October 9, 2019

DEVELOPMENTAL AND REPRODUCTIVE RISKS TO CONSUMERS AND WORKERS FROM ACUTE EXPOSURES TO 1-BROMOPROPANE: KEY EPA FINDINGS

On August 12, 2019, EPA released its draft risk evaluation for 1-Bromopropane (1-BP) under section 6(b) of the Toxic Substances Control Act (TCSA).[1] 1-BP is a solvent with widespread consumer and industrial uses and significant potential for exposure. There are long-standing concerns about 1-BP's harmful effects on human health. EPA's draft risk evaluation confirms these concerns, finding that 1-BP causes cancer, reproductive harm, damage to developing fetuses, and kidney, liver and neurological effects. Accordingly, it concludes that 1-BP presents an unreasonable risk of injury for most use and exposure scenarios under TSCA.

The EPA Science Advisory Committee on Chemicals (SACC) reviewed the draft evaluation on September 10-12. According to SACC members and comments by stakeholders, while EPA's draft correctly identifies 1-BP's harmful effects, it understates the risks that these effects pose to workers, consumers and vulnerable subpopulations.[2] Nonetheless, even with these limitations, the draft evaluation makes clear that acute exposure to 1-BP presents a serious and imminent risk of harm to pregnant women and developing fetuses. The Agency must act immediately to protect consumers and workers from these harmful effects while it works to finalize the evaluation. The health risks from acute exposure to 1-BP are too serious to delay action until completion of the risk evaluation and follow-up rulemaking, a process that will take several years.

To validate the need for immediate action, this paper describes EPA's assessment of 1-BP's acute developmental and reproductive toxicity and then reviews its determinations of risk for these effects under anticipated exposure levels during use of consumer products and in the workplace.

Robust Evidence of Adverse Developmental and Reproductive Effects Following Acute Exposure

The draft risk evaluation states that "[r]eproductive and developmental toxicity were identified as critical targets for 1-BP exposure based on a constellation of effects reported across studies, including a two-generation reproduction study (WIL Research, 2001), which showed adverse effects on male and female reproductive parameters, and the developing conceptus" (p. 160). According to the Agency, "adverse effects were observed in all of these systems in rats exposed to 1-BP by inhalation in the range of 100 – 1000 ppm (LOAELs)." EPA concluded that there was "high confidence" in these studies because

[1] 84 Federal Register 39830 (August 12, 2019); https://www.epa.gov/sites/production/files/2019-08/documents/01._1-bp_draft_risk_evaluation_hero_links_external.pdf.

[2] For example, EPA fails to address the significant air emissions from facilities manufacturing or processing 1-BP, which represent an additional source of exposure and risk for workers and the general population, including consumers who use 1-BP-containing products. It also does not quantify aggregate risks from dermal and inhalation exposure, although both routes are significant, and fails to address risks to consumers of using multiple products containing 1-BP simultaneously or using these products over an extended period of time. EPA also fails to use human evidence of 1-BP's neurotoxicity in estimating risks for this endpoint. Finally, EPA's evaluation of workplace risks erroneously assumes that workers will wear respirators and use gloves, an implausible assumption for which EPA lacks any supporting evidence.

they ”were of longer duration with effects observed more consistently than other high-quality studies that were evaluated.”

The Agency emphasized that “[e]vidence supporting fetal development as a sensitive target of 1-BP exposure is provided by a number of laboratory animal studies.” It elaborated that:

> Overall, the general consistency of findings indicative of impaired development across species, as reported in multiple studies from independent laboratories, *is taken as evidence of a causative association between 1-BP exposure and developmental toxicity.* (Emphasis added) (p.160)

EPA then assessed reproductive and development risks for both acute and chronic exposure. Explaining its decision to evaluate risks of acute effects, the Agency said that “multiple publications suggest that some developmental effects (e.g., decreased live litter size and increased post-implantation loss) may result from a *single exposure during a critical window of development*.” (Emphasis added) (p.185) The Agency indicated that developmental effects were “considered the most sensitive [endpoints] identified for an acute exposure duration, and are considered to be biologically relevant to the potentially exposed or susceptible subpopulation (i.e., adults of reproductive age and their offspring).”

To examine these acute risks, EPA selected Points of Departure (PODs) for acute developmental effects[3] from animal studies. After making adjustments to reflect differences in metabolism and uptake between rodents and humans, EPA converted them to a Human Equivalent Concentration (HEC) for inhalation and a Human Equivalent Dose (HED) for dermal exposure. EPA used the 8-hour HECs and HEDs to assess risks for acute occupational exposure. Expressed as an 8-hour acute HEC, EPA determined that the POD for the decreased live litter size was 31 ppm and the POD for the increased post-implantation loss was 17 ppm. (p.171) The HEDs calculated by EPA were 19 mg/kg/day (decreased liter size) and 11/mg/day (post implantation loss). These HECs, along with other developmental, reproductive, and neurological effects, were notably low (others were in the range of 100-530 ppm) indicating greater risk. Additionally, EPA used Benchmark Response Levels (BMRs) of both 5% and 1% to highlight the severity of these particular endpoints. (p. 167-173)

EPA also calculated 24-hour HECs and HEDs to assess the risks of consumer exposure. The 24-hour HECs were 10 ppm (decreased live litter size) and 6 ppm (post-implantation loss). The 24-hour HEDs were the same that were used to assess occupational risks -- 19 mg/kg-day and 11 mg/kg-day, respectively.[4] (p.189-190)

Acute Risks from Consumer Product Exposure

Having determined PODs/HECs for acute developmental effects, EPA then examined how they compared to human exposure levels for consumer product use.

[3] “EPA defines a POD as the dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on the dose for an estimated incidence, or a change in response level from a dose-response model (*i.e.*, BMD), a NOAEL or a LOAEL for an observed incidence or change in the level of response.” (p. 164)

[4] This seems to be a mistake. Since they were calculated on a 24-hour basis, the consumer HEDs should be lower than the worker HEDs, which were calculated on an 8-hour basis.

According to the draft evaluation, 1-BP is used in the following consumer products:

Table 2-42. Consumer Uses and Routes of Exposure Assessed

Consumer Uses	Routes of Exposure
1. Adhesive Accelerant (Liquid Pump Spray) 2. General Purpose Spray Cleaner (Liquid Spray/Aerosol) 3. Spot Cleaner and Stain Remover (Liquid Spray/Aerosol) 4. Mold Cleaning and Release Product (Liquid Spray/Aerosol) 5. General Cleaners and Degreasers (Liquid Spray/Aerosol) 6. Electronics Degreasers (Liquid Spray/Aerosol)	Inhalation and Dermal
7. Coin and Scissors Cleaner (Liquid Bath) 8. Automobile AC Flush (Liquid)	Inhalation and Dermal
9. Insulation (Off-gassing)	Inhalation

Using established modeling techniques, EPA determined low, medium and high intensity use scenarios for short-term exposures to each product type and calculated corresponding 24-hour Time Weighted Average (TWA) exposure levels. These scenarios were developed for both direct users and bystanders and for inhalation (all uses) and dermal (only 3 uses) pathways of exposure. EPA then compared its product-by-product exposure estimates to the HECs/HEDs and derived margins of exposure (MOEs) – a ratio of the HEC/HED to human exposure levels. (p. 192)

To determine how risky the consumer uses are, EPA compared these actual MOEs to a "benchmark MOE" of 100.[5] This benchmark accounts for "uncertainty/ adjustment factors" in predicting effects in humans on the basis of animal studies and is used by EPA as a 'yardstick' for determining the seriousness of risks. As EPA uses this methodology, it presumes that an unreasonable risk exists where the actual MOE is **below** the benchmark MOE. As the gap between the actual and benchmark MOE widens, the level of risk increases—that is, the **lower** the actual MOE is below the benchmark MOE, the riskier the use/exposure.

For numerous products and use scenarios, EPA's draft risk evaluation found that actual consumer exposures were above or alarmingly close to the HEC/HED. As a result, in many cases, the MOEs were below 1 (boxed in red in the Appendix tables) and, in nearly all instances, were far lower than the benchmark EPA used to determine unreasonable risk. (Figures 1-3)

Table 4-26 (Appendix) from the draft evaluation illustrates the remarkably small inhalation MOEs EPA calculated for nearly all consumer uses.

[5] The benchmark MOE of 100 reflects a 10X UF for inter- and intra-species variability and another 10X UF for extrapolation from a Lowest Observed Adverse Effect Level (LOEAL) to a No Observed Adverse Effect Level (NOAEL). Based on this calculation, EPA is only adjusting for animal and human variability (Inter- and Intraspecies). By setting the UF_L at 1, EPA indicates that there is no need to adjust from LOAEL to NOAEL despite that NOAEL can represent upwards of 10% of the BMR. (Wignell et al. Available: http://rusynlab.org/publications/2014/Wignall%20et%20al%202014.pdf)

Figure 1a. Risks of concern for developmental effects (post-implantation loss) by consumer product users for all uses and scenarios

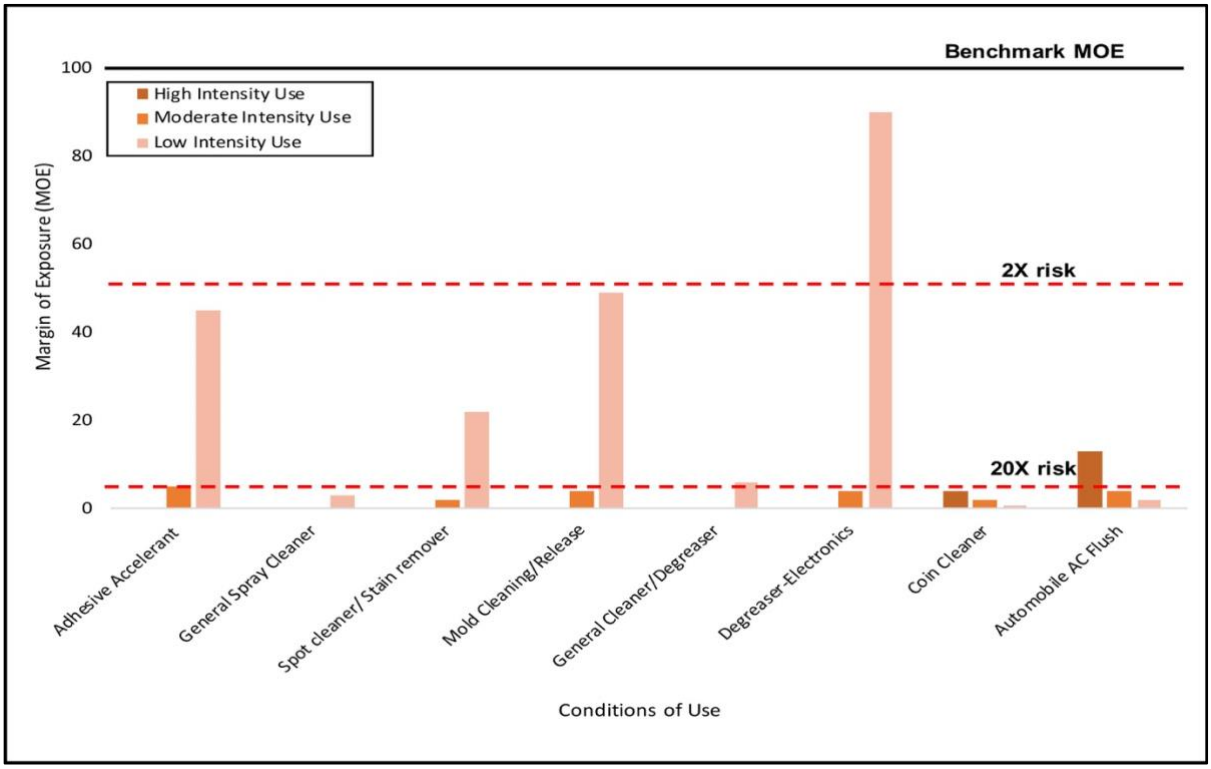
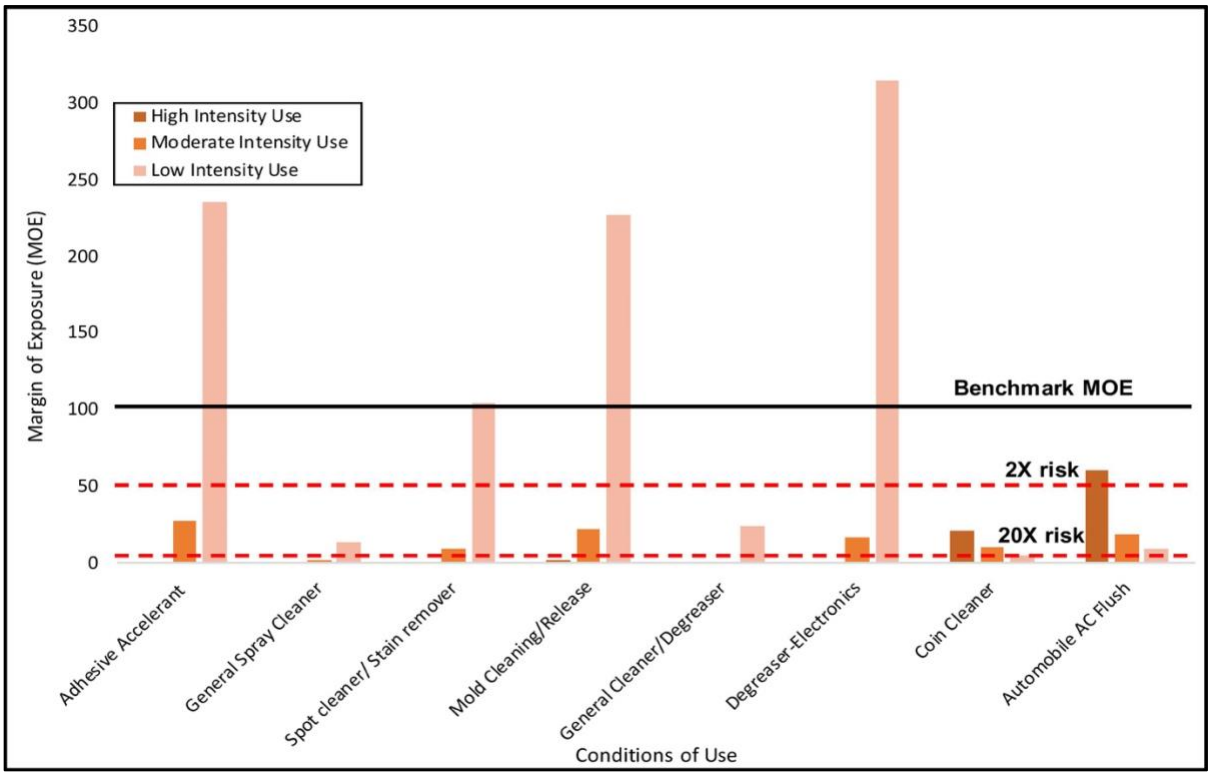


Figure 1b. Risks of concern for developmental effects (post-implantation loss) by consumer product bystanders for all uses and scenarios

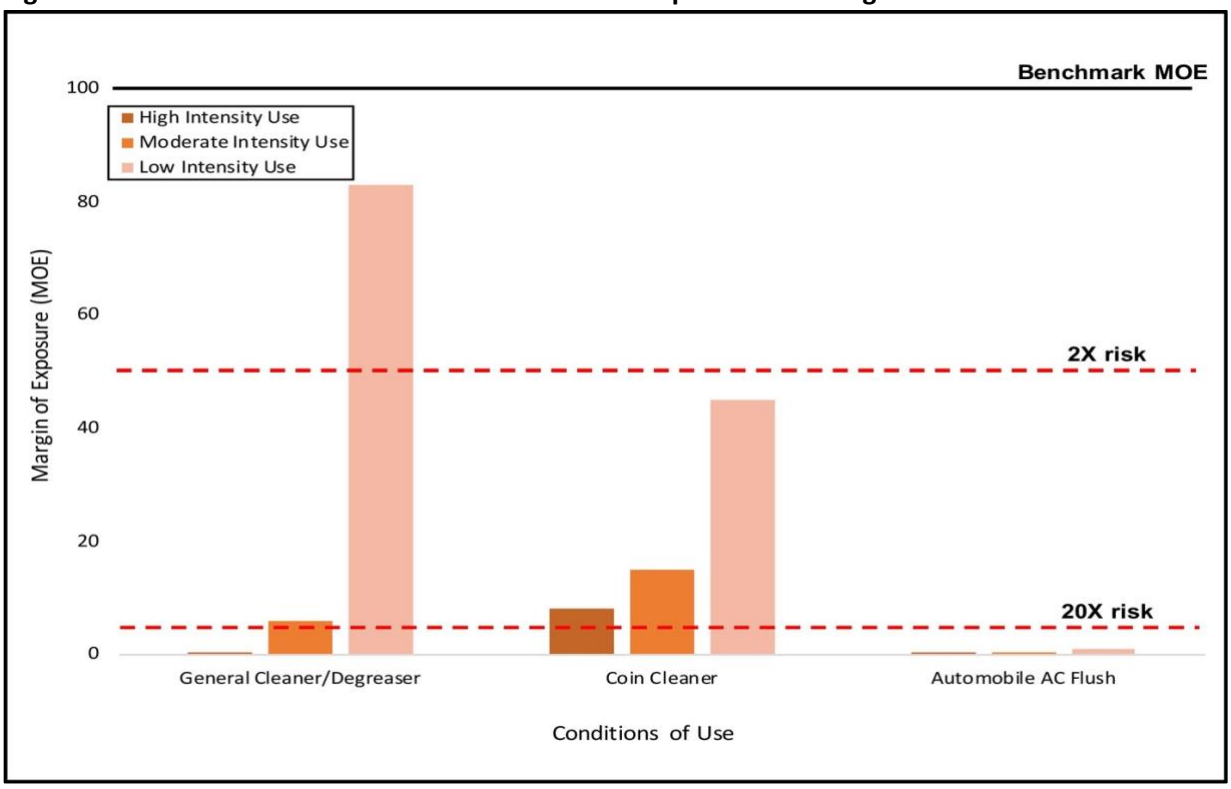


Figures 1a and 1b compare the MOEs for high, moderate, and low intensity use of 1-BP for both users and bystanders to the benchmark MOE of 100 (represented by the red line). These charts represent a subset of the data on 1-BP's developmental effects, specifically post-implantation loss for the F0 generation (the originally affected generation, not subsequent birth cohorts). The full dataset can be found in Table 4-26 in the Appendix.

As shown in Figures 1a and 1b, MOEs were below the benchmark for all high- and medium-intensity use scenarios and nearly all low-intensity use scenarios. In almost all cases, MOEs were not protective for both direct consumer users and bystanders and for both of the adverse developmental effects (reduced liter size and post-implantation loss) linked to acute 1-BP exposure.

EPA also calculated dermal exposure MOEs for three types of consumer products (general cleaner/degreaser, coin cleaner, and automobile AC Flush) for which it determined that exposure by this route was likely. [6] (Figure 2 below, Appendix Table 4-54)

Figure 2. Non-cancer risk estimates for 24-hr dermal exposure following adult consumer uses of 1-BP



Again, most MOEs were well below the benchmark and some were below the HED, meaning that human exposure levels were **higher** than the doses predicted to cause adverse effects. As all of these products also result in inhalation of 1-BP, the risks of dermal exposure would be additive, making the overall MOE even smaller (and the use/exposure riskier). However, EPA did not aggregate dermal and inhalation risks and thus overestimated the MOEs; it also did not address the contribution of other pathways of

[6] It is not explained why EPA felt that the other consumer products lacked the potential for dermal exposure. By their very nature, these products would seem likely to result in inhalation and dermal contact during use.

exposure like air emissions to aggregate exposure or the possibility that more than one consumer product might be used at the same time or particular products would be used over a multi-day period.

Significantly, the draft evaluation underscores the reality that consumers have no realistic ability to protect themselves from exposure because there is little possibility that they would use Personal Protective Equipment (PPE) during product application:

> *The use of personal protective equipment or natural/engineered controls by a consumer during product use is uncertain at best. It is not expected that consumers will utilize personal protective equipment like full face respirators, self-contained breathing apparatus, or engineering controls*… Although the use of gloves could reduce dermal exposure, if used improperly (for example fully immersing hands into a product) could allow for leakage into the glove leading to an occluded scenario that is not otherwise expected. (Emphasis added) (p. 134)

Further demonstrating that consumers lack meaningful protections, Safer Chemicals Healthy Families' review of product labels for selected consumer products confirmed the absence of prominent warnings about the acute developmental risks of 1-BP and the need to avoid exposure.

Acute Risks from Workplace Exposure

The draft risk evaluation also identified numerous industrial and commercial applications of 1-BP. Several of these applications involve open processes with the potential for significant worker exposure, such as:

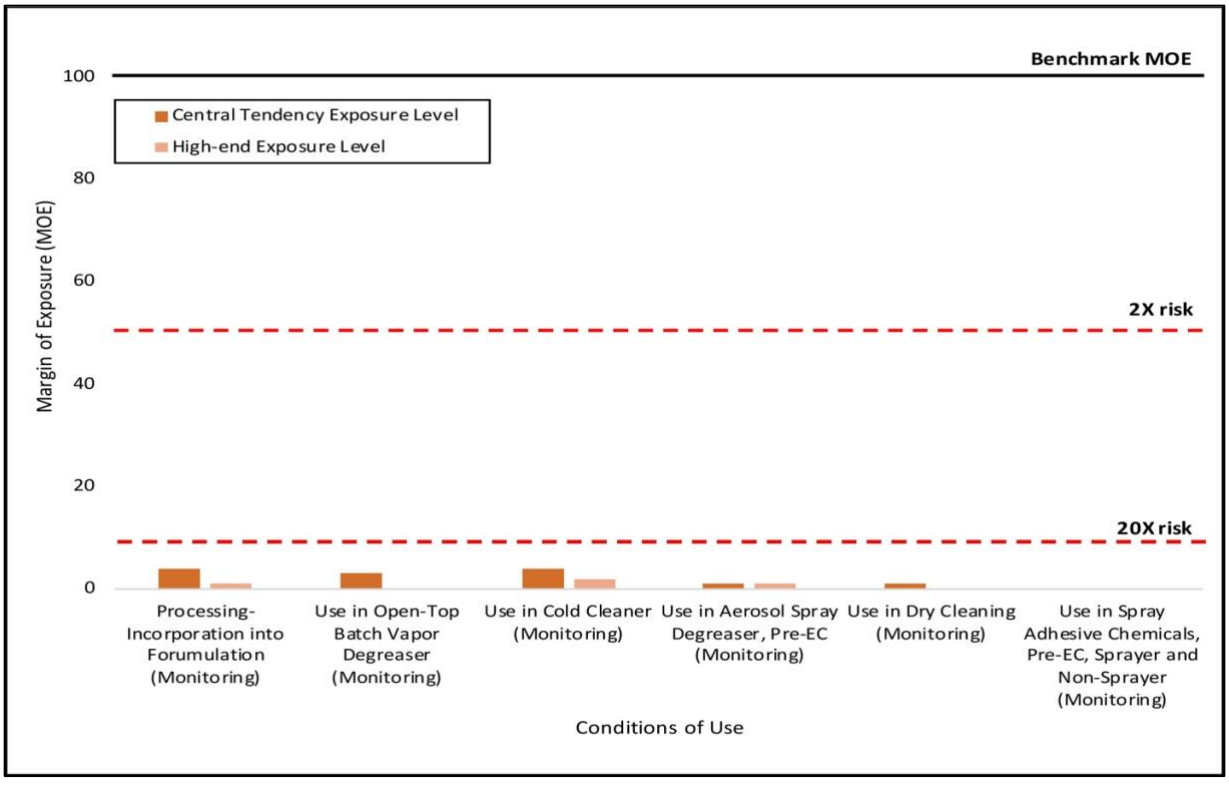
- Formulation of mixtures containing 1-BP
- Industrial and commercial use as solvent for cleaning and degreasing, including vapor degreaser (batch vapor degreaser – open top and closed loop, inline vapor degreaser), cold cleaner aerosol spray degreaser/cleaner.
- Industrial and commercial use as adhesives and sealants.
- Industrial and commercial use as cleaning and furniture care products, including dry cleaning, spot cleaner and other liquid, spray and aerosol cleaners.
- Other industrial and commercial uses: arts, crafts, hobby materials (adhesive accelerant); automotive care products (engine degreaser, brake cleaner, refrigerant flush); anti-adhesive agents (mold cleaning and release product); building/construction materials not covered elsewhere (insulation); electronic and electronic products and metal products; functional fluids (close/open-systems) – refrigerant/cutting oils; asphalt extraction; laboratory chemicals; and temperature indicator – coatings.

These uncontrolled applications occur at numerous small sites and involve a large worker population. For example, EPA estimated that between 22 and 99 sites formulate 1-BP into mixtures and employ up to 1,046 workers; that between 500 and 2,500 establishments use 1-BP as a vapor degreaser and employ up to 24,000 exposed workers; that 1,000 to 5,000 businesses use 1-BP-based aerosol solvents, with up to 12,300 exposed workers; and that 100 to 280 facilities use 1- BP spray adhesive products in

foam cushion manufacturing, with up to 4,200 exposed workers. EPA found that at least half of these exposed workers are women. (p. 22).

For each of these 1-BP applications, the draft risk evaluation used monitoring data (where available) and modeling to estimate acute exposure levels for exposed workers. Using the same procedure it applied to consumer products, it then compared these levels to 8-hour HECs representing the exposure levels at which acute developmental and reproductive effects would be expected to occur in workers inhaling 1-BP. Using this comparison, EPA calculated MOEs for each exposure scenario and acute developmental effect and determined whether these MOEs were above or below the benchmark MOE of 100. As shown in Tables 4-8, 9, 13, 15, 18 and 23 in the Appendix and in the figure below, MOEs were again below the benchmark by up to three orders of magnitude for all workers and many occupational non-users (ONUs) and in a few instances were 1 or even below (meaning that actual exposures were equal to or higher than the HEC).

Figure 3. Risks of concern for developmental effects (post-implantation loss) workers for all uses and scenarios



As the tables indicate, EPA calculated alternate MOEs based on the unsupported assumption that workers would wear and be protected by respirators (APF=50). As EPA explained, the MOE "estimates for these respirator scenarios assume workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity where there is potential exposure to 1-BP" (p. 194). However, even when applying these highly unrealistic assumptions about the additional exposure reduction provided by respirators, for many use scenarios, the MOEs still remained below the benchmark. Moreover, the likelihood of any respirator use (let alone respirator use for all workplace operations, as assumed by EPA) during the 1-BP conditions of use addressed in the risk evaluation is

extremely small. The risk evaluation acknowledges that "[f]ew literature sources indicate the use of respirators in 1-BP conditions of use" and states that "small commercial facilities performing dry cleaning and spot cleaning are unlikely to have a respiratory protection program." (p. 24). There is no OSHA Permissible Exposure Limit (PEL) for 1-BP and monitoring data cited by EPA shows that workplace levels are often two or more orders of magnitude above the NIOSH recommended exposure limit (REL) of 0.3 parts per million (ppm). In addition, Safer Chemicals Health Families' review of product labels and SDSs indicates that they generally fail to highlight the adverse reproductive and developmental effects of acute exposure to 1-BP and do not recommend aggressive respirator use. Finally, dry cleaners and other small facilities that use 1-BP typically lack the expertise and resources for advanced worker protection programs and are unlikely to make respirators available and assure compliance.

For these reasons, in EPA's proposed TSCA rules banning use of trichloroethylene (TCE) in aerosol and vapor degreasing operations, the Agency rejected respirator use as a worker protection strategy and concluded that eliminating worker exposure was the only effective mechanism for managing TCE's health risks. As EPA explained the inadequacy of respirators:[7]

> Not all workers can wear respirators. Individuals with impaired lung function, due to asthma, emphysema, or chronic obstructive pulmonary disease for example, may be physically unable to wear a respirator…Also, difficulties associated with selection, fit, and use often render them ineffective in actual application, preventing the assurance of consistent and reliable protection, regardless of the assigned capabilities of the respirator… In addition, respirators may also present communication problems, vision problems, worker fatigue and reduced work efficiency (63 FR 1156, January 8, 1998). According to OSHA, 'improperly selected respirators may afford no protection at all (for example, use of a dust mask against airborne vapors), may be so uncomfortable as to be intolerable to the wearer, or may hinder vision, communication, hearing, or movement and thus pose a risk to the wearer's safety or health. (63 FR 1189-1190).

These considerations apply equally to 1-BP, a volatile solvent with a very similar use profile to TCE. As EPA concluded for TCE, the only effective way to protect workers from acute developmental effects is to "ensure that employees are no longer at risk from exposure."[8]

In conclusion, although EPA's 1-BP evaluation understates risks, its findings about the developmental and reproductive risks to consumers and workers from acute exposure raise very serious concerns and require immediate action to protect these exposed and susceptible subpopulations.

[7] 82 Federal Register 7432, 7445 (January 19, 2007).
[8] Id at 7444.

Appendix:

Acute Risks from Consumer Product Exposure

Table 4-26. Non-Cancer Risk Estimates for Acute 24-hr Inhalation Exposure Following Consumer Uses of 1-BP (Benchmark MOE = 100) Based on Modeling

Condition of Use	Scenario Description	Acute Non-Cancer MOE (24-Hour TWA)			
		Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)		Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001)	
		User	Bystander	User	Bystander
Adhesive Accelerant	High Intensity Use	0.5	2	0.3	1
	Moderate Intensity Use	9	47	5	28
	Low Intensity Use	74	393	45	236
General Spray Cleaner	High Intensity Use	0.1	0.3	0.1	0.2
	Moderate Intensity Use	0.7	4	0.4	2
	Low Intensity Use	4	23	3	14
Spot Cleaner/ Stain Remover	High Intensity Use	0.2	1	0.1	0.6
	Moderate Intensity Use	3	15	2	9
	Low Intensity Use	37	173	22	104
Mold Cleaning/ Release	High Intensity Use	0.5	2	0.3	2
	Moderate Intensity Use	7	37	4	22
	Low Intensity Use	81	379	49	228
General Cleaner/ Degreaser	High Intensity Use	0.1	0.2	0.1	0.2
	Moderate Intensity Use	0.5	2	0.3	1
	Low Intensity Use	10	40	6	24
Degreaser-Electronics	High Intensity Use	0.4	1	0.2	0.7
	Moderate Intensity Use	7	29	4	17
	Low Intensity Use	150	526	90	315
Coin Cleaner	High Intensity Use	6	34	4	21
	Moderate Intensity Use	3	16	2	10
	Low Intensity Use	1	7	0.7	5
Automobile AC Flush	High Intensity Use	21	100	13	61
	Moderate Intensity Use	6	32	4	19
	Low Intensity Use	3	15	2	9
Insulation	Living Area	N/A	3000	N/A	1800
	Attic	N/A	562	N/A	337
	Crawlspace	N/A	462	N/A	277
Overall	Maximum	150	526	90	315
	Minimum	0.1	0.3	0.1	0.2

Note: Acute HEC = 6 ppm (decreased live litter size) and 10 ppm (post-implantation loss).

Values in the red boxes represent Margins of Exposure under 1.

Table 4-54. Non-Cancer Risk Estimates for Acute 24-hr Dermal Exposure Following Consumer Uses of 1-BP

Condition of Use	Scenario Description	Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001) HED = 19 mg/kg-day			Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001) HED = 11 mg/kg-day		
		Adult	Youth A	Youth B	Adult	Youth A	Youth B
General Cleaner/Degreaser	High Intensity Use	0.7	0.7	0.7	0.4	0.4	0.4
	Moderate Intensity Use	106	11	10	6	6	6
	Low Intensity Use	144	153	141	83	89	81
Coin Cleaner	High Intensity Use	13	14	13	7	8	7
	Moderate Intensity Use	16	27	25	15	16	14
	Low Intensity Use	77	82	75	45	48	43
Automobile AC Flush	High Intensity Use	0.2	0.3	0.2	0.1	0.2	0.1
	Moderate Intensity Use	0.5	0.5	0.5	0.3	0.3	0.3
	Low Intensity Use	2	2	1	0.9	0.9	0.8
Overall	Maximum	144	153	141	83	89	81
	Minimum	0.2	0.3	0.2	0.1	0.2	0.1

Values in the red boxes represent Margins of Exposure under 1.

Table 4-8. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Processing – Incorporation into Formulation Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)	31	Central tendency	8	95	409	100
		High-end	2	19	82	
Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001); NCTR Model	17	Central tendency	4	52	224	100
		High-end	1	11	45	

Table 4-9. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Batch Vapor Degreaser (Open-Top) Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)	31	Central tendency	5	1,550	231	100
		High-end	1	14	31	
Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001); NCTR Model	17	Central tendency	3	850	127	100
		High-end	0.3	8	17	

Values in the red boxes represent Margins of Exposure under 1.

Table 4-13. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Cold Cleaner Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)	31	Central tendency	7	12	360	100
		High-end	4	12	209	
Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001); NCTR Model	17	Central tendency	4	7	198	100
		High-end	2	7	115	

Table 4-15. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Aerosol Spray Degreaser Based on Monitoring Data (Pre-EC)

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		APF=50	Benchmark MOE
			Worker	ONU	Worker	
Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)	31	Central tendency	2	No data	97	100
		High-end	1	No data	49	
Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001); NCTR Model	17	Central tendency	1	No data	53	100
		High-end	1	No data	27	

Note: EPA did not identify exposure monitoring data for ONUs. EPA estimated exposure level for ONU through modeling.

Table 4-18. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Dry Cleaning Based on Monitoring Data

Health Effect, Endpoint and Study	Acute HEC (ppm)	Exposure Level	Acute MOE		Benchmark MOE
			Worker	ONU	
Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)	31	Central tendency	1	3	100
		High-end	1	2	
Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001); NCTR Model	17	Central tendency	1	1	100
		High-end	0.3	1	

Values in the red boxes represent Margins of Exposure under 1.

Acute Risks from Workplace Exposure

Table 4-23. Non-Cancer Risk Estimates for Acute Inhalation Exposures Following Occupational Use of 1-BP in Adhesive Chemicals (Spray Adhesive) Based on Monitoring Data (Pre-EC)

Health Effect, Endpoint and Study	Exposure Level	Acute MOE			APF=50		Benchmark MOE
		Sprayer	Non-Sprayer	ONU	Sprayer	Non-Sprayer	
Developmental Effects Decreased live litter size (F_1) (WIL Research, 2001)	Central tendency	0.2	0.2	10	12	12	100
	High-end	0.1	0.1	0.2	6	7	
Developmental Effects Post-Implantation Loss (F_0) (WIL Research, 2001); NCTR Model	Central tendency	0.1	0.1	6	6	7	100
	High-end	0.1	0.1	0.1	3	4	

Note: Based on acute HEC of 31 ppm and 17 ppm.

Values in the red boxes represent Margins of Exposure under 1.