVERAGE AIR CONCENTRATIONS IN THE VICINITY OF AN AVERAGE ADHESIVE USING OPERATION LOCATED IN AN URBAN ROW-HOUSE-TYPE WAREHOUSE USING N-PROPYL BROMIDE

Distance	Vented Vertical Release Scenario*	Non-Vented Vertical Release Scenario	Non-Vented Horizontal Release (natural vent) Scenario	Non-Vented Horizontal Release (w/fans) Scenario	Reference Concentration Level
(m)	(ppm)	(ppm)	(ppm)	(ppm)	(ppm)
3	0.00	0.00	0.06	0.24	1
5	0.00	0.00	0.06	0.19	1
10	0.00	0.00	0.04	0.13	1
20	0.00	0.01	0.03	0.08	1
30	0.03	0.01	0.01	0.05	1
40	0.03	0.01	0.01	0.04	1
50	0.03	0.01	0.01	0.04	1
60	0.01	0.01	0.01	0.03	1
70	0.01	0.01	0.01	0.03	1
80	0.01	0.01	0.00	0.01	1
90	0.01	0.01	0.00	0.01	1
100	0.01	0.01	0.00	0.01	1

* Maximum cavity region annual average concentration of 0.02 ppm assuming half of all hours when facility is operating are conducive to downwash conditions

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LABORATORY REPORT
(Air Sampling)

Batch No: 2010090365

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PO No:

Date Received: September 13, 2010
Date Reported: September 20, 2010

Date(s) Analyzed: 09/20/10

xposure results are the average concentration for the period of time monitored. ND = None Detected. The results relate only to the items tested. Unless noted below, samples were received in acceptable condition, all applicable uality control were within method specifications, lab blanks were subtracted before a result was reported, and any customer supplied field blanks were not subtracted from sample results. The molar volume at 22 C (24.1 L/mole) as used to calculate parts per million, ppm. Air concentrations reported are based upon field sampling information provided by the customer. For assistance with the content of this report, please visit the Customer Services ection of our web site at http://www.assaytech.com or contact Technical Support at 1-800-833-1258.

ab Sample ID / Lab Code	Date Sampled	Media Code - Client Sample ID	Media Lot / Serial #	Chemical Analyzed (Method, Chemist)	Quantity Found (µg)	Reporting Limit (µg)	Sample Volume (L)	Sample Time (min)	Concentration/Exposure (mg/M3)	Concentration/Exposure (ppm)	Reporting Limit (mg/M^3)	Reporting Limit (ppm)
2010033281 - ATOH	9/9/10	J566A - PRESS STATION 10FT	11D09 - HA2331	N-PROPYL BROMIDE (1,101)	4.8	2	2.03	300	2.4	0.47	1	0.2
2010033282 - ATOH	9/9/10	J566A - 2 FEET FROM DOOR	11D09 - HA2426	N-PROPYL BROMIDE (1,101)	14	2	2.03	300	6.7	1.3	1	0.2

Messages

Lab Sample ID	Message	Method	Method Name	Chemist Analyzed By	Approved By
		1 MOD OSHA 7		101 K. TAYLOR	W. EWING

Fabrisolv®

Dry Cleaning Solvent

Dry Cleaning Plant
Operator Manual

Poly Systems

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Dry Cleaning
Operation and Information Manual

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1. Introduction

Fabrisolv® is an environmentally friendly dry-cleaning solvent. It is an alternative to perchloroethylene (perc) used in many Dry Cleaning Machines.

Fabrisolv® can be used in all dry-dry type perc machines. It is compatible with typical seals, pumps, valves, and gaskets used on such machines. The most significant difference between perc and Fabrisolv® is that Fabrisolv® has a much lower boiling point and than Perc. Therefore a dry-cleaning machine which utilizes Fabrisolv® consumes less energy and operates at lower temperatures.

The benefits of Fabrisolv® are no flash point, superior cleaning abilities, a shorter dry time and a lower boiling point than Perc.

The wash cycle of Fabrisolv® is typical of Perc except that each element of the cycle takes less time. Fabrisolv® also does not require filtering, eliminating the purchase and disposal costs of filters.

Fabrisolv® is continually distilled during the operation of the dry cleaning machine. This distillation ensures fresh and clean solvent for each and every wash cycle. The low boiling point of Fabrisolv® allows for fast distillations and guarantees clean solvent for subsequent cleaning cycles.

Fabrisolv® contains various corrosion inhibitors to prevent rust formation in your machine. These inhibitors have been specially formulated to assure that they are not affected by the action of the still or water separator. They will always be present in your solvent providing machine protection.

To handle Fabrisolv® in a safe and responsible manner please read the Technical Data Sheet (TDS) and Safety Data Sheet (SDS).

2. Fabrisolv® – Overview

This manual is designed to give the operator general information regarding the use of Fabrisolv cleaning solvents. It is not designed to replace your machines operating instructions. This information is only supplemental to your operating manual.

Below you will find abbreviated information regarding the use of Fabrisolv®. It will give the user and those who do not like to read directions all the information needed to operate a dry cleaning machine with Fabrisolv cleaning products. More information on these sections can be found in the Discussion Section following this Overview Section.

2.1. Solvent requirement

4 gallon Fabrisolv® for 10 lb clothing.
Actual range is between 10 to 30 gallons for 50 Lb load.

2.2. Detergents

Fabrisolv® can handle both cationic and anionic detergents. The only limitation is that the detergent can not contain perchloroethylene as an ingredient. Low quality detergents may contain perc and this will build up in Fabrisolv. It is also preferred that the detergent be added to the wash cycle by an injection method.

The charged method of adding detergent to the tank can not be used with Fabrisolv.

(Detergents containing primary and secondary amines can not be used with Fabrisolv®.)

2.3. Cleaning Cycle

A typical Fabrisolv® cleaning process comprises of four cycles as follows:

4 minute wash cycle
2 minute extraction cycle
12 minute drying cycle
8 minute cool down cycle

2.4. Steam Pressure

Fabrisolv boils at a lower temperature than perc (almost 100°F less). Fabrisolv has a boiling point of 158°F (70°C) and perc has a boiling point of 250°F (121°C). This lower boiling point requires a lower operating pressure for steam than the perc. If the steam pressure is not reduced excessive solvent losses will occur.

The recommended steam pressure for distillation of Fabrisolv® is 5 – 10psi. The steam pressure affects the rate of the distillation, the higher the steam-pressure, the faster the distillation. The final steam pressure value is dependant on the cooling capacity of condensation column on the machine. Higher steam pressures can be used as long as the distillation column can condense the distillation vapors.

Optimization of the steam pressure is described below

2.5. Distillation

Distillation is the area where the use of perc and Fabrisolv differ the most. The difference is that the still is always on with the use of Fabrisolv.

Fabrisolv® is continually distilled during the cleaning process. Extracted Fabrisolv from a cleaning cycle is sent to the still for distillation and not thru filters or reused for other loads. It is always distilled to provide clean solvent for subsequent loads.

The low boiling point and continuous distillation of Fabrisolv has the following advantages:

- Short distillation times
- Efficient use of detergents (it is not removed by the carbon filters)
- Eliminates the expense purchasing and disposing of filters
- Provides clean solvent for each wash cycle

An optional second type of distillation can be performed prior to the clean out of the still called a steam sweep. The steam sweep reduces solvent losses from the still bottoms. Still bottoms can contain over 25% Fabrisolv if steam-sweep is not performed. If a steam-sweep is carried out, this level can be reduced to less than 5% solvent. The steam sweep is described below.

2.6. Still Cleanout

A clean still requires lower steam-pressure and uses less steam for distillation. The more sludge that accumulates in the still the higher the energy consumption for distillation and higher temperatures are required to keep an acceptable distillation rate. Therefore it is recommended that the still be cleaned on a regular basis (once or twice per week).

Clean out and disposal of the still bottoms are the same as those of perc. However, prior to disposal of the still bottoms steam sweeping them will allow the user to recover solvent from the still bottoms. The steam sweep processes reduces solvent losses to the still bottoms from over 25% to less than 5%. The steam sweep is described below.

2.7. Water Separator

The water separator separates water from Fabrisolv® during the distillation process. The water separator will work in the same manner with Fabrisolv as with perc. In order for the separator to work effectively, there must always be a water layer of about 1" or more on top of the Fabrisolv®.

The water overflow valve should always be open. This is especially important during the heat up of the still. Failure to follow either of these will result in excessive solvent losses, premature seal failures, and excessive pressure buildup. (See the water separator section below for more details.)

2.8. *Tanks*

Since clean solvent is used for all loads most machines operating with Fabrisolv use only one or two tanks. There is no distinction between solvent for 'whites' or 'colors', the solvent is always clean and fresh.

It is recommended that the solvent from the still go to a separate tank and after the distillation process is complete transferred to the main working tank. This ensures that if problem with the distillation process occurs all of the solvent is not contaminated.

2.9. *Filters*

Fabrisolv® does not require any filtering. The solvent is continually distilled during the use of the dry cleaning machine. This keeps the detergents in the solvent where they can clean cloths and eliminates their removal by the carbon filters.

However, Fabrisolv® is compatible with all common filters used in the dry cleaning industry and it can be filtered as any other dry cleaning solvent. Both carbon and carbon core filters are acceptable. Use of filters will add additional expense and eliminate many advantages of not using filters.

3. Operating Routines

This manual is designed to give the operator general information regarding the use of Fabrisolv cleaning solvents. It is not designed to replace your machines operating instructions. This information is only supplemental to your operating manual.

When following tasks are properly carried out your machine will operate without any difficulties. Failure to follow these operating procedures will result in excessive solvent usage and increased solvent emissions.

4. Fabrisolv® Cleaning Cycle – Discussion

4.1. *Solvent Usage*

The optimum solvent to garment weight ratio that should be used, is 4 Gallon Fabrisolv® per 10 lb cloths. More or less Fabrisolv® solvent can be used depending on the type of the garment being washed and the amount and type of soils on the garment.

Using less Fabrisolv® creates more mechanical action (rubbing) that result in better elimination of spots and stains but it may result in more lint and more chafing. Using larger quantity of Fabrisolv® will result in superior cleaning, better "hand" and the less stress on the garment. Too much solvent will cause the garments to float on the solvent and eliminate much of the tumbling action; rubbing and scrubbing. A load of 50 Lb should use not less than 10 gallon and not more than 30 gallons.

4.2. Detergents

Fabrisolv® can handle both cationic and anionic detergents. The only limitation is that the detergent can not contain perchloroethylene as an ingredient. Low quality detergents may contain perc and this will build up in Fabrisolv.

Some detergents may contain amines as additives for pH control. These detergents are incompatible with Fabrisolv can not be used.

Addition of Detergents

Fabrisolv cleaning solvents require that detergent be injected or added to each load. Cationic or anionic detergents work equally well. The same amount of detergent can be used as the detergent manufacture suggests for perc. Since Fabrisolv does not use carbon filters less detergent can be used with the same cleaning performance.

The "charge" method of adding detergent to the holding tank can not be used with Fabrisolv. This method is ineffective since the solvent is distilled after each wash cycle. This distillation process removes all of the detergent from the solvent and the detergent remains in the still bottoms and is not available for subsequent wash cycles.

4.3. Cleaning Cycle

A typical Fabrisolv® cleaning cycle is as follows:

4 minute immersion-wash cycle
2 minute extraction cycle
12 minute drying cycle
8 minute cool-down cycle

This is a typical cleaning cycle for use with Fabrisolv. The operator can change the cycle as needed in accord with the operating manual supplied by the equipment manufacturer. Our testing has shown this to cycle to clean the garments with a minimum of time, energy, and solvent losses.

Fabrisolv® requires less time during the cleaning cycle than Perc. This is due to its superior cleaning characteristics to perc. Fabrisolv® has greater solvency for oils, greases, and soils than Perc allowing for shorter cleaning times.

However, this increased solvency can also affect elastics, poor quality buttons, and other plastic or rubber components on clothing. Therefore it is important to check the compatibility of certain suspected accessories (buttons, beads) before starting a cleaning cycle with Fabrisolv®.

4.4. Steam Pressure

The recommended steam pressure for distillation of Fabrisolv® is 5 – 10psi. The steam pressure affects the rate of the distillation, the higher the steam-pressure, the faster the

distillation. The final steam pressure value is dependant on the cooling capacity of condensation column on the machine. Higher steam pressures can be used as long as the distillation condenser can condense the distillation vapors.

Lower steam pressures are required because Fabrisolv's boils 92° lower than perc. Fabrisolv® has a boiling point of 158°F (70°C) and perc has a boiling point of 250°F (121°C). This difference in boiling points saves significant amount of energy. If the steam pressure is not reduced the excessive heat will cause losses of solvent.

A distillation rate which is to fast will allow uncondensed solvent vapor to pass thru the condenser and into the shop. This will then increase the solvent odor in your shop and needlessly expose your employees to solvent vapors. A distillation rate which is too fast will thus increase your solvent losses.

Non-condensed solvent vapors can also interfere with the operation of the water separator. They will cause solvent to exit the water separator with the water if a distillation rate is too fast. This will increase your solvent usage and expense.

Foam-over of the still can also result from excessive distillation rates. Excess heat can cause your still to foam. If the heat is not reduced when this occurs the foam can actually enter into the condenser and fall into your solvent tank contaminating the solvent. This dirty solvent would then affect your next wash load.

A good rule of thumb for steam pressure optimization is for the distillation of the solvent to take the same time as a wash cycle.

4.5. Distillation

The lower boiling point of Fabrisolv allows for continuous, steady and efficient distillation.

Before attempting to distill Fabrisolv make sure that the machine Steam-pressure has been reduced to 5-10psi.

Fabrisolv® is continually distilled during the cleaning process. Extracted Fabrisolv from a cleaning cycle is sent to the still for distillation and not thru filters or reused for other loads. It is always distilled to provide clean solvent for subsequent loads.

The low boiling point and continuous distillation of Fabrisolv has the following advantages:

- Short distillation times
- Efficient use of detergents (it is not removed by the carbon filters)
- Eliminates the expense associated with purchasing and disposing of filters
- Provides clean solvent for each wash cycle

The fact that the solvent is distilled continuously requires that the water separator valve remain open at all times. If this valve is closed excessive pressures will build up in the machine causing seal failures and excessive solvent losses. (See the water separator section below for more details).

4.6. Water Separator

The water separator separates water from Fabrisolv®. The source of this water is from the detergent, clothing, and humidity in the air. As with perc if this water enters into a wash cycle with solvent it will cause re-deposition on wet garment and poor cleaning. Therefore it is essential that the water separator work properly.

In order for the separator to work effectively, there must always be a water layer on top of the Fabrisolv®. ***One inch*** or more of water on top of the solvent is acceptable. On machine start up it is important that water is added to the water separator to assure that there is water in the separator to prevent solvent losses.

For the system to work properly the water overflow valve be open at all times (especially during the heat up of the still). Failure to follow either instruction will result in excessive vapor losses.

Heating a cold still will cause the air to expand. If the water separator valve is closed the pressure in the machine will increase. If this valve is closed during system heat-up, when it opens this excess pressure will vent thru this valve at a high rate and carrying with it excessive amount of solvent. This will then increase your solvent usage. It can also result in premature seal and gasket failures.

Common sense may tell a person that if this valve is closed they will loose less vapors, especially during the wash cycle, cool down cycle, and or dry cycle. This common sense approach is ***WRONG***. Closing this valve during any time of the cleaning cycle increases solvent losses.

Closing this valve can also result in unwanted pressure built-up in the machine. This fact is true for all solvent operated machines.

Tests have shown that the amount of solvent lost thru this valve during a cycle vary between 1/2 to 1 oz. (This test was conducted on a 20 year old Hamilton Dry Cleaning Machine). Operating this machine with the valve closed, always increased the solvent losses, sometimes significantly.

4.7. Still Cleanout

A clean still requires less steam-pressure for distillation. The reason for this is that the oils, dirt, and residue in the still bottoms have a higher heat capacity and boiling point than the Fabrisolv®. Therefore this sludge will cause losses of energy. The higher the oil, dirt and residue concentrations, in the sludge, the higher the energy consumption.

The Fabrisolv still bottoms must be disposed of in a similar fashion to those of perc. It is recommended that the still be cleaned every 1 or 2 weeks depending on usage. Under normal conditions these still bottoms will contain over 25% Fabrisolv. This is a major source of solvent losses for a machine using Fabrisolv. Steam sweeping the solvent can recover these solvents.

4.8. Steam Sweeping

Steam sweeping is a process that will allow you to remove solvent from your still bottoms. Remember, your still bottoms can contain more than 25% Fabrisolv®.

When the steam sweeping procedure is carried out can be determined by the operator. Some do a steam strip every time they clean the still while others collect still bottoms over several months and then re-add them to the still for one big steam strip. This choice is left to the operator.

HOWEVER – Once the steam strip is to be carried out the procedure must be followed exactly. Short cuts may result in solvent that has a bad odor, color, or high amounts of water.

Note - Steam Sweeping is similar to a chemical process called Steam Distillation and Steam Stripping. More information on this can be found on the internet.

To carry out the steam stripping operation a live steam line must be attached to the still. This steam line will introduce live steam into the still and remove Fabrisolv. This live steam will carry with it small amounts of oils and greases from the still bottoms. These oils and greases must be removed by a conventional distillation or they will foul future wash loads.

4.9. Steam Sweep Procedure

The steam sweep procedure is described below. It is important to follow all of the steps to ensure that no problems arise. This includes the steam strip procedure as well as the water separator cleanout.

A. Have a steam line installed to deliver live steam to the still. This can be a manual or electronically controlled valve. A 3/8" line with 5-10psi steam is more than adequate.

B. Completely empty a tank to collect the steam stripped solvent from the still.

C. Turn on the heat to the still. The still must be hot before starting the steam sweep procedure. It is best to perform the steam sweep immediately after a distillation cycle. This ensures a hot still, which speeds up the distillation process.

D. When the still is hot, open the live steam line to the still and start the steam sweep operation. You will see solvent and water dripping in the water separator. The solvent can be seen falling thru the water layer. *(If the still is not hot at the start of this operation excessive water will condense in the still and reduce the solvent recovery)*

E. When only water drips into the water separator and no solvent is seen falling thru the water the steam sweep is complete. Turn off the steam to the still and turn off the live steam line and clean the still completely.

F. After completing the still clean out transfer all of the recovered solvent from the steam strip back into the still for re-distillation. This re-distillation will remove the oils that came over in the steam strip. Failure to do so may result in solvent with a bad odor.

G. Rinse the tank with some fresh solvent to assure that all of the steam stripped material is removed.

H. Drain and clean the water separator by draining the solvent from the water separator to the still. This solvent will also contain small amounts of oil from the steam sweep and must be re-distilled.

I. Drain the water from the water separator to a bucket and discard. This water will also contain small amounts of oils from the steam sweep and begin to stink if it is not removed.

J. Add fresh water to the water separator to a level of about 2-3 inches.

K. Redistill the steam swept solvent and the rinse solvent. This can be done immediately or the next time the unit is operated. The solvent that distills over will be clean of all oils and ready for re-use.

The steam sweep is very effective in removing solvent from the still bottoms. However this process will also remove small amounts of oils from the still bottoms (body oils, fatty acids, ink etc.). The oils that come over during the steam strip can not be prevented since it is inherent in the steam stripping process. Therefore, the steam stripped solvent must be redistilled. If it is not redistilled this solvent will have a bad odor that can affect future loads.

The water separator must also be drained because this will contain distilled solvent that also contains these oils. If it is not drained this may contaminate future loads.

The rinsing of the tank with fresh solvent ensures that all these oils are removed from the still receiving tank. Redistilling the solvent under normal conditions (not using live steam) will distill clean solvent and keep the small amount of oils in the still bottoms.

4.10. Filters

Fabrisolv® does not require any filtering. The solvent is continually distilled during the use of the dry cleaning machine. Fabrisolv® and good quality detergents will keep the soils in suspension and will prevent re-deposition.

The elimination of filters increases the effectiveness of detergents and shortens the wash cycle. Typical carbon or carbon core filters will remove the detergent faster than it takes for the detergent to interact with the clothing during wash cycles and in order for the detergent action to be effective a much longer cycle would be required.

However Fabrisolv® is compatible with all common filters used in the dry cleaning industry and it can be filtered as any other dry cleaning solvent. Both carbon and carbon core filters are acceptable.

5. Machine - Retrofit.

To change Perc machine to use Fabrisolv®

5.1. Parts Needed

- Low pressure steam regulator
- Viton, chloroprene seals

5.2. Procedure

- Remove Perc from all the tanks and still and the machine Clean machine
- Empty and clean the water separator
- Reduce steam pressure – change regulator if needed
- Perform system maintenance – replace needed gaskets and seals
  What works for perc will work for Fabrisolv
  Viton and Chloroprene seals are best
- Add Fabrisolv Solvent
- Add 2" of water to the water separator
- If Desired add valve and steam line for Steam Sweeping
  1/4" - 3/8" insulated line with valve

5.3. Set-Up

- Steam pressure to the still should be set between 5 and 10 psi.
- Cooling tower thermostat should be set to start water flow at 115°F
- Water overflow valve, in the water separator, should be in 'Open' position at all times.

6. Conclusion

Perc has been successfully used in the dry cleaning industry for many decades. As you are aware many options are currently available to dry cleaning as replacements to perc. However many of these are very costly and more complicated to operate than the traditional per machine. Fabrisolv is a relatively drop in replacement. The only major modification is the reduction in steam pressure to the machine. All your years of experience with perc will probably be applicable with the use of Fabrisolv. Therefore there is no need for extensive retraining of the operators.

We hope that your conversion to Fabrisolv is smooth and trouble free. If you have any questions regarding the use of our products feel free to call for technical support.

The above information is furnished in good faith and believed to be accurate and reliable. Neither representations nor warranties are made, expressed or implied. User should make their own tests and determine suitability of the product to their needs. Nothing in here shall be construed as permission for a use which might infringe upon a patent.

APPENDIX I –
AIR MANAGEMENT REGULATION XIV – CONTROL OF EMISSIONS FROM DRY CLEANING FACILITIES
(AS APPROVED BY THE AIR POLLUTION CONTROL BOARD ON 11/17/10)

AIR MANAGEMENT REGULATION XIV
CONTROL OF EMISSIONS FROM DRY CLEANING FACILITIES

I. **DEFINITIONS**
II. **PROHIBITIONS**
III. **WORK PRACTICE STANDARDS**
IV. **LEAK DETECTION AND REPAIR**
V. **MONITORING**
VI. **RECORDKEEPING**
VII. **REPORTING**
VIII. **PROPERTY OWNERS AND OPERATORS RESPONSIBILITIES**
IX. **EFFECTIVE DATE**

I. DEFINITIONS:

(a) For the purpose of this regulation, the definitions of the Philadelphia Air Management Code and all regulations promulgated thereunder apply.

(b) For the purpose of this regulation, the following definitions also apply:

(1) *Alternative Cleaning Technology*. A textile cleaning technology which may include, but is not limited to: water-based wet cleaning, carbon dioxide (CO_2) cleaning, decamethylcyclopentasiloxane or volatile methyl siloxane, or petroleum hydrocarbon solvents.

(2) *Ancillary Equipment*. The equipment used with a dry cleaning machine in a dry cleaning system including, but not limited to, emission control devices, pumps, filters, muck cookers, stills, solvent tanks, solvent containers, water separators, exhaust dampers, diverter valves, interconnecting piping, hoses and ducts.

(3) *Articles*. Clothing, garments, textiles, fabrics, leather goods, and other items that are dry cleaned.

(4) *Carbon Adsorber*. An air cleaning device that consists of an inlet for exhaust gases from a dry cleaning machine; activated carbon in the form of a fixed bed, cartridge, or canister, as an adsorbent; an outlet for exhaust gases; and a system to regenerate or reclaim saturated adsorbent.

(5) *Cartridge Filter*. A replaceable cartridge filter that contains one of the following as the filter medium: paper, activated carbon, or paper and activated carbon. Cartridge filters include, but are not limited to: standard filters, split filters, "jumbo" filters, adsorptive filters, and all carbon polishing filters. Adsorptive Cartridge Filters contain diatomaceous earth or activated clay.

(6) *Closed-loop Machine*. Dry cleaning equipment in which washing, extraction, and drying are all performed in the same single unit (also known as a dry-to-dry unit) and which recirculates Perc-laden vapor through a primary control system (e.g. refrigerated condenser) with no exhaust to the atmosphere during the drying cycle. A closed-loop machine may allow for venting to the

ambient air through a local exhaust ventilation system, such as a door fan, after the drying cycle is complete and only while the machine door is open.

(7) *Co-commercial.* A facility sharing a common wall, floor or ceiling with another commercial or industrial business/site.

(8) *Co-located.* A facility sharing a common wall, floor or ceiling with a residence/residential site, sensitive facility, commercial business/site, or industrial business/site.

(9) *Co-residential*. A facility sharing a common wall, floor, or ceiling with a residence/residential site.

(10) *Co-sensitive.* A facility sharing a common wall, floor, or ceiling with a sensitive facility.

(11) *Colorimetric Detector Tube*. A glass tube (sealed prior to use), containing material impregnated with a chemical that is sensitive to Perc and is designed to measure the concentration of Perc in air.

(12) *Condenser*. An air cleaning device that removes condensable vapors by a reduction in the temperature of the exhaust gases or, in the case of a surface condenser, by contact of the exhaust gases with structures that are cooled by a circulating cooling fluid.

(13) *Cool-down*. The portion of the drying cycle that begins when the heating mechanism deactivates and the refrigerated condenser continues to reduce the temperature of the air recirculating through the drum to reduce the concentration of Perc in the drum.

(14) *Department*. The City of Philadelphia Department of Public Health.

(15) *Desorption.* Regeneration or stripping of an activated carbon bed, or any other type of vapor adsorber by removal of the adsorbed solvent using hot air, steam, or other means.

(16) *Diverter Valve.* A flow control device that prevents room air from passing through a refrigerated condenser when the door of a dry cleaning machine is open.

(17) *Drum.* The rotating cylinder or wheel of the dry cleaning machine that holds the articles being cleaned.

(18) *Dry Cleaning Control System.* Equipment or device (*e.g.*, Carbon Adsorber, Refrigerated Condenser, azeotropic unit) used to reduce the amount of air pollutant(s) in an air stream prior to discharge to the atmosphere.

(19) *Dry Cleaning Equipment.* Any machine, device, or apparatus used to dry clean articles.

(20) *Dry Cleaning Facility*. An establishment with one or more dry cleaning systems.

(21) *Dry Cleaning System*. All of the following equipment, devices, and apparatuses associated with the Perc dry cleaning operations: dry cleaning equipment; filter or purification systems; waste holding, treatment, or disposal systems; Perc supply systems; dip tanks; pumps; gaskets; piping, ducting, fittings, valves, or flanges; and

dry cleaning control systems.

(22) *Drying Cycle.* The operation used to actively remove the Perc remaining in the materials after washing and extraction. For closed-loop machines, the heated portion of the cycle is followed by cool-down and may be extended beyond cool-down by the activation of a control system. The drying cycle begins when heating coils are activated and ends when the machine ceases rotation of the drum.

(23) *Drying Sensor*. A device that senses when articles being cleaned are relatively dry and automatically controls the drying cycle. Drying sensors include but are not limited to: infrared analyzers, float switches, and resistance probes. The device detects the concentration of synthetic solvents in the drying air or that the liquid solvent recovery rate is at a minimal rate. The drying sensor extends the drying cycle for a minimum time beyond the activation point to ensure dry articles.

(24) *Dry-to-Dry Machine.* A one-machine dry cleaning operation in which drying and washing are performed in the same machine.

(25) *Equivalent Closed-loop Vapor Recovery System.* A device or combination of devices that achieves, in practice, a Perc recovery performance equal to or exceeding that of refrigerated condensers.

(26) *Facility*. All emission sources located at one or more adjacent or contiguous properties under common control, and owned or operated by the same person or persons.

(27) *Fifth (5th) Generation Equipment.* A dry cleaning machine with all the features of Fourth Generation Equipment, plus a monitor inside the machine drum and an interlocking system to ensure that the concentration is below approximately 300 ppm before the loading door can be opened.

(28) *Filter Muck.* The residue from a filter using loose diatomaceous earth, which must be replaced periodically.

(29) *Fourth (4th) Generation Equipment.* A primary closed-loop refrigerated dry cleaning machine that has a "secondary control system" (e.g., closed-loop refrigerated condenser with a drying sensor and an integral carbon adsorber).

(30) *Fugitive Emissions*. Emissions of air contaminants which could not reasonably pass through a stack, vent, chimney, or other functionally equivalent opening.

(31) *General Exhaust Ventilation System.* A mechanical exhaust ventilation system consisting of fresh air makeup inlets and one or more exhaust fans in a Dry Cleaning Facility. This type of system would commonly be used to exhaust a dry cleaning workroom or a room enclosure.

(32) *Halogenated-hydrocarbon Detector*. A portable device capable of detecting and reporting vapor concentrations of Perc.

(33) *Hazard*. An event which may result in any Perc release, Perc spill, fire or explosion.

(34) *Liquid Leak.* A Perc emission which is in a liquid state at the point(s) of discharge into the atmosphere.

(35) *Major Source*. A Dry Cleaning Facility that emits or has the potential to emit more than 9.1 megagrams per year (10 tons per year) of Perc to the atmosphere. In lieu of measuring a facility's potential to emit Perc or determining a Facility's potential to emit Perc, a Dry Cleaning Facility is a major source if it includes only Dry-to-Dry Machine(s) and has a total yearly Perc consumption greater than 8,000 liters (2,100 gallons).

(36) *Muck Cooker*. A device for heating filter muck to drive off Perc vapors for reclaiming.

(37) *Openings*. Any window, door or air intake point.

(38) *Leak*. Any Perc vapor or liquid leaks that are obvious from the odor of Perc, pools or droplets of Perc or by passing a finger over the surface of the equipment; or as detected by an appropriate portable monitoring instrument.

(39) *Perc*. A colorless volatile chlorinated hydrocarbon. Perc is also known as perchloroethylene, tetrachloroethylene, tetrachloroethene, and PCE. The chemical formula for Perc is $Cl_2C{:}CCl_2$. The CAS registry number for Perc is 00127-18-4.

(40) *ppb*. Parts per billion by volume in air or by weight in water.

(41) *ppm*. Parts per million by volume in air or by weight in water.

(42) *Portable Gas Analyzer*. A portable device capable of detecting Perc vapor concentrations of 25 ppm by volume.

(43) *Primary Control System.* A Refrigerated Condenser or equivalent *closed-loop vapor reco*very system approved by the Department.

(44) *Process Ventilation Emission.* The emission from any dry cleaning machine that occurs when the machine door is open.

(45) *n-Propyl Bromide (n-PB),* Also called 1-bromopropane, C3H7Br, it is a colorless nonflammable organic solvent used for the cleaning of metal surfaces, removal of soldering residues from electronic circuit boards, and as an adhesive solvent. Its Chemical Abstracts Service Registry Number (CASRN) is 106-94-5.

(46) *Refrigerated Condenser*. A closed-loop vapor recovery system into which Perc vapors are condensed by cooling below the dew point of the Perc using a mechanical refrigerated system.

(47) *Residence*. Any dwelling or housing which is occupied or intended to be occupied by the same person for a period of 180 days or more.

(48) *Secondary Control System*. A device or apparatus that reduces the concentration of Perc in the recirculating air at the end of the drying cycle beyond the level achievable with a Refrigerated Condenser alone. For example, an integral Carbon Adsorber used in fourth generation equipment constitutes a secondary control system. An *"integral"* secondary control system is designed and offered as an integral part of a production package with a single make and model of Dry Cleaning Machine and Primary Control System.

(49) *Self-service Dry Cleaning Machine.* A Perc dry cleaning machine that is loaded, activated, or unloaded by the customer.

(50) *Sensitive Facility*. Any educational facility for minors including, but not limited to, schools for kindergarten through twelfth (K-12) grade or preschools or other early childhood education facilities; and health and community care facilities including, but not limited to, hospitals, long-term or child care centers, and family day care homes.

(51) *Stand-alone Facility*. A facility that is not co-located.

(52) *Still*. Distillation equipment used to volatilize and recover Perc from contaminated solvent removed from the cleaned articles.

(53) *Trained Operator.* A person who can effectively administer the requirements of the 'Work Practice Standards' and 'Leak Detection and Repair' sections of this regulation, and is conversant with the applicable devices and methods listed under Section IV (a)(1) of this regulation.

(54) *Transfer Machine*. Perc Dry Cleaning Equipment in which washing and extraction are performed in one unit and drying is performed in a separate unit. (First generation equipment)

(55) *Vapor Adsorber.* A bed of activated carbon or other adsorbent into which vapors are introduced and trapped for subsequent desorption.

(56) *Vapor Barrier.* A material surface or coating that is impermeable to Perc.

(57) *Vapor Leak.* A fugitive emission of Perc vapor from unintended openings in the dry cleaning system. A vapor leak can be indicated by a rapid audible signal or visual signal from a halogenated-hydrocarbon detector or other approved instrument.

(58) *Water Separator.* A vessel that uses gravity to physically separate liquid Perc from liquid water.

II. PROHIBITIONS:

(a) As of the effective date of this regulation, no person shall:

(1) Build, erect, install, alter or replace Perc Dry Cleaning Equipment or Perc Ancillary Equipment without first obtaining an Air Management permit for such installation and construction.

(2) Operate or use any Perc Dry Cleaning Equipment or Perc Ancillary Equipment without a current operating license as specified by the Air Management Code and regulations promulgated thereunder.

(3) Use any Perc Dry Cleaning Equipment as a Transfer Machine.

(4) Use Perc in any Co-residential or Co-sensitive Facility established, created, or constructed after the effective date.

(5) Use Perc in conjunction with any Dry Cleaning Equipment installed after the

effective date at any Co-residential or Co-sensitive Facility.

(6) Install, use or offer for use any Self-Service Perc Dry Cleaning Machine(s).

(7) Evaporate Perc from the untreated water effluent of solvent water separators into the atmosphere without use of air control devices approved by the Department.

(8) Vent Perc emissions from Dry Cleaning Equipment or Dry Cleaning Control Systems into the Dry Cleaning Facility, or any Co-residential, Co-sensitive or Co-commercial site.

(9) Use n-PB as a dry cleaning solvent in any Co-residential or Co-sensitive Facility. Subject to the conditions set forth in Section IX, n-PB may be used at Stand-alone or Co-commercial facilities.

(b) After December 31, 2013:

(1) No person shall operate, use, or allow the operation or use of, Perc or Perc Dry Cleaning Equipment at any Co-located Facility.

(2) On or before July 1, 2013, Co-commercial Dry Cleaning Facilities may petition the Department to continue using Perc beyond the December 31, 2013 phase out date. Pursuant to Section V (a), the petitioners must demonstrate that the airborne concentration of Perc in adjoining commercial or industrial sites is at or below 40 ppb.

(c) Any installation of new, or relocation of used, Perc Dry Cleaning Equipment shall comply with the deadlines in 40 CFR 63 Subpart M.

III. WORK PRACTICE STANDARDS:

(a) Equipment Standards:

(1) *Stand-alone Perc Facilities*. Within two years of the effective date of this regulation, all Stand-alone Perc Dry Cleaning Facilities shall use:

(i) Fourth (4th) Generation Equipment or better if the Perc Dry Cleaning Facility is a non-Major Source.

(ii) Fifth (5th) Generation Equipment or its equivalent approved by the Department if the Perc Dry Cleaning Facility is a Major Source.

(iii) All such Equipment required by Sections III (a)(1)(i)-(ii) shall be installed with, or if already in use shall be upgraded with, the following:

(A) A spill containment system capable of containing 125 percent of the capacity of the largest dry cleaning Perc tank or vessel associated with the Dry Cleaning System; and

(B) A Drying Sensor.

(2) *Co-located Perc Facilities*. Within one year of the effective date of this regulation, *in addition* to the equipment listed in Section III (a)(1)(iii) hereof, all Co-located Perc Dry Cleaning Facilities shall:

(i) Modify Process Emissions Ventilation Points or install appropriate control devices, as approved by AMS, so that the airborne concentration of Perc at any air intake, window, doorway, or similar penetration of neighboring residential, commercial, or sensitive facilities be less than or equal to 40 ppb.

(ii) Either (A) seal off the rooms containing Perc Dry Cleaning Equipment from the rest of the Facility with Vapor Barriers and installation of a separate General Exhaust Ventilation System for these rooms, or (B) install a professionally designed exhaust ventilation system that produces one air change every five minutes and maintains negative air pressure for the entire Facility.

(3) *All Perc Dry Cleaning Facilities*. Within 30 days of the effective date of this regulation, all Perc Dry Cleaning Facilities must be equipped with:

(i) Adequate spill control equipment including sorbent materials, or an alternative method for absorbing spills; and

(ii) Vapor-proof containers for storing spill-contaminated material and labeled 'FOR SPILL CONTAINMENT USE ONLY'.

(b) Operation and Maintenance Requirements:

(1) Each owner or operator of a Perc Dry Cleaning Facility shall comply with the following operation and maintenance requirements, as applicable:

(i) Operate Refrigerated Condensers so as to ensure that exhaust gases are recirculated until the air-vapor stream temperature is 45° F or less at the outlet. The temperature must be determined at least weekly with a thermometer with a temperature range of from 32° F (0° C) to 120° F (48.9° C) to an accuracy of 2° F (1.1° C).

(A) If equipped with pressure gauges, the refrigeration system's high and low pressure during the drying phase must be kept within the range specified by the manufacturer. Refrigerated system pressure readings must be made on a weekly basis.

(ii) Operate Vapor Adsorbers used with a Primary Control System or Secondary Control System so as to ensure that exhaust gases are recirculated at the temperature specified for optimum adsorption.

(iii) Operate Carbon Adsorbers, lint filters, and exhaust fans in accordance with manufacturer's specifications.

(iv) Drain Cartridge Filters in the filter housing, before disposal, for no less than 24 hours for Cartridge Filters and 48 hours for Adsorptive Cartridge Filters. The General Exhaust Ventilation System must be operated during this activity.

(v) Keep all steam and condensing coils free of lint and hard lint build-up on interior surfaces.

(vi) Replace door gaskets in accordance with manufacturer's specifications.

(2) *Preparedness and prevention.*

(i) Each owner or operator of a Perc Dry Cleaning Facility must:

(A) Maintain aisle space to allow proper inspection of the Dry Cleaning Equipment.

(B) Keep a reasonable supply of spare parts for repairing Dry Cleaning Equipment available at the Dry Cleaning Facility.

(C) Keep parts of the Dry Cleaning System including solvent containers where Perc may be emitted to the atmosphere closed at all times except when access is required for proper operation and maintenance.

(3) *Perc-contaminated wastewater discharges.*

(i) Each owner or operator of a Perc Dry Cleaning Facility must operate and maintain all Dry Cleaning Systems so as to ensure that Perc releases are contained and do not migrate to sewer systems or groundwater.

(ii) Each owner or operator of a Perc Dry Cleaning Facility must treat Perc-contaminated wastewater that is discharged to the public sewer system by physical separation (Water Separator) and double carbon filtration, or by an equivalent control technology which has been approved by the Department. Any water discharged to the sewer must meet Philadelphia Water Department Regulations.

(iii) Except as provided for by Section III (b)(3)(ii), no person may discharge into the public sewer system any Perc-contaminated wastewater or wastes resulting from Dry Cleaning Systems including, but not limited to, Still bottom or sludge residues, dirt, lint, soils, or any other deposits or residues extracted as a result of dry cleaning processes.

(iv) No person shall discharge into the public sewer system filters or other filter media used in Dry Cleaning Systems.

(4) *Perc-contaminated wastes:*

(i) Each owner or operator of a Perc Dry Cleaning Facility must store all Perc-contaminated wastes (including spent Cartridge Filters, spent carbon, Still bottoms, and lint) in tightly sealed containers, which are impermeable to the solvent, so that no Perc is emitted to the atmosphere.

(A) Containers must be appropriately labeled and stored in a designated area.

(B) Containers must be in good condition and must be kept closed except when necessary to add or remove waste.

IV. LEAK DETECTION AND REPAIR:

(a) *Leak check requirements.* As of the effective date of this regulation, a Trained Operator must inspect the Dry Cleaning System weekly for Liquid and Vapor Leaks and other Fugitive Emissions. The Trained Operator, or a designee, must record the status of each component on a Department-approved inspection checklist as required in Section VI (c) of this regulation.

(1) *Devices and methods permitted.* One of the following devices or methods must be used for detecting Vapor Leaks:

(i) a Halogenated-hydrocarbon Detector;

(ii) a Portable Gas Analyzer;

(iii) an air sampling pump and Colorimetric Detector Tube; or

(iv) an alternative method approved by the Department.

(2) *Weekly inspections.* The following components of the Dry Cleaning System must be inspected weekly:

(i) While the Dry Cleaning System is operating, the following components shall be inspected for the presence of Liquid and Vapor Leaks and for proper operation:

(A) hose and pipe connections, fittings, couplings and valves;

(B) door gaskets and seatings;

(C) filter gaskets and seatings;

(D) pumps;

(E) solvent (including spent solvent) tanks and containers;

(F) Water Separators;

(G) Muck Cookers;

(H) Stills;

(I) exhaust dampers;

(J) Diverter Valves; and

(K) Cartridge Filter housings.

(ii) Carbon Adsorber vents (for Vapor Leaks);

(iii) The temperature of the vapor stream on the outlet side of a Refrigerated Condenser; and

(A) If equipped with pressure gauges, refrigeration system high and low pressure readings; and

(iv) Preparedness and prevention equipment and conditions, as required in Section III (b)(2) of this regulation, to ensure proper operation and maintenance. A notation must be made on the checklist at the time of inspection.

(b) *Repair of detected Leaks.* Except for loading and unloading of textiles following the completion of the Drying Cycle, and any short-term maintenance operations that requires opening any part of the Dry Cleaning System for inspection or repair, a Fugitive Emission concentration of 25 ppm or more of Perc emanating from any part of the Dry Cleaning System is a violation. If a Leak or Hazard is detected, the Trained Operator must:

(1) Note on the checklist, as required in Section VI (c) of this regulation, any Liquid Leak, Vapor Leak, or malfunction that has been detected.

(2) Where a Hazard is imminent or has already occurred, shut down the Dry Cleaning System, and take immediate remedial action;

(3) Report immediately all releases, spills, fires or explosions to the Department and appropriate emergency response agencies, as required in Section VII (b) of this regulation;

(4) Repair the Leak within 24 hours unless repair parts are not available at the Perc Dry Cleaning Facility;

(5) Mark or tag any leaking component that cannot be repaired at the time the Leak is detected in a manner that is readily observable by an inspector;

(6) Order all unavailable repair parts within two working days of detecting the Leak and install such repair parts within five working days after their receipt;

(7) Shut down leaking Perc Dry Cleaning Equipment that has not been repaired 15 working days after the Leak was detected; and

(8) Record the date the repair was completed on the checklist as required by Section VI (c).

V. MONITORING

(a) One year after the effective date of the regulation, a Co-commercial Perc Dry Cleaning Facility must collect a minimum of one air sample over 24-hours per quarter from an adjoining Co-commercial business/site. The sample must be submitted to an independent laboratory for analysis. The air sample must be taken:

(1) From and within the adjoining commercial or industrial business/site where the airborne concentration of Perc is highest.

(2) On days the Perc Dry Cleaning Equipment at the Co-commercial Perc Dry Cleaning Facility is operated.

(b) The Department may collect ambient air samples at an occupied space Co-located to a Dry Cleaning Facility and analyze them for Perc. When the Department directs, the owner or operator of a Dry Cleaning Facility shall provide duplicate normal operating conditions during periods of sampling.

(c) If the Perc concentration of any collected air sample exceeds 200 ppb, the owner or operator of a Co-located Perc Dry Cleaning Facility shall cease all Perc operations immediately. Said operations shall remain ceased until the owner or operator has taken any and all corrective action to reduce and maintain the airborne concentration of Perc in the co-located, occupied space at 40 ppb or below.

(d) If the Perc concentration of any collected air sample exceeds 40 ppb but is below 200 ppb, the owner or operator of a Co-located Perc Dry Cleaning Facility shall immediately take any and all corrective action to reduce and maintain the airborne concentration of Perc in the co-located, occupied space at 40 ppb or below. Said period for corrective action shall not exceed thirty (30) days from the date of the exceedance. In the event that the owner or operator can not demonstrate that the airborne concentration of Perc within the occupied space is at or below 40 ppb within the thirty (30) days, the owner or operator shall cease all Perc operations immediately. Said operations shall remain ceased until compliance with the 40 ppb limit can be demonstrated.

(e) The owner or operator of a Perc Dry Cleaning Facility shall reimburse the Department for the cost of collecting and analyzing ambient air samples whenever the Perc concentration result exceeds 40 ppb.

VI. RECORDKEEPING:

(a) Owners or Operators of all Perc Dry Cleaning Facilities or their designees shall record the following:

(1) A written description of any emergency response action, including, at a minimum:

(i) The date, duration and nature of any malfunction, spill or incident of the Dry Cleaning System;

(ii) The quantity of any spill;

(iii) The notification procedures followed; and

(iv) The corrective actions taken.

(2) The date of maintenance performed on any air cleaning component or exhaust system;

(3) The date the Carbon Adsorbers, lint filters, and exhaust fans are replaced per manufacturer's specifications;

(4) The date any maintenance is performed on the Drying Sensors;

(5) The date and volume of any Perc-contaminated hazardous waste shipments;

(6) The date any Perc-contaminated wastewater treatment unit carbon cartridge is replaced; and,

(7) The date the door gaskets are replaced per manufacturer's specifications.

(b) Each owner or operator of a Perc Dry Cleaning Facility shall keep receipts of Perc purchases, including a log of the following:

(1) *Monthly consumption.* On the first day of the month, for the preceding month, the volume of Perc purchased that month by the Dry Cleaning Facility as recorded from Perc purchases; and

(2) *Yearly consumption.* The total sum of the volume of all Perc purchases made in each of the previous twelve months, as recorded in the log described above.

(c) Each owner or operator of a Perc Dry Cleaning Facility shall record the following information on a Department-approved inspection checklist:

(1) The dates when the Dry Cleaning System components are inspected for Leaks, as specified under Section IV (a)(2)(i) of this Regulation, and the name or location of Dry Cleaning System components where Leaks were detected;

(2) The date, time and monitoring results as specified in Section IV (a)(2) and Section V of this Regulation; and

(3) The dates of repair and records of written or verbal orders for repair parts to demonstrate compliance with the requirements in Section IV (b)(4)-(5) and Section V of this Regulation.

(d) Each owner or operator of a Perc Dry Cleaning Facility shall retain, on-site, a copy of the design specifications, manufacturer's specifications, and the operating manuals for each Dry Cleaning System and each Dry Cleaning Control System located at the Dry Cleaning Facility.

(e) All records, including air monitoring record and inspection checklist, must be maintained on-site for five years, and shall be made available to the Department upon request.

VII. REPORTING

(a) The owner or operator of a Perc Dry Cleaning Facility shall submit a permit application within six months of the effective date of this regulation. The permit application shall include all of the following information:

(1) Facility name, Facility address, owner/operator name, and telephone number;

(2) The distance from the center of the Facility to the property line of the nearest commercial/industrial building, and to the nearest Residence;

(3) A listing of all Sensitive Facilities located within 100 feet from the center of the Perc Dry Cleaning Facility;

(4) Annual operating information for the preceding year, including pounds of clothes cleaned, solvent type, gallons of solvent purchased, gallons of solvent at the Perc Dry Cleaning Facility at the beginning of the year, gallons of solvent remaining at the end of the year, gallons of Still residue waste produced, number and type of filter cartridges disposed, and copies of recent waste manifests;

(5) Equipment original date of purchase, or equipment manufacture date and equipment generation type; and

(b) The owner or operator shall report immediately all releases, spills, fires or explosions to the Department and appropriate emergency response agencies.

(c) The owner or operator shall report within three days any monitoring result that exceeds 40 ppb per Section V (a).

VIII. PROPERTY OWNER AND OPERATOR RESPONSIBILTIES

(a) The owner or operator of a property on which Perc, Perc Dry Cleaning Equipment or a Perc Dry Cleaning Facility is located shall:

(1) Ensure the operation and maintenance of said property in accordance with the Air Management Code and regulations promulgated thereunder, including but not limited to the instant regulation; and

(2) Where required by the Department, take all necessary action or cause the forbearance therefrom to effect compliance with the provisions of the Air Management Code and regulations promulgated thereunder, including but not limited to the instant regulation.

(b) The failure of an owner or operator of a property on which Perc, Perc Dry Cleaning Equipment, or a Perc Dry Cleaning Facility is located to abide by the terms of this Regulation shall subject said owner or operator to any and all actions and remedies available under the Air Management Code and regulations promulgated thereunder, including but not limited to the assessment of penalties for non-compliance.

IX. REQUIREMENTS AND SPECIFICATIONS FOR n-PB

(a) All n-PB Dry Cleaning Facilities must comply with the prohibitions, work practice standards, leak detection and repair requirements, monitoring requirements, recordkeeping requirements, reporting requirements, and property owner and operator responsibilities outlined for Perc Dry Cleaning Facilities in Sections II-VIII, with the following modifications:

(1) Per Section VII (a), Stand-alone and Co-commercial facilities must obtain an Air Management permit, prior to any installation or modification of existing Dry Cleaning Equipment using n-PB, and an operating license.

(2) Co-commercial facilities, per Section II (b)(2) and pursuant to Section V (a), must demonstrate that the airborne concentration of n-PB in adjoining commercial or industrial sites is at or below 40 ppb. Venting of n-PB into adjoining commercial

or industrial sites is prohibited.

(3) Per Section IV (b), a Fugitive Emission concentration of 10 ppm or more of n-PB emanating from any part of the Dry Cleaning System is a violation.

(4) Per Section V (c), the owner or operator of a Co-commercial n-PB Dry Cleaning Facility shall cease all n-PB operations immediately if the n-PB concentration of any air sample exceeds 225 ppb.

(5) Per Section V (d), if the n-PB concentration of any collected air sample exceeds 40 ppb but is below 225 ppb, the owner or operator of a Co-commercial n-PB Dry Cleaning Facility shall immediately take any and all corrective action to reduce and maintain the airborne concentration of n-PB in the Co-commercial, occupied space at 40 ppb or below. Said period for corrective action shall not exceed thirty (30) days from the initial date of the exceedance.

X. EFFECTIVE DATE:

This regulation shall be effective on xx.xx.xxxx.